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MORTALITY FOLLOWING WIDOWHOOD:
THE ROLE OF PRIOR SPOUSAL HEALTH

BY

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MORTALITY FOLLOWING WIDOWHOOD: THE ROLE OF PRIOR SPOUSAL HEALTH

By

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Ph.D., The Pennsylvania State University, 1992
M.S., The Pennsylvania State University, 1987
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An abstract of
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Abstract

MORTALITY FOLLOWING WIDOWHOOD:
THE ROLE OF PRIOR SPOUSAL HEALTH

By
Debra A. Heller

Previous studies have demonstrated that widowhood is associated with increased mortality risk. Although prior research suggests that the context of the predeceased spouse's death may affect this association, information is limited regarding how the rapidity of the decedent's health decline affects the survival of the bereaved spouse. The goal of this study was to combine two methods – group-based trajectory modeling and survival analysis – to identify decedents' end-of-life morbidity trajectories and to examine their association with post-widowhood survival in bereaved spouses.

Subjects included 9,967 married couples enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) Program. Using the predeceased spouse's death date as an index date, predeceased and bereaved spouses' morbidity trajectories in the prior year were evaluated for three morbidity measures: the Combined Comorbidity Score, inpatient hospitalized days, and ambulatory visits. Kaplan-Meier and Cox proportional hazards models were used to evaluate associations between morbidity patterns and post-widowhood survival over three years.

Multiple trajectories were identified for each predeceased morbidity measure, including six patterns for Combined Comorbidity, four for inpatient days, and six for ambulatory visits. Among hospice users, stable low or late onset predeceased Combined Comorbidity trajectories were associated with elevated mortality rates in the bereaved, relative to chronic high morbidity (HR=1.47 and 1.62, respectively); no effect was apparent in non-hospice users. Relative to stable medium ambulatory visits, chronic high predeceased visits were associated with a lower mortality rate in the bereaved (HR=0.67; 95% CI: 0.48, 0.92), while a stable zero visit pattern was associated with a higher rate (HR=1.32; 95% CI: 1.14, 1.53). The effects of spousal morbidity on survival were neither confounded with nor modified by age, sex, race, or place of death. However, for Combined Comorbidity and ambulatory visits, the predeceased morbidity trajectory was confounded with the widowed subject's own morbidity trajectory.

These results demonstrate the utility of group-based trajectory modeling for describing end-of-life health decline. However, the impact of spousal morbidity trajectory on post-widowhood survival was not consistent across measures, and was confounded with subjects' own morbidity. More research is needed to examine the complex pathways through which spousal illness trajectories affect post-widowhood mortality.

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CHAPTER I: INTRODUCTION

Rationale

The death of a spouse is widely acknowledged to be one of the most traumatic events that can occur during a person's lifetime. Numerous studies have demonstrated that widowed individuals experience increased risk for a number of adverse outcomes – including their own death – following spousal loss. Although increases in mortality following widowhood, frequently referred to as the "bereavement effect," have been clearly shown in prior research, questions still remain regarding the factors that may confound or modify the effects of bereavement on health and mortality. One area which is not yet well understood is the extent to which the predeceased spouse's pattern of health decline before their death affects the subsequent likelihood of mortality of the bereaved spouse. The goal of this study, therefore, is to examine the association between elderly married decedents' end-of-life health trajectory patterns and the subsequent survival of the decedents' bereaved spouses.

Problem Statement

Results of many cross-sectional studies suggest that married persons experience better health and have lower mortality risk than those who are unmarried (1, 2). Marital status differences may reflect, at least in part, marriage selection effects whereby persons who marry – and who remain married – may be healthier than other persons (3, 4). Yet the observation that husbands and wives sometimes die in close succession has also been noted throughout history (5, 6), and longitudinal studies of bereavement have demonstrated increased mortality among widowed persons following the loss of a spouse

(7-9). Frequently the death of the bereaved spouse may be attributed informally by family or friends to the effects of acute shock or grief, or to the belief that one spouse simply did not want to live without the other. However, the formal research that has been conducted to date on this topic suggests considerable complexity with respect to the factors that may contribute to the effect of bereavement on mortality. For example, differences in the degree of post-bereavement mortality risk according to gender, time since bereavement, and the specific circumstances of the first spouse's death have been suggested by a number of prior studies, yet much remains unknown about the causal pathways involved.

Several general groups of theories have been proposed to explain the mortality risk elevations that have been shown to be associated with spousal loss, and some level of support for each theory can be drawn from various lines of research. The first group of theories focuses on the importance of selection and shared environmental effects in causing spouses to be similar in their health status and mortality risk (10, 11). For example, assortative mating may be reflected in persons choosing spouses who share specific characteristics (e.g., body size, socioeconomic factors) or health-related behaviors (e.g., dietary habits, exercise, smoking, alcohol use) that may predispose both spouses to either an early or a late death. Spouses may also adopt similar lifestyles and health-related behaviors over the course of a lifetime spent together, which may also increase their concordance for health-related risks.

Secondly, acute stress and crisis bereavement theories suggest that the trauma of spousal loss, as reflected in grief and depression, increases the risk of illness and death in the surviving spouse (12). Studies linking traumatic or complicated grief to poorer health

outcomes provide evidence that psychological trauma and distress may contribute to the bereavement-mortality association (13, 14), and research on stress-induced physiological changes, such as those occurring within psychoneuroimmune pathways, suggests plausible biological mechanisms through which bereavement distress may operate (15).

Thirdly, social support and role-based causal theories of bereavement (16-18) argue that spouses provide critical social integration and social support which may promote health. As a general conceptual framework that is relevant to these theories, social cognitive theory emphasizes the reciprocal interactions of personal, behavioral, and environmental factors, as well as the importance of self-efficacy in health promotion (19, 20). Research on health-related social control has shown that married spouses are an important source of health-related support, and spouses may both directly and indirectly influence each other's health-related behaviors and health care access (21-24). Bereavement is associated with the loss of support that the deceased spouse provided, forcing the surviving spouse to take on new roles and responsibilities pertaining to his or her own health. For many widowed elderly, the loss of financial resources following bereavement may further compound the loss of role-based and health-related social support.

The potential public health impact of bereavement is especially great among the elderly, given that the likelihood of experiencing spousal loss increases steadily with advancing age. According to 2010 U.S. Census data, 6.4% of men and 21.2% of women aged 65-74 are already widowed, and for those aged 85 or older, the proportion of the population that is widowed increases to 34.6% of men and 72.9% of women (25). Many widowed elderly experience greater vulnerability due to other factors, as well, such as

higher levels of frailty, comorbidity, cognitive or other functional impairment, and economic constraints (26).

Results of prior research suggest that the context of the predeceased spouse's death – including the duration and nature of the illness which led to death – has a bearing on how well the surviving spouse adapts to the loss. While a number of studies of bereaved elderly have demonstrated differential mortality according to the recorded causes of death of the predeceased spouse, the cause-of-death classifications and the study methodologies employed have been varied (27-29). Other research suggests that the expectedness or suddenness of death is important, with unexpected or sudden deaths exacting a greater psychological toll on survivors (18, 30, 31). Some research suggests that the place of death may be important, as well (32). However, place of death has not been well-studied outside of the setting of palliative care. Other research suggests that the use of specialized end-of-life support, such as hospice care, may improve not only the quality of death experienced by dying persons, but may also benefit surviving spouses in important ways (33, 34). However, few studies have analyzed the historical health services utilization of the predeceased spouse as a means of characterizing the context of spousal loss. In particular, health trajectories, which have been used increasingly in gerontological research to describe patterns of health or functional status change over time, have not been previously applied to studies of bereavement.

Health trajectory analysis, which is used to describe the rate and pattern of health change over time, represents a promising area of analysis. Over the last decade, gerontologists have increasingly utilized health trajectory analysis as a means of studying aging-related changes in health and functional status. Recent developments in statistical

modeling capabilities, particularly through group-based trajectory modeling, have made the analysis of health trajectories more feasible within a wide array of study settings (35, 36). Despite these promising advances, health trajectory analysis has not yet been incorporated into bereavement research, based on publications to date. However, its application as a means of measuring spousal death context seems reasonable, given that trajectory patterns are likely to capture more information about the nature and rapidity of decedents' health decline than diagnosis-specific measures such as cause of death. In addition, a conceptual precedent already exists within the gerontological literature for considering end-of-life trajectories as a way to understand the dying process (37-39).

Purpose Statement

The primary purpose of this research is to examine the extent to which survival among newly widowed persons is associated with the end-of-life health trajectory patterns of their predeceased spouses. Evaluating the impact of other factors reflecting the circumstances of the predeceased spouse's death, including the place of death and the use of Medicare hospice benefits, on subsequent survival is a secondary goal.

Research Questions

The research questions for this research will be addressed in two broad study phases: the first phase of research will focus on evaluating morbidity trajectory patterns among deceased and widowed spouses. Key questions to be addressed in this phase of research pertain to whether there is heterogeneity in trajectory patterns and how many trajectory patterns are discernible. Related to this is the ancillary goal of considering whether the observed trajectory patterns are interpretable, and whether the decedents' patterns are consistent with theoretical patterns of end-of-life decline which have been

previously proposed (37, 39). The second phase of research will evaluate whether the predeceased spouse's morbidity trajectory pattern group membership is associated with the survival, over a period of up to three years, of the bereaved spouse. The specific research questions and their associated null hypotheses are outlined below.

- Research Question 1: What are the discernible patterns of health trajectory among decedents and their spouses? How many trajectory patterns optimally describe the heterogeneity within the sample?

  Null Hypothesis 1: Either a single trajectory pattern (suggesting little heterogeneity) exists, or no discernible trajectory patterns are present.

- Research Question 2: Does the health trajectory pattern of the predeceased spouse affect the survival of the bereaved spouse, after adjustment for potential confounding variables?

  Null Hypothesis 2: There is no difference in survival time associated with the categorized health trajectory pattern of the predeceased spouse, after adjustment for confounding variables.

- Research Question 3: Does the bereaved spouse's own health trajectory pattern confound or modify the effect of spousal health trajectory pattern on survival?

  Null Hypothesis 3: There is no confounding or modifying effect of the bereaved spouse's trajectory pattern on the association between spousal health trajectory pattern and survival time.

- Research Question 4: Do demographic characteristics – including gender, age, or race – confound or modify the effect of spousal health trajectory pattern on the survival of bereaved spouses?

  Null Hypothesis 4: There is no confounding or modifying effect of gender on the association between spousal health trajectory pattern and survival time.

- Research Question 5: Do other circumstances surrounding the predeceased spouse's death – specifically, the place of death and the use of hospice before death – modify the effect of spousal health trajectory pattern on the bereaved spouse's survival?

  Null Hypothesis 5: Place of death and use of hospice before death does not modify the effect of spousal health trajectory on survival time.

Significance Statement

Results of previous studies have suggested that marital status is associated with health, and that widowhood increases the risk of mortality. Prior research results also suggest that the context of the predeceased spouse's death may have a bearing on the subsequent health and mortality risk experienced by the bereaved spouse. However, relatively few studies have examined variability in mortality as a function of historical health-related characteristics of the predeceased spouse. Furthermore, no known published studies to date have combined the use of group-based trajectory modeling to empirically evaluate end-of-life patterns of health change in the predeceased spouse with the survival of the bereaved spouse. The present research seeks to contribute to the body of knowledge by combining these two concepts, in order to explore how the predeceased spouse's trajectory of morbidity during the last year of their life affects the subsequent

survival of the bereaved spouse. It seeks, further, to evaluate the potential confounding or effect modifying roles of gender, age, place of death, use of hospice benefits, and the bereaved spouse's own baseline comorbidity level, on survival. Gaining a better understanding of the impact of specific factors related to the context of the predeceased spouse's death on the bereaved spouse's subsequent survival may help health care providers, social service providers, and family members to identify bereaved elderly who may be at greater risk for adverse health outcomes following widowhood. Understanding which aspects of spousal health are most associated with mortality may also point to new strategies for support-based interventions among bereaved elderly.

Definition of Key Terms

BIC – Bayesian Information Criterion, a criterion for model selection.

CHF – Congestive heart failure.

COPD – Chronic obstructive pulmonary disease.

CI – confidence interval.

CMS – Centers for Medicare and Medicaid Services.

Crude mortality rate –the cumulative number of deaths/total person-years of follow-up.

Crude mortality risk –the cumulative number of deaths/total persons in the cohort.

Elderly – The chronological age of persons considered elderly varies across settings, but in gerontological research the term is most frequently reserved for persons aged 65 or older.

HR – Hazard ratio.

ICD-9-CM – The International Classification of Diseases, Ninth Revision, Clinical Modification. ICD-9-CM is based on the World Health Organization's Ninth Revision,

International Classification of Diseases, but includes clinically-modified codes used for diagnoses associated with clinical health care in the United States. ICD-9-CM codes are present on the diagnoses obtained from Medicare Parts A and B health care claims data used in this study.

ICD-10 – International Classification of Diseases, 10th Revision, is the disease classification system used by the World Health Organization. When used for mortality data, the original ICD-10 coding system is used, not the Clinical Modification variation. ICD-10 coding is used for the cause-of-death codes present on the death certificate data that were analyzed in this study.

Index date – For this study, the date that a widowed person's spouse died.

IRB – Institutional Review Board.

PACE – Pharmaceutical Assistance Contract for the Elderly, a state prescription drug assistance benefit program for Pennsylvania residents aged 65 and older who meet income eligibility requirements.

RR – risk ratio.

Trajectory – The pattern of change progression in a measure over time.

U.K. – United Kingdom.

U.S. – United States.

CHAPTER II: REVIEW OF THE LITERATURE

Introduction

It is important to place the present study's rationale and aims within the context of a large body of existing literature pertaining to marriage, bereavement, and health. To support this goal, a literature review was undertaken using a variety of electronic sources available through the Woodruff Health Sciences Center Library at Emory University. The primary electronic tools employed included the PubMed database and the Thomson-Reuters Web of Science Citation Index database. Other search strategies included searching for selected terms through Google and Google Scholar, as well as reviewing articles listed in the bibliographies of articles already accessed. The review is organized into broad sections relating to the evidence for general effects of marriage on health, the impact of bereavement on mortality and other health outcomes, the importance of the context of death of the predeceased spouse, and the potential for new bereavement research approaches offered by health trajectory modeling.

Marital Status and Mortality

Results of numerous studies over the last century have suggested that marital status affects health and mortality, with married persons generally having a lower risk of dying within a given time period than those who are not married. Reviewing early research in this area from a historical context is beneficial, because the evolution of theories pertaining to marriage and health provides a valuable framework within which we will later consider how bereavement affects mortality.

The first comprehensive study of marital status and mortality was published by the British statistician William Farr in 1858 (40). Farr combined 1851 French census population counts with counts of all deaths recorded in France during 1853 to compute one-year age-specific mortality risk among married, never-married, and widowed persons. For both men and women across most age groups examined, the married had lower age-adjusted risks than the never-married or widowed groups. Farr's findings led him to conclude that "Marriage is a healthy estate. The single individual is more likely to be wrecked on his voyage than the lives joined together in matrimony" (40). Yet Farr also provided a thoughtful discussion on a number of diverse factors that may have contributed to his findings, including potential selection effects and economic considerations. Other early studies, such as those reported by March in 1912 (41) and Bliss in 1915 (42), found patterns of mortality that were similar to what Farr had shown. March (41) compared age-specific mortality rates among married, never-married, and widowed or divorced persons in France, Prussia, and Sweden between 1886 and 1895, and found that mortality was consistently lowest among married groups (41). Three years later, Bliss published more detailed comparisons of married and unmarried mortality rates, using 1861-1864 census data from Scotland (42), and concluded that marriage was associated with distinct survival advantages for men, with less advantage apparent for women. By the middle of the twentieth century, a number of other formal scientific investigations using data from the U.S. and other countries had reported lower mortality rates among married when compared with non-married, with apparent marriage advantages observed in both genders and across multiple age groups (10, 17, 43, 44).

The population mortality comparisons conducted in these earlier studies have a key limitation in that they are essentially cross-sectional. Most have evaluated relative mortality ratios – the ratio of the mortality rate among an unmarried group to the mortality rate among married persons – using aggregate data on deaths and population counts. The limitations of these data, including potential errors in the numerator and denominator data used for such studies, have been noted by a number of authors (45-48). Still, although the authors of these earlier studies acknowledged the inherent limitations of the data examined, they generated important hypotheses which have remained as key themes in subsequent research on marriage and mortality. One central hypothesis, first offered by Farr in his 1858 presentation, is that marriage selection effects -- in which persons who become married tend to already be healthier or are inherently more likely to have healthier lifestyles than are persons who remain unmarried or who become divorced or widowed -- may explain a large portion of the married-unmarried mortality difference (40, 43, 44, 49). A second central hypothesis arising from these earlier studies is that marriage itself is causally protective, by causing people to be healthier or to adopt behaviors that are associated with a reduced risk of death, which may be mediated at least in part through social roles (2, 17).

The recognition that social roles conferred by marriage may play a part in mortality risk was further solidified when the concept of social support was advanced as important in moderating the health effects of stress (50-52). In particular, the publication by Berkman and Syme (53) of data on social networks and mortality from the Alameda County Study -- a population-based prospective cohort study of lifestyle, health, and mortality that began in 1965 in Alameda County, California -- provided important new

insights regarding the potential pathways through which marriage and other social contacts may affect health and mortality. The authors constructed a weighted Social Network Index which incorporated information on both the number and importance of baseline social contacts, with more intimate contacts (e.g., spouses, relatives) receiving greater weight than more distant social ties (e.g., church or group acquaintances), and related it to mortality during follow-up. One particular finding -- that unmarried persons who had many friends had lowered mortality risk similar to that of married persons -- suggested that social support is a primary means by which marriage reduces mortality risk (53). Berkman and Syme hypothesized that the mechanisms by which social support affects mortality may reflect lifestyle factors (i.e., social isolation may be associated with unhealthier behaviors), or that, alternatively, psychological and physiological responses to social isolation may lower host defenses and thus increase disease susceptibility (53).

By 2005, a rapidly-growing number of studies had established that marriage was associated with lower mortality in a number of developed countries, with generally greater effects observed in men than women (4, 54). Increasing numbers of studies had also employed either retrospective cohort or prospective cohort designs, and used multivariate methods such as logistic regression to estimate mortality risk and to adjust for other measures, rather than focusing on simple comparisons. In attempt to synthesize the results of studies with a focus on the elderly, Manzoli et al. (1) conducted a meta analysis of cohort studies published between 1995 and 2005 which had examined marital status and mortality in the elderly. The overall risk ratio for married versus all non-married individuals estimated from the meta analysis was 0.88 (95% CI: 0.85, 0.91), with

no substantial differences found on the basis of gender, study quality, or geographic region.

In the aggregate, numerous studies on marriage and mortality conducted since the time of Farr's report through the present have provided strong evidence that marital status has a bearing on health and mortality. However, most of the studies reviewed have utilized data that do not allow analysis of the impact of changes in marital status on subsequent health and survival. Therefore the ability of these studies to inform us regarding the impact of bereavement on mortality risk is limited. The next section of this review will therefore focus on studies that have explicitly related spousal loss to subsequent mortality.

Bereavement and Mortality

Early Cohort Studies

The 1960's marked the beginning of a series of longitudinal investigations aimed at studying the degree to which widowhood affects mortality risk among surviving spouses. The first of these studies was a prospective cohort study conducted by Young et al. (55) of 4,486 British widowed men aged 55 and older whose wives died in 1957. Using vital records, Young et al. obtained information on subsequent deaths among the widowers, and computed age-specific mortality risks at six-month and yearly intervals for up to five years after widowhood. They then compared the risks to those expected among married men of the same age, with the intent of determining whether there was a "duration effect" of widowhood. Using a weighted average of the mortality ratios, they estimated that widowhood was associated with a 40% increase in mortality risk during the first six months after bereavement, with risk then falling to about 5% over that

expected among married men during later intervals. Following the publication of Young et al.'s findings, Cox and Ford (56) conducted a retrospective analysis of British women, using actuarial data on widows that had been previously compiled between 1927 and 1933. Compared with Young et al.'s findings for men, Cox and Ford's analyses suggested less impact of widowhood among women – with a maximum of 8% excess mortality occurring in the second year (56). A third important study occurring in the 1960's was a population-based cohort study by Rees and Lutkins (57) of 903 relatives of 371 decedents from a rural area of Wales, along with a comparison group of 878 non-bereaved persons. The degree of relationships examined included spouses, parents, children, and siblings of the deceased. Rees and Lutkins found that 4.76% of bereaved relatives died in the first year after bereavement, compared with 0.68% of non-bereaved, a finding that was very highly significant ($p<0.001$). They found that widows and widowers experienced much greater mortality risk than did parents, children, or siblings, with 12.2% of the widowed dying in the first year of bereavement, and further found that risk was higher for widowers than for widows (57).

As discussed by Jacobs and Ostfeld (58), these and other early cohort studies provided important information about the basic patterns of mortality risk following bereavement. Taken together, the results suggested that risk is greatest during the first six months to two years following widowhood, that widowed men experience greater risk elevation than widowed women, and that younger widowers experience greater risk increases compared with older individuals.

Gender, Age, and Duration of Bereavement

As methodological advances in computing and epidemiologic analysis occurred, studies on bereavement and mortality became more rigorous and began to explore the role that other variables may play in the bereavement-mortality association. In 1981, Helsing and Szklo (46) published the results of a retrospective cohort study using 1963-1975 health census and vital records data from Washington County, Maryland. The authors used matched-pair analytic techniques to compare mortality risk among 4,032 widowed and 4,032 married persons, while adjusting for the effects of other variables related to socioeconomic status (SES) and health behaviors. They found that widowed males had significantly greater mortality than did married men of the same age, even after adjusting for SES and other factors. However, they found no significant difference in mortality risk between widowed and married women. In a subsequent study using the same Washington County, Maryland data, Helsing et al. (59) examined the impact of several factors on mortality rates based on person-years at risk, including remarriage and movement into new residence settings. They found that for both sexes, compared with living with other persons, living alone or moving into a long term care setting after widowhood was associated with a higher mortality rate. Although remarriage did not appear to affect mortality rates among widowed women, men who remarried had a significantly lower mortality rate than widowers who did not remarry.

Using a nationally representative sample of 503 older widowed persons in England, Bowling and Charlton (60) surveyed 361 subjects approximately five months, on average, after they were widowed in 1979, and then followed the cohort for up to six years (60). The study found no excess mortality among male widowers aged 65-74 or among widowed women of any age, but found that for men aged 75 or older, widowhood

was associated with a two-fold increase in mortality risk during the first six months of the study. Subsequent follow-ups in the same population by Bowling (61) and Bowling and Windsor (62), utilizing 13.5 years of data, confirmed that most of the excess mortality associated with bereavement occurred during the first several years.

Data from U.S. studies have also supported similar conclusions. For example, Johnson et al. (47) analyzed bereavement data from the National Longitudinal Mortality Study, a retrospective cohort study which linked data from the U.S. Current Population Survey and the National Death Index. Increases in mortality risk after widowhood were apparent immediately and up to five years after bereavement. While there was some suggestion in these data that risk was elevated most during the first year post-bereavement, effects persisted for at least five years.

Using a unique data resource dating spanning the 19th and 20th centuries, Mineau et al. (63) utilized historical data for four Utah marriage cohorts of spousal pairs who were married between 1860 and 1904, with linked mortality data obtained from a combination of Utah death certificates and the Centers for Medicare and Medicaid Services (CMS). Cox proportional hazards modeling indicated that for men, widowhood was associated with higher mortality rates at all ages, although results were stronger among younger men. For women, at younger ages widowhood was associated with a lower mortality rate, which the authors attributed to the effects of maternal deaths among married women; however, after age 55 widowhood was associated with modest increases in rates but much less than those observed in men. In addition, cohort differences were observed, with a greater apparent impact of widowhood observed for the more recent cohorts. A strength of Mineau et al.'s work is that it used a wide span of historical data,

and thus tested to some degree the generality of the bereavement effect. However, their finding of temporal variability in the magnitude of effects across the four marriage cohorts suggests that societal contexts which vary over time may also be important in the response to widowhood.

Several large cohort studies of mortality among widowed persons have been conducted in the Scandinavian countries and have taken advantage of the comprehensive patient registries available. One example is Mellstrom et al.'s study of nearly 360,000 persons in Sweden who were widowed between 1968 and 1978 (64). Mellstrom et al. found excess mortality among older widows and widowers to be highest during the first three months of bereavement; the risk subsequently lessened but remained elevated for up to 11 years. A second representative Scandinavian study was published by Kaprio et al. in 1987, and linked data from the Finnish population and vital status registries to identify and follow widowed persons over a five-year period. Consistent with the majority of studies reviewed here, Kaprio et al. also found greater bereavement effects in men than in women. Based on standardized mortality ratios, excess deaths in this study were primarily found during the first week, month, and half-year after bereavement, particularly for ischemic heart disease, suggesting that acute responses to grief may precipitate illness and death among the newly bereaved (65). Results of other Scandinavian studies, such as a Finnish study by Martikainen and Valkonen (66) provided confirmatory evidence that post-bereavement mortality effects appear to be larger in men than in women, and are greatest during the initial period following bereavement.

Cause-Specific Mortality of Bereaved Spouses

While most studies have evaluated all-cause mortality in the bereaved, some studies have also examined cause-specific mortality. In a 9-year follow-up study of the widowed British men that had initially been studied by Young et al. (55), Parkes et al. (12) broadly categorized deaths among the widowers by their cause, and found that coronary diseases appeared to account for most of the excess mortality. Several of the Scandinavian registry studies also examined differential risk depending on the cause of death of the bereaved spouse. For example, Mellstrom et al. (64) examined excess mortality by the bereaved spouse's cause of death, and found the effects to be concentrated in the categories of cancer, cardiovascular deaths, accidents, suicides, and alcohol-related deaths. Kaprio et al. (65) similarly categorized deaths among Finnish widowed into natural causes (infections, cancer, ischemic, cerebrovascular, other cardiovascular, and all other natural causes) or violent causes (traffic accidents, suicides, and other violent causes). Early post-widowhood mortality risk, in particular, was greatest for ischemic heart disease. A later Finnish study by Martikainen and Valkonen (66) also categorized mortality among the bereaved based on cause, and found that excess mortality was greatest for accidents, violent causes, and alcohol-related deaths, was moderate for ischemic heart disease and lung cancer, and was smaller for all other causes analyzed. In general, the results of studies which examined the cause of death of the bereaved spouse support the general theory of emotional stress and grief immediately after spousal loss. Authors such as Martikainen and Valkonen (66) concluded that a large part of the excess mortality is general rather than disease-specific; this may reflect a generally lowered ability to withstand disease among the widowed. These authors further theorized that because even diseases with long latencies have been shown to be

associated with short-term excess mortality effects, this may reflect an acceleration or exacerbation of existing diseases, rather than the initiation of new disease processes.

Studies Addressing Shared Environmental Effects

Several studies have attempted to control for confounding caused by environmental effects shared by spouses. For example, Martikainen and Valkonen (67) used the same Finnish cohort discussed above (66) to examine potential confounding due to a shared environment. To control for shared socioeconomic factors, they included measures of housing tenure and disposable family income; adjustment for these measures in Poisson models had only a minor effect on the relative mortality rates. To attempt to control for other spousal similarity, Martikainen and Valkonen examined the categorized cause of death of both the predeceased and bereaved spouse, using broad causal groups which they categorized as "risk-taking" (accidents, violence, and alcohol-related deaths) and all other causes. Excess mortality remained even after adjusting for these broad cause of death measures, suggesting that bereavement indeed has a causal effect, and does not simply reflect selection effects caused by environmental factors shared by spouses.

Using a different approach, Schaefer et al. (29) also sought to evaluate shared environmental factors as an alternative explanation to bereavement effects being due to the stress of the loss. This study employed a retrospective cohort design to analyze data on spousal pairs aged 40 and older from the U.S. Kaiser Foundation Health Plan. All study subjects had participated in a multiphasic health checkup between 1964 and 1973 which collected data on medical history, symptoms, smoking, and alcohol use. In Cox proportional hazards survival models, there was an interaction of baseline health with

bereavement among males, with a diminished effect among men who had the most health problems. Schaefer et al. also analyzed Cox models which included interaction terms for both the subject's and spouse's risk factors and interaction terms for their joint effects. Adjustment for the spouse's covariates and the interaction terms, as well as the person's own covariates, did not change results from what had been found with only the person's covariates, and none of the spouse's covariates or the interaction terms were significant. The authors concluded that shared environmental effects had only a negligible effect on the bereavement effect, and concluded that post-widowhood increases in mortality rates reflect responses to bereavement rather than the selective effects of shared environmental factors.

Meta Analyses of Bereavement and Mortality

Two recently-published meta analyses have consolidated findings from multiple bereavement studies (9, 68). A 2011 meta analysis published by Moon et al. (9) focused on 15 longitudinal studies conducted between 1960 and 2009, and estimated the pooled long-term mortality risk ratio among widowed persons, relative to married persons, to be 1.12 (95% CI: 1.10, 1.15). The meta-analysis also revealed substantial heterogeneity in effects with respect to gender, with a mortality risk ratio of 1.22 found for males (95% CI: 1.18, 1.26) compared with a risk ratio of only 1.03 for females (95% CI: 1.00, 1.07). Significant differences in effect size over time were also confirmed by Moon et al.'s meta analysis: the mortality risk ratio during the first six months was estimated to be 1.41 (95% CI: 1.26, 1.57) compared with 1.14 after the first six months (95% CI: 1.10, 1.18). A second meta analysis on widowhood and mortality published by Shor et al. in 2012 (68) was not limited only to longitudinal studies following bereavement, but also

included cross-sectional studies comparing widowed persons with married persons, or to the general population. Shor et al. converted risk ratios to hazard ratios for the meta analysis in order to estimate the impact of bereavement on mortality rates. Relative to non-widowed, Shor et al. estimated an overall hazard ratio of 1.23 (95% CI: 1.19, 1.28) associated with widowhood. Like Moon et al., Shor et al. also found larger estimated effects for men (HR=1.27, 95% CI: 1.19, 1.35) than for women (HR=1.15, 95% CI: 1.08, 1.22). Shor et al. also found the greatest hazard ratios during the first six months of widowhood (HR=1.58, 95% CI: 1.32, 1.88), but the combined study results also indicated widowhood-associated elevations in mortality rates persisting for 20 years or more.

Impact of Bereavement on Other Health Measures

Although the increases in mortality that accompany widowhood have been well-demonstrated in the studies discussed above, the mechanisms involved in the mortality effect are unclear. Cross-sectional studies of marital status differences, as well as longitudinal studies of bereavement, have suggested that widowhood is associated with increased risk for a number of adverse health outcomes, including greater morbidity, disability, and institutionalization (2, 8, 69-71). The extent to which pre-existing baseline differences in health may explain these effects is not well understood, however. A 2011 United Kingdom study by Shah (72) found that Cox models which controlled for comorbid conditions both at baseline and throughout follow-up did little to attenuate the effect of bereavement on mortality. Findings from the earlier research conducted by Schaefer et al. (29) and Boyle et al. (27) discussed above suggest that individuals in better health at baseline may actually experience greater bereavement-associated mortality than those in poorer baseline health. The results of these studies suggest that

acute effects may be most salient in explaining post-widowhood mortality. However, literature on grieving suggests that although acute grief is generally of limited duration for many bereaved persons, some individuals go on to experience *complicated or traumatic grief*, a prolonged period of severe distress which has been proposed as a specific syndrome that differs from usual grief and depression (14, 73). In a U.S. study, Prigerson et al. (13) further found that persons experiencing traumatic grief were at the greatest risk for worsening physical health, and concluded that traumatic grief, rather than acute grief, was most damaging to physical health. Moreover, a U.S. study of 328 bereaved persons by Utz et al. (74) found that individuals who were in poorer health at the time of widowhood experienced the greatest risk for complicated grief, suggesting that there is considerable complexity in the relationships among preexisting health problems, complicated grief development, and subsequent adverse health outcomes.

A number of studies have also examined the extent to which bereavement may produce changes in the level and quality of health care received by widowed persons. Results across studies have been varied with some studies suggesting increases in health services use, but others suggesting declines in health service utilization. Guldin et al. (75) reported that, on average, spouses of cancer patients in Denmark increased their health services and medication use during the months preceding the loss through several years following it. In another Danish study, Oksuzyan et al. (76) found increases in the daily overall and system-specific medication use and the annual number of physician visits of widowed persons before and after bereavement, and concluded that there was little evidence that poorer medical care after bereavement could explain the overall bereavement effect on mortality or sex differences in the mortality effect. However, in a

U.S. study of widowed women, Prigerson et al. (77) found that although widowed women were more likely than divorced or separated women to experienced worsened physical and psychological health, they were not more likely to seek medical help or to increase their use of health services, suggesting that failure to seek appropriate health care could potentially be a factor in the bereavement effect.

A richer understanding of bereavement-associated changes in health services use has been gained from two recent studies which obtained multiple health utilization measurements on large samples of older adults. Simeonova (78) conducted a study of U.S. widowed male veterans, examining three dimensions of health care quality – 1) patient medication adherence assessed from prescription refill data, 2) average clinical quality of care, which reflected the extent to which participants' physicians followed a number of established clinical guidelines for patients within their medical practice, and 3) continuity of care, which quantified the extent to which the participant's medical care during the year was fragmented across multiple providers. Results indicated that bereavement was associated with increased fragmentation of care and reduced clinical quality of care; however, the author concluded that those changes explained less than five percent of the mortality effect of bereavement. These findings are similar to those that were obtained by Jin and Christakis (79) in a U.S. study of 475,313 elderly couples enrolled in Medicare. Jin and Christakis examined the extent to which patterns of health care use and quality of health care changed following bereavement, and also examined the extent to which those changes contributed to elevations in the mortality rate. In an attempt to measure health care quality across several dimensions, these authors examined the extent to which recommended preventive screenings and vaccinations were received,

and also identified the occurrence of "preventable" hospitalizations (i.e., hospitalization for ambulatory care-sensitive conditions such as asthma, diabetes, and hypertension) and early readmissions after hospitalization, which were defined as any readmission for the same principal diagnosis less than two weeks after a prior discharge. Results suggested a decline in quality of health care before and around the time of spousal death. However, including the quality-of-care indicators in survival models had little impact on the magnitude of the bereavement effect on the mortality hazard. The authors concluded that their findings supported a crisis model of bereavement impact, in which widowed persons undergo short-term changes in health care access, but then may subsequently increase their access to appropriate health care services.

Context of the Predeceased Spouse's Death

Health Conditions of the Predeceased Spouse

Results of a number of different lines of research suggest that factors related to the context of the predeceased spouse's death may be important in determining the health effects of bereavement on the surviving spouse. The context of death may include the specific health conditions that the person had before they died, the duration of illness that they experienced, the expectedness or suddenness of the death, whether spousal caregiving was involved, the place of death, and the availability of specialized support services, such as hospice care. Primary literature on the importance of each of these contextual factors is briefly summarized below.

Although the number of studies demonstrating that bereavement is associated with increased risk is fairly extensive, fewer studies have examined the impact of the predeceased spouse's health prior to their death on the bereavement-mortality

association. The studies that have addressed spousal health have used varied approaches. One U.S. study, published by Schaefer et al. in 1995 (29), examined spousal health and health habits in an attempt to evaluate the extent to which shared marital environment may influence mortality rate increases following bereavement. Their Cox survival analyses included terms for both spouse's symptom counts and health behavior indicators for smoking and alcohol use, and included interaction terms for the bereaved and predeceased spouse's terms. This study detected no significant interactions involving the bereaved and predeceased health behavior measures (e.g., smoking, alcohol), which they interpreted as indicating that the effects of shared environment were minimal in explaining the bereavement effect. A strength of Schaefer et al.'s study was the availability of data on health status and health habits of both spouses prior to the widowhood event. However, the focus of the study was primarily on detecting shared environmental effects, and the measurement of the predeceased spouse's prior health status was limited to counts of self-reported health conditions, which may limit the generalizability of the findings.

Other research has focused on the recorded cause of death of the predeceased spouse. In a Scottish longitudinal study, Boyle et al. (27) examined post-bereavement hazard ratios according to official causes of death, which were broadly grouped in three different ways: 1) using Espinosa's and Evans' (80) classification of "informative" (related to socioeconomic factors) versus "non-informative" deaths; 2) using a three group classification of amenable, preventable, and unavoidable deaths proposed by Page et al. (81), and 3) using Martikainen and Valkonen's (66, 67) previously-described classification of risk-related deaths (accidents, violence, smoking, alcohol use) versus all

other deaths. Cox proportional hazards models treated widowhood as a time-varying covariate, with all other predictors fixed at baseline. Effect modification was evaluated through interaction terms for widowhood by spousal cause of death, widowhood by duration of bereavement, and widowhood by SES characteristics. The impact of bereavement was greatest for men and women during the first six months of widowhood, but remained elevated over the following ten years. Inconsistent results were obtained with respect to the predeceased spouse's cause of death, with no significant interaction terms for women. For men, only the risk behavior-related death classification yielded a significant interaction (adjusted HR=1.64 for risk-related causes, versus 1.37 for not risk-related). There were no clear differences on the basis of the amenable/preventable/ unavoidable or informative/noninformative classification schema. The authors concluded that there was little evidence that bereavement-associated mortality rates varied by the predeceased spouse's cause of death.

Other studies, however, have found that the predeceased spouse's cause of death has a bearing on the subsequent health outcomes of the bereaved spouse. In a large study of Medicare-enrolled couples in the U.S., Elwert and Christakis (28) studied the impact of spousal death on the surviving partner's subsequent mortality over nine years of follow-up. Cause-specific associations – both of the predeceased spouse's cause of death and cause-specific hazard of death in the surviving spouse – were evaluated in Cox models. Overall results indicated that bereavement was associated with an 18% increase in the all-cause mortality rate for men (adjusted HR=1.18, 95% CI: 1.16, 1.19) and a 16% increase in the all-cause mortality rate for women (adjusted HR=1.16, 95% CI: 1.14, 1.17). An important finding was that although bereavement was associated with some

degree of elevation in the hazard regardless of the cause of death of the predeceased spouse, variability across the 17 grouped causes of death was apparent. The greatest impact for men was seen when their wives died of lung cancer, infections or sepsis, chronic obstructive pulmonary disease (COPD), other heart or vascular diseases, or diabetes. No impact for men was apparent if their wives died of Alzheimer's or Parkinson's disease. For women, rates were highest if their husbands had died of COPD, influenza, or pneumonia. As was also seen for men, there was no significant hazard elevation seen for women whose husbands died of Alzheimer's or Parkinson's disease.

In a related study using the same U.S. Medicare database, Christakis and Allison (82) studied the relationship between spousal hospitalization and/or death and subsequent mortality in the other spouse. Using Cox proportional hazards survival models, the authors examined the differential impact of spousal death due to any cause, as well as the impact of hospitalization both for any cause and for the same 17 grouped diagnostic indications studied by Elwert and Christakis (28). Similar general patterns of hazard ratios were observed for men and women in this study. While spousal death increased the mortality rate by 21 percent for men and 17 percent for women, the adjusted hazard ratios for death due to spousal hospitalization were 1.05 for men (95% CI: 1.04, 1.06) and 1.03 for women (95% CI: 1.19, 1.22), with greater effects apparent when the time course for follow-up was limited to 30 days post-hospitalization. The authors also found variability in mortality rates based on the grouped spousal hospitalization reasons. Greatest rate increases were seen when subjects' spouses were hospitalized for dementia, psychiatric disease, COPD, congestive heart failure (CHF), and hip fracture – which the authors noted are all associated with significant functional limitations. It is possible that

the results may reflect caregiving stress; alternatively, the impact of function-limiting illnesses may also result in other changes in spousal roles and spousal support (82).

Expectedness of Death

The expectedness or suddenness with which spousal loss occurs may be an important factor influencing the association of prior spousal health with bereavement outcomes. Based on a survey of bereaved relatives in Belgium, Merlevede et al. (31) concluded that sudden and traumatic deaths, especially when death occurs outside of a hospital, are associated with more residual questions and greater psychological distress among bereaved. Using 1971-1982 linked data from the U.S. Panel Study of Income Dynamics Study and corresponding vital records, Smith and Zick (18) used the estimated time of onset of the condition(s) that led to death, if recorded on the death certificate, to categorize spousal deaths as "unexpected", "expected", and "unknown". For non-elderly, but not elderly, widowers, unexpected spousal loss was associated with elevated hazard ratios in Cox survival models; for elderly women, long-term illness was associated with apparent protective effects. Although the authors urged caution due to the small sample sizes of a number of cells, as well as limitations with respect to the validity of the duration onset recorded in death certificates, this study nevertheless serves as a useful example of how categorizing spousal deaths based on their expectedness may provide important information about the potential impact on the surviving spouse.

A retrospective cohort study by Fosbol et al. (83) linked data from several large Danish national registries in order to examine the relationship of fatal and non-fatal acute myocardial infarction (AMI), and fatal and non-fatal occurrences of other health conditions, on spouses' subsequent use of anti-anxiety medication, use of antidepressant

medication, depression-associated hospitalization, and suicide. One key finding from Poisson models was that the occurrence of AMI, regardless of whether it was fatal or non-fatal, was associated with increased incidence of depression, and that AMI differed from other health conditions with respect to its apparent impact. The impact of spousal AMI appeared to be greater for men than for women. Fosbol et al. suggested that the results may reflect the fact that AMI mortality is frequently sudden and unexpected, in contrast to deaths caused by many other conditions.

One important theoretical construct that relates to the expectedness of death is the concept of "anticipatory grief, " a term that was first introduced by Lindemann (84) in his landmark study of psychiatric symptoms associated with grief. "Anticipatory grief" describes the process by which persons facing either the possibility or certainty of a loved one's impending death go through the phases of grieving, including emotional adaptation to the expected loss. Theoretically, it appears reasonable that anticipatory grief associated with expected deaths – such as those due to prolonged terminal illness – may serve to reduce the intensity of post-bereavement grief experienced by widowed elderly. However, results of empirical studies spanning several decades have been inconclusive, with some study results suggesting that death forewarning mitigates grief reactions (85, 86) , and other studies suggesting either the opposite or no effect (87, 88).

The U.S. Changing Lives of Older Couples (CLOC) study has yielded important insights into the psychological impact of the expectedness or suddenness of spousal loss (30, 89, 90). The CLOC study investigators initially recruited and interviewed 1,532 married individuals in the Detroit metropolitan area during 1987-1988, and then monitored the sample for spousal loss using a combination of vital records and obituaries.

Widowed persons were re-interviewed at 6 months, 18 months, and 48 months after the predeceased spouse's death. In a 2001 study of CLOC respondents, Carr et al. (30) examined the association between death expectedness (termed "forewarning" by the authors) on the subsequent psychological distress of the bereaved spouse. It should be noted that, in contrast to the above-discussed study by Smith and Zick (18), the CLOC study relies on the self-reported assessment of the surviving spouse to determine the suddenness or expectedness of the pre-deceased spouse's death. Carr et al. (30) found complex patterns involving the predeceased spouse's mode of death, with sudden, unexpected death increasing the likelihood of intrusive thoughts at 6 months post-bereavement. The presence or absence of forewarning had no significant impact on depression, anger, shock, or overall grief. However, prolonged forewarning was associated with greater anxiety at the 6-month and 18-month post-bereavement follow-ups. In a 2007 follow-up publication, Lee and Carr (91) analyzed additional CLOC data with the goal of examining the impact of spousal loss on physical functioning of the bereaved. Lee and Carr found that if the predeceased spouse had serious ongoing health problems before their death, the surviving spouse was more likely to report greater perceived functional limitations at 18 months and 48 months after bereavement. However, effects were primarily concentrated in widowers, suggesting that there may be important gender differences in how bereaved individuals respond to prolonged spousal illness before death.

Caregiving Burden

One challenge in evaluating the importance of the expectedness or suddenness of death is in separating the effects of death timing *per se* from spousal caregiving that may

have occurred before the spouse died. A considerable proportion of the research that has addressed spousal health has focused on the impact of caregiving, with a substantial body of literature demonstrating that caring for an ill or disabled spouse can be associated with significant stress for the caregiver, and that caregiving stress can persist for at least several years after the person for whom care was provided has died (92, 93).

As part of the U.S. CLOC study described above, Carr (89) measured eight potentially-important aspects of death quality as perceived by the surviving spouse: the dying person's acceptance of death, pain during final days, timeliness of death, spousal interactions in the final days, dying in the presence of family members, dying in a nursing home, degree of burden to family, and having led a full life prior to death. Results indicated that several aspects of the spouses's death were especially important in determining the bereaved spouse's responses to widowhood. Being present at the moment of death, in particular, was found to be beneficial for the survivor, reducing intrusive thoughts as assessed at follow-up. Somewhat surprisingly, caregiving burden was not related to the spouse's distress level six months after bereavement, leading the authors to speculate that the stress of caregiving may be balanced by compensatory rewards such as greater closeness with the spouse for whom care is being given. These results appear to be consistent with the finding by Keene et al. (94) that longer periods of pre-widowhood caregiving were associated with greater adaptation and lower depressive symptoms after widowhood.

In another U.S. study of the CLOC cohort, Burton et al. (95) examined the relative impact on depressive symptoms of the expectedness of death and caregiving simultaneously. Spousal deaths were categorized into four groups: unexpected loss,

expected loss without caregiving, expected loss with low-stress caregiving, and expected loss with high-stress caregiving. The authors used multilevel modeling (96) to examine change over time, by group. In this study, unexpected death was a more important predictor of depression at 6 and 18 months than was caregiving. However, high stress caregiving was associated with reduced social activity and support, suggesting greater isolation after bereavement.

With respect to mortality, studies examining the impact of caregiving have yielded mixed findings. In the U.S. Caregiver Health Effects Study (an ancillary study of the larger Cardiovascular Health Study), Schulz and Beach (97) compared the four-year survival of elderly individuals who were married to spouses having difficulties with activities of daily living with a comparison group of elderly whose spouses had no such limitations. Results of Cox proportional hazards survival analysis indicated that persons who provided care and who felt that their caregiving was associated with mental and emotional strain experienced an elevated hazard of death (HR=1.63, 95% CI: 1.00, 2.65). However, the results of other research, such as a 2013 propensity-matched study by Roth et al. (98) who used Cox survival models to analyze data from the U.S. Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, suggests that caregiving may actually be associated with modestly lower, not higher, mortality rates. The seeming inconsistencies across studies may be at least in part explained by the common finding that mortality effects appear to be largely concentrated in the subset of caregivers who perceive high levels of strain (97-99).

Other research suggests that greater perceived levels of a spouse's suffering – regardless of whether caregiving is involved – predisposes the non-suffering spouse to

greater depression and disease. Using data from the U.S. Cardiovascular Health Study, Schulz et al. (100) attempted to quantify suffering across three domains – physical symptoms, existential/spiritual suffering, and depressive symptoms – and examined the impact of spouses being exposed to their partner's perceived suffering. Schulz and his colleagues found for both genders, exposure to high levels of spousal suffering increased the likelihood of concurrent and future depressive symptoms. In addition, husbands exposed to wives with high levels of suffering were more likely to have prevalent coronary heart disease.

The Importance of Place of Death

Other research has explored whether the place of death influences the response to bereavement. Consideration of place of death is important for at least two reasons. First, depending on the cause of death, place of death may be associated with the extent to which there was forewarning or expectedness of the death, and may also be associated with the extent to which medical care was administered to the dying person (58). Secondly, place of death has become an important consideration with respect to end-of-life quality, particularly in the context of palliative care for persons with terminal illness. In its 1997 publication "Approaching Death: Improving Care at the End of Life," the Institute of Medicine defines a "good death" as "one that is free from avoidable distress and suffering for patients, families, and caregivers; in general accord with patients' and families' wishes" (101). In the United States, the evolution of hospice care has included an emphasis on allowing patients to live their last days at home, in familiar surroundings and with family, and a number of studies have found that a majority of terminally ill patients express a preference for dying at home, as reviewed by Higginson et al. (102).

Addington-Hall & Karlsen (32) reported data from the Regional Study of Care for the Dying, a population-based retrospective study in 20 English health districts which assessed bereaved persons' responses to their loved one's deaths 10 months after bereavement. In this study, which focused on cancer deaths, caregivers of cancer patients who died at home were found to have more psychological distress than when death had occurred elsewhere. However, in another U.K. study, Grande et al. (103) found that location of death was not associated with psychological response to bereavement. Only one aspect of location – whether the caregiver felt that the patient's wishes regarding place of death had been met – showed a significant trend with better mental health on the part of the caregiver. One factor that may limit the generalizability of prior research on death location is that the studies that have focused on location have for the most part been focused on palliative care for persons terminally ill with cancer. Studies examining the impact of place of death in the general population are far fewer. One early study addressing the importance of location was conducted in Wales by Rees and Lutkins (57), who compared mortality risk for bereaved whose relatives had died at home, in the hospital, or in other settings. They found that hospital deaths were associated with greater post-bereavement mortality risk than home deaths, but greatest risk was apparent when deaths occurred in public settings, attributed by the authors to reflect traumatic, sudden deaths. Similar findings were reported by Merlevede et al. (31) in their survey of sudden death victims' relatives in Belgium. Given the small number of studies that have examined the impact of place of death in contexts other than terminal cancer care research, more research is warranted on the potential impact of the predeceased spouse's place of death on the bereaved spouse.

Use of Hospice Services

The use of hospice benefits prior to death may help to provide information about both the expectedness of death and the inclusiveness of support given to the dying person. Christakis and Iwashyna (33) conducted a matched retrospective cohort study of U.S. Medicare elderly to test if hospice use among decedents affected mortality rates among the surviving spouses. This sample included only persons whose spouses died, and separate analyses were conducted for men and women. Persons whose predeceased spouse had used hospice care were matched to persons whose spouse had not used hospice, using propensity score matching. The dependent variable was time from bereavement to death of the surviving spouse. For women, prior hospice use by the predeceased husband decreased the mortality rate by 9%, controlling for other factors (HR=0.91, 95% CI: 0.82, 0.98). Results for men suggested a similar trend but were non-significant (HR=0.93, 95% CI: 0.84-1.02).

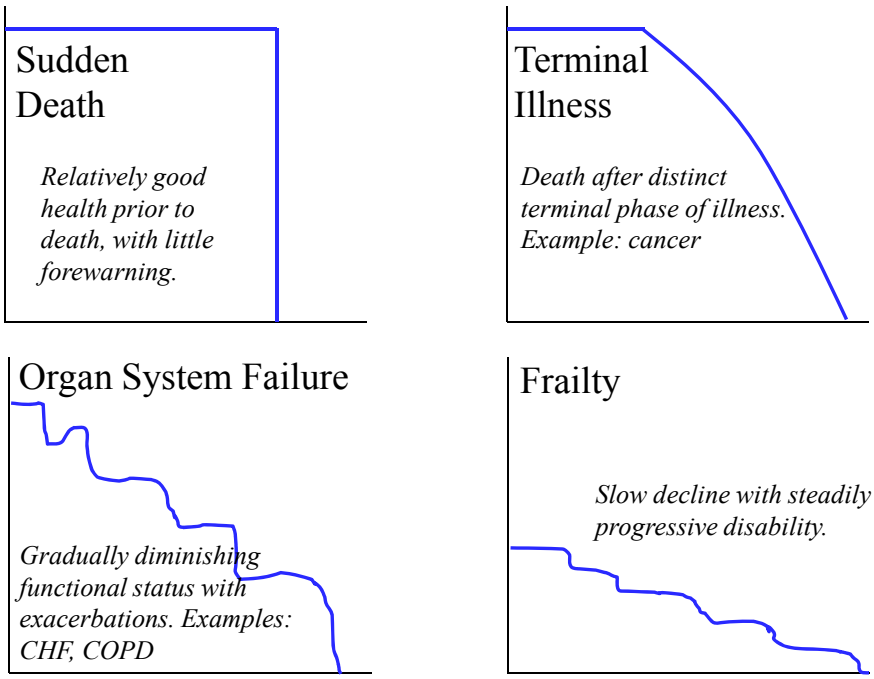
End-of-Life Health Trajectories

As described above, a number of prior studies have used varying approaches to examine how the health of the predeceased spouse prior to their death affects mortality among the surviving widows or widowers. However, to our knowledge, no prior studies have explicitly examined how the *trajectory* of health change in the predeceased spouse at the end of their life may affect the subsequent survival of the bereaved spouse.

However, the concept of health trajectories, particularly at the end of life, has been utilized in a number of different ways in prior gerontological research settings. Glaser and Strauss (37, 104) first proposed that there are several common patterns of decline observed as part of the dying process. Building on the work of Glaser and

Strauss, Lunney et al. (39) proposed four theoretical trajectories differing in their shape of decline at the end of life. As illustrated in Figure 1, the authors described these as: 1) *sudden death*, in which the person has no forewarning or obvious health decline prior to death – this pattern is consistent with the compression of morbidity introduced by Fries (105); 2) *terminal illness*, whereby sharp decline occurs over an approximate six-week

Figure 1
End-of-Life Trajectories Proposed by Lunney et al. (2002)



Modified from: Lunney et al. (2002) Profiles of older Medicare decedents. *J Am Geriatr Soc* 50:1108-1112

period before death, 3) organ failure, meaning a serious systemic failure such as congestive heart failure (CHF) or chronic obstructive pulmonary disease (COPD), characterized by gradually declining function with periodic sharp exacerbations of

illness, and 4) frailty, indicating a slow decline resulting from steadily progressing illness or disability which finally culminates in death. Using Medicare claims data for a 0.1% random sample of all U.S. Medicare beneficiaries, Lunney and her colleagues sought to develop claims-based group profiles during the last year of life, using the above-described theoretical patterns of decline. The authors first established rule-based criteria to assign Medicare-enrolled decedents to one of the above four groups. Persons under age 80 who had less than $2,000 in total Medicare costs were assigned to the "sudden death" group (7% of the study sample), persons with multiple claims indicating a cancer diagnosis were assigned to the "terminal illness" group (22% of the sample), persons with diagnoses of CHF or COPD were assigned to the "organ failure" group (16% of the sample), persons who had diagnoses related to stroke, dementia, Parkinson's disease, hip fracture, pneumonia, and selected other conditions were assigned to the "frailty" group (47% of the sample), and the remaining 8% of decedents were classified as "other." Although the assignment of individuals to the four groups was to some extent arbitrary, Lunney et al. found that the types of care and associated Medicare costs during the last year of life were distinct across the four groups, and that these distinct profiles fit general clinical expectations.

In a subsequent and closely-related study, Lunney et al. (38) further validated the four proposed trajectory definitions using functional status data from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) study, a U.S. community-based longitudinal study. In this second study, Lunney et al. assigned 4,190 decedents whose last EPESE interview occurred within one year prior to their death to one of the four trajectory groups described above, using the same rules-based assignment they had

used in their first study. They then computed mean activities of daily living (ADL) functional scores for each of 12 monthly cohorts corresponding to how soon before death the final interview had occurred (e.g., one month before death, two months before death, and so forth). Although the 12 cohort means do not reflect longitudinal monthly measurements obtained on the same persons, when the 12 average monthly ADL values were graphed for each of the four trajectory groups, the resultant functional decline patterns fit the clinically-expected patterns of decline that had originally been theorized for the four trajectory groups. The two studies by Lunney and colleagues thus provided important evidence that variability in functional decline at the end of life can be organized into distinct patterns that appear to be clinically relevant.

Subsequent work by other researchers have used other statistical approaches to assign persons to trajectory groups based on empirical observation of actual patterns of change in functional status measures. In a U.S. study, Gill et al. (106) used group-based trajectory modeling – a statistical method developed by Nagin et al. (35) to cluster observations based on patterns of change – in order to identify distinct trajectories of disability progression during the last year of life. Gill and his colleagues identified five relevant patterns of change which they interpreted as persistently severe disability, progressive disability, accelerated disability, catastrophic disability, and no disability. A further important finding of this study was that for most decedents, the pattern of disability change in the last year of life did not follow predicted patterns based on conditions leading to their death. This suggests that the diseases that lead to death and the functional decline experienced as part of the dying process are not isomorphic, and

that considerable heterogeneity exists in how people experience functional decline during the last part of their life.

The identification and analysis of end-of-life health and functional trajectories appears to hold great promise for increasing our understanding of the dying process. However, the extent to which such end-of-life trajectories among predeceased spouses may have a bearing on the subsequent survival of bereaved widows and widowers has not been previously addressed.

Summary of Current Problem and Study Relevance

A wealth of prior research has demonstrated that marital status is associated with health, and that the event of widowhood is associated with subsequently increased risk on the part of the surviving spouse for a number of adverse health outcomes, most notably death. Results of combined meta analyses suggest that bereavement increases mortality by about 25% on average for males, but less so for females. Results of numerous studies also suggest that the bereavement effects are greatest during the first six months of widowhood, but may persist for up to 20 years. Research to date has not revealed clear mechanistic pathways to explain how mortality risk is increased. Prior research suggests that the context of the predeceased spouse's death – such as whether the death was expected – generally appears to have a bearing on how well the surviving spouse does. However, the number of studies that have examined variability in mortality as a function of specified characteristics of the predeceased spouse's death – especially using multivariate analysis – is limited. Furthermore, no known published studies to date have combined the use of group-based trajectory modeling to empirically evaluate end-of-life patterns of health decline in predeceased spouses with formal analysis of the subsequent

survival of the bereaved spouses. The present research therefore seeks to make a contribution to the body of knowledge by combining these two concepts, in order to explore how the predeceased spouse's trajectory of morbidity during the last part of their life affects the subsequent survival of the bereaved spouse.

CHAPTER III: METHODOLOGY

Introduction

Using a retrospective cohort study design, the goal of this study is to examine the relationship between the pre-death trajectory of health change in the predeceased spouse – as well as the widowed spouse's own pre-bereavement health trajectory pattern – on the subsequent survival of the bereaved spouse.

Data analyses for the project include secondary analyses of existing administrative data collected by the Pennsylvania Assistance Contract for the Elderly (PACE) Program. The data were originally collected by PACE for its internal use supporting health care operations, administration, research, and evaluation purposes. The linked data sets that were analyzed for this study are not considered public use files, but prior to their release for use in this thesis, the data were fully de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule's Safe Harbor method. Therefore all names, information on geographic subdivisions below state (except for the first three digits of the zip code, which is permitted under the Safe Harbor method provided that the associated Census population exceeds 20,000 persons), Social Security numbers, medical records numbers, health plan beneficiary or account numbers, and dates were removed from the files.

As part of the de-identification process, dates were converted to simple interval counts of days between the original date and the subject's *index date*, which was the date that they were widowed and thus entered the retrospective cohort. The precise index date was not retained in the de-identified file; but the year of widowhood was kept so that possible temporal effects over the course of the study could be evaluated. Age was retained as whole years, but all ages over 89 were aggregated to a single value for 90 and older.

After reviewing the proposed de-identification procedures and data set variables, the Emory University Institutional Review Board (IRB) determined that the de-identified research did not require IRB review because it does not constitute research on human subjects according to the definition used in federal regulations, as set forth in Emory's Policies and Procedures. (The letter from the Emory IRB documenting this decision is provided in Appendix A.)

Population and Sample

The PACE Program

The population and setting for this study is the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) Program. PACE is a state program, funded by Pennsylvania state lottery proceeds, which provides pharmacy benefits to Pennsylvania state residents aged 65 or older who meet its income eligibility requirements. Since its inception in 1984, PACE has provided medication assistance to over one million elderly Pennsylvanians.

PACE includes two separate benefit tiers: the traditional PACE benefit program, which has current income limits of $14,500 for single individuals and $17,700 for

married persons, and the PACE Needs Enhancement Tier (PACENET) introduced in 1996, which currently covers single individuals with incomes between $14,501 and $23,500, and married persons with incomes ranging from $17,701-$31,500. PACENET includes higher copays and a monthly premium which is collected out of the point of sale drug cost when prescriptions are filled at the pharmacy. Individuals may not concurrently receive prescription benefits through the Pennsylvania Medical Assistance (Medicaid) program, and most individuals enrolled in PACE have incomes that are too high to qualify for Medicaid. Since 2006, PACE/PACENET has facilitated concurrent enrollment in selected Medicare Part D partner plans, and provides wrap-around benefits to Medicare Part D.

Widowed Cohort

The sample for this retrospective cohort study includes all enrolled persons who were widowed between 2000 and 2006, and who survived their spouse by at least one day. In addition, to be included in the sample, individuals had to meet additional study eligibility criteria, as described below.

Medicare Enrollment: Both the widowed person and their predeceased spouse had to be enrolled in the Medicare Fee-for-Service Program on the date of the predeceased spouse's death. This requirement means that valid and unambiguous matches to Medicare's denominator and vital status files had to have been obtained for both spouses by PACE when it acquired Medicare Part A and B claims data from CMS. To ensure that complete health-care based comorbidity data are present, both spouses also had to have been continuously enrolled in the Medicare Fee-for-Service Program during the preceding 24 months before the index date on which the predeceased spouse

died. Persons with any period of enrollment in a Medicare Advantage plan (i.e., a managed care health maintenance organization arrangement) during the prior 24 months were excluded, because encounter-level health utilization claims processed through the Medicare Advantage plan are not available from CMS. Widowed persons who switched from the Medicare Fee-for-Service Program to a Medicare Advantage Plan after their index date and before the end of the follow-up period were eligible to remain in the study cohort, because their date of death would still be recorded and available from CMS.

PACE/PACENET Enrollment: The widowed spouse had to be actively enrolled in PACE or PACENET on the date of death of the predeceased spouse (i.e., the study index date), in order to ensure that follow-up data on vital status and other health status measures would be available from PACE. Widowed persons in the study cohort could have later disenrolled from PACE after their index date and before the end of the follow-up period, but were censored from the Cox proportional hazards survival analysis models as of their date of disenrollment from PACE. This censoring was necessary because, over the present study's time period, there is no guarantee that all dates of death occurring after disenrollment from PACE would still be captured by PACE.

Research Design

The research design for this thesis is an observational retrospective cohort study, with secondary analysis of de-identified linked PACE enrollment records, Medicare Part A and B health care claims and enrollment data, and vital records data.

Procedures

Pre-Research Preparatory Activities. Prior to initiating the thesis research, and as a condition of employment with Magellan Health Services and the PACE Program, the

study investigator worked closely with PACE to coordinate the preparatory linkage of data sets and the creation of the data sets that are used for the thesis research. The Emory IRB was informed that the study investigator had access to identifiable PACE data as a Magellan Health Services employee, but that only the resulting Safe Harbor de-identified data authorized by PACE would be accessed when conducting the thesis research.

Preliminary Data Processing: Using the de-identified data sets provided by PACE, monthly Combined Comorbidity Scores (107) were calculated for both members of each spousal pair at monthly intervals during the year before the index date. Total numbers of inpatient hospitalization days and ambulatory visits were also computed for the 12 months before the index date. To support Cox proportional hazards modeling, each widowed person's event date (the date that they died, if applicable) or their censoring date was computed. The duration of time in days from the index date until the censoring date or the event date were computed, and a censoring indicator variable was created to show whether the person experienced the event of death or alternatively was censored. Persons who did not die during the three-year follow-up period, and who did not disenroll from PACE, were censored with a study duration value of 1,095 days. Age group categories were created corresponding to 65-69, 70-74, 75-79, 80-84, and 85 and older.

Instruments

The instruments for this study include variables obtained from PACE enrollment records, Medicare Part A and B health services records, and vital records information obtained from the Pennsylvania Department of Health and CMS. Instruments also

include computed measures, including Gagne et al.'s (107) Combined Comorbidity Score, the number of inpatient hospitalized days, and the number of ambulatory visits.

Data Files

Three de-identified data files were provided by PACE for the thesis research. Preparatory to research, each person in the widowhood cohort was assigned a unique study identifier by PACE which was randomly generated and which did not encrypt any PACE or other health plan number or other identifier. The unique study ID was present in all three PACE data files, so that records could be aggregated and linked across the three de-identified data files, but not to other data sources.

File 1: De-identified person-level data file (one record per person)

- Study ID (randomly generated, does not encrypt any other identifier data).
- Spouse's Study ID – the randomly-generated ID of the predeceased spouse.
- Year of index date (study entry) – the year the predeceased spouse died.
- PACE enrollment status for 24 months before through 36 months after each subject's index date – number of days enrolled during each sequential month in PACE or PACENET for months -1 to -24 pre-index, and month 0 to 36 post-index.
- Medicare Part A, B, and C (i.e., Medicare Advantage) monthly enrollment status indicators for the 24 months before through 36 months after each subject's index date – data included indicators for months -1 to -24 pre-index, and months 0 to 36 post-index.
- Sex (male, female).
- Race (white, black, and other race).
- Residence type as of index date (community, long-term care).

- Total annual income in dollars as of the index date.
- First three digits of zip code of residence at index point (each 3-digit combination present in Pennsylvania contains more than 20,000 people).
- Age as of the index date (whole years for ages 65-89; ages>89 aggregated to 90+)
- Source of death information on predeceased spouse (Pennsylvania vital statistics match, CMS match, or other).
- ICD-10 coded cause of death of predeceased spouse.
- Place of death (e.g., occurring at home, hospital, or nursing facility) of predeceased spouse, as recorded on the death certificate.
- For surviving spouses, the interval of time between their predeceased spouse's death and their own death, if applicable.

File 2: De-identified pharmacy claims data file (multiple records per person):

- Study ID (randomly generated and does not encrypt any other identifier, as described above).
- Recoded dispensing date (expressed as interval of days between indexed study entry and Rx fill).
- National Drug Code (NDC).
- Drug strength.
- Metric quantity of medication dispensed.
- Days supply of medication dispensed.
- American Hospital Formulary Service (AHFS) therapeutic class.
- Total drug cost.
- Subprogram (PACE or PACENET).

File 3: De-identified Medicare Parts A and B claims data (multiple records per person)

- Study ID (randomly generated and does not encrypt any other identifier, as described above).
- Data claim source: inpatient hospitalization, outpatient hospitalization, physician (carrier) visits, hospice care.
- Recoded admission or visit date (expressed as interval of days between indexed study entry and either an admission or visit date).
- Admission source (inpatient data).
- Type of admission (inpatient data).
- Patient status at discharge (inpatient data).
- Length of stay in days (inpatient data).
- Facility type.
- Total Medicare payment.
- Primary diagnosis, ICD-9-CM coded.
- Up to 13 secondary diagnoses depending on data claim source, ICD-9-CM coded.

Computed Measures

Comorbidity. ICD-9 based comorbidity was assessed using a validated combination of the Charlson (108) and Elixhauser (109) comorbidity scores. The Charlson comorbidity index was originally developed to maximally predict subsequent one-year mortality based on inpatient hospitalization diagnoses in 19 categories (108). Subsequent adaptations of the original Charlson have sought to maximize mortality prediction from administrative claim diagnoses; of these modifications, the Romano et al. (110, 111) and Deyo et al. (112, 113) versions of the Charlson have been the most widely

adopted. An alternate comorbidity score – the Elixhauser index – is based on 30 diagnostic categories and was originally developed to predict hospital charges, hospital length of stay, and in-hospital mortality (109). Although the original Elixhauser implementation recommended including all 30 comorbidities as separate binary predictor variables, subsequent modification by van Walraven et al. (114) yielded a well-validated single Elixhauser summary score. A number of studies have compared the ability of the Charlson-Romano, Charlson-Deyo, and Elixhauser to predict mortality and other health outcomes, with varying results. In a Canadian sample, Southern et al. (115) found that the Elixhauser score predicted mortality better than the Charlson-Deyo; similarly, Chu et al. (116) found better mortality prediction in a Taiwanese sample for the Elixhauser score than either the Charlson-Deyo or the Charlson-Romano scores. However, as discussed by Gagne et al. (107), a potential weakness of the Elixhauser scale is that it omits several diagnostic categories found in the Charlson which have consistently been shown to be associated with substantial mortality in elderly populations, including myocardial infarction and stroke. In attempt to synthesize the predictive capabilities of both the Charlson and the Elixhauser indices, Gagne et al. (107) tested a combined version of the Charlson-Romano and Elixhauser scores in two elderly samples – persons enrolled in the New Jersey Pharmacy Assistance for the Aged and Disabled (PAAD) program, and persons enrolled in PACE, the Pennsylvania pharmacy assistance program from which the present study's sample is drawn. Gagne et al.'s final Combined Charlson-Elixhauser Comorbidity Score, which includes 20 diagnostic entities, performed better than either the Charlson-Romano or the Elixhauser score in predicting mortality among the elderly samples studied (107). The Combined Comorbidity Score has been subsequently used as

a comorbidity adjustment score in a number of other settings (117, 118). Due to its prior validation as a useful mortality predictor in the PACE population and a similar elderly population, the Combined Comorbidity Score was selected as the primary ICD-9 based comorbidity measure for the present study. Using code specifications provided by Gagne et al. (107) , the Combined Comorbidity Score coding algorithm was applied to all primary and secondary diagnoses present on Medicare inpatient hospital, outpatient hospital, and physician visit records.

For ICD-9-based comorbidity indices, including the Combined Comorbidity Score employed in the present study, using a full year of "lookback" data history to construct the index is recommended (119). Therefore, although updated comorbidity scores were created for each month during the year before the predeceased spouse's death, the preceding 365 days were used to provide the lookback diagnostic data at each monthly measurement point.

Other measures of morbidity burden. In addition to Gagne et al.'s (107) Combined Comorbidity Score, two other summary claims-based health-related measures were also explored as global measures of morbidity burden. The following two measures were computed for both spouses of each married pair for each month during the year prior to the predeceased spouse's death:

Inpatient hospitalized days: This measure was constructed as the total number of days within the monthly period which were spent as part of an inpatient stay in a hospital facility, based on Medicare inpatient hospitalization data.

Ambulatory visits: Ambulatory visits were identified from Medicare outpatient, carrier, and hospice claim types, using a combination of codes relating to the place of

service and procedure performed. To be captured as an ambulatory visit, the Medicare claim's place of service code had to indicate that care occurred at a physician's office, patient's home, hospital outpatient setting, hospital emergency room, rural health clinic, public health clinic, urgent care center, or ambulatory surgical center. Because carrier data, in particular, include records for physician services performed in both inpatient and outpatient settings, additional criteria were applied to select procedures related to ambulatory evaluation and management. In addition to these criteria, to be counted as an ambulatory visit the encounter also had to have occurred on a date which did not fall within any portion of an inpatient hospital stay.

Although prescription drug fill data were available from the PACE program, drug data were not used as pre-index date comorbidity measures because prior research results suggest that ICD-9 based comorbidity indices perform significantly better at predicting mortality than do prescription-based measures alone (120). A second consideration is the fact that PACE's authorizing legislation does not permit the program to pay for prescriptions dispensed during inpatient stays. Relying on prescription drug data alone to measure comorbidity, particularly when constructing the end-of-life trajectories among the deceased subset of the sample, could therefore exclude important information.

Plans for Data Analysis

Statistical analysis was performed using SAS 9.3 software (SAS Institute Inc., Cary, North Carolina). Data analysis for the project was divided into two broad phases.

Phase 1: Health Trajectory Analysis

Trajectory model overview. The first phase of analysis entailed analysis of the health trajectory patterns of each person in the study cohort. Trajectories were analyzed

for the 365-day period preceding the index date. Parallel analyses were undertaken for each of the three morbidity measures, including the Combined Comorbidity Score, ambulatory visit counts, and inpatient hospitalization day counts. In addition, separate models were initially fit for the total sample (i.e., both the predeceased and bereaved spouses) and for the subsample of predeceased spouses only.

The statistical method used for the health trajectory analysis was group based trajectory modeling, developed by Daniel Nagin and his colleagues (35, 36, 121). The goal of group-based trajectory modeling is to identify clusters of individuals (trajectory groups) who follow similar developmental trajectories that are modeled with polynomials, for some measure or outcome over time. Group-based trajectory modeling employs maximum likelihood estimation and represents a specialized application of finite mixture modeling (35, 122). Other alternative approaches for the analysis of developmental data include growth curve modeling, including latent curve analysis and hierarchical or multi-level modeling (96, 123). An advantage of Nagin's group-based trajectory modeling approach is that it does not require any *a priori* assumptions or classification rules about the trajectory shapes. To conduct the group-based trajectory modeling, the publicly-available executable SAS add-in named PROC TRAJ, authored by Jones et al. (124), was used.

The group-based trajectory model seeks to identify a finite number of groups which are defined by their patterns of change over time in a measure *y*. The group-based model specifies that for individual, i, the values of measure *y* over time period *T* are described by vector $Y_i = [y_{i1}, y_{12}, \ldots, y_{iT}]$. The model employs maximum likelihood estimation to identify a set of parameters, Ω, which maximizes the probability of Y_i, or

P(Y_i). The particular form of Ω is distribution-specific, depending on the type of measurements that the vector Y_i comprises. Distributions available in PROC TRAJ include the censored normal (tobit) distribution, zero-inflated Poisson distribution, and the binary logit distribution. From among these choices, the zero-inflated Poisson distribution was selected as the most appropriate distribution for the three morbidity measures included in this study. Assuming a Poisson process to describe the underlying distributions of these variables is appropriate because each measure represents a discrete count (i.e., numbers of selected and weighted diagnoses, monthly days spent in the hospital, and monthly ambulatory visits). However, these measures do not conform to a traditional Poisson process because of the large number of cases having zero values for each measure, resulting in substantial overdispersion. (That is, the variance is substantially greater than the mean and thus does not fulfill the Poisson assumption of equal mean and variance.) The zero-inflated Poisson model, however, accommodates the excess values clustered at zero and is thus ideal for modeling the morbidity measures.

Regardless of the underlying distribution that is assumed to describe variability in measure y, the parameter set Ω defines the shape of the trajectories over time and the probability of trajectory group membership, where:

$$P(Y_i) = \sum_{j}^{J} \pi_j P^j(Y_i)$$

In the above equation, $P(Y_i)$ is the unconditional probability of individual i's sequence of observed *y* measurements. This unconditional probability equals the sum across *J* groups of the probability of membership in group *j* (denoted as π_j) multiplied by the conditional probability of Y_i, given membership in group *j*. This equation represents a

finite mixture model because it sums across a finite number (i.e., *J*) of unobserved groups which together constitute the population being studied (35). The likelihood function for a sample of *N* individuals is the product of the individual likelihood functions across all individuals in the sample, so that:

$$L = \prod^{N} P(Y_i)$$

Members of a group *J* are assumed to all follow a common trajectory of change, and each group's trajectory shape is described by a specific polynomial of *y* and time. PROC TRAJ allows the specification of zero order (constant), first-order (linear), second order (quadratic), or third order (cubed) functions of time. These specifications thus allow groups to be defined which may show no change with time, may increase or decrease linearly, may show accelerating or decelerating rates of change over time, or may even reverse direction.

Trajectory model selection procedures. The first goal of model selection is to determine the optimal number of groups (*J*) that are needed to describe the finite mixture of trajectory patterns in the population. In general, the objective is to identify the smallest (most parsimonious) number of groups needed to adequately describe the trajectory variability of the sample being studied. Identifying the optimal group number requires models with the same basic model specifications – but differing in the number of groups – to be compared. As a general approach, Nagin (35) recommends beginning with a two-group quadratic specification and then adding additional quadratic-specified groups until improvements in model fit cease.

Determining whether meaningful improvement in model fit is achieved with additional groups is not straightforward, however. Classical hypothesis testing is based

on large sample theory and requires that the null hypothesis model be nested as a special case within an alternative model to which it is compared (125). However, alternative mixture models are not unambiguously nested; therefore, likelihood ratio comparisons and their associated chi-square tests cannot be validly used to evaluate improvements in model fit (125, 126). One widely-used alternative to classical hypothesis testing is the Bayesian Information Criterion (BIC). Proposed by Schwarz (127), BIC implements a Bayesian approach to hypothesis testing as set forth by Jeffreys in 1935 (128). (See Kass and Raftery (129) or Burnham and Anderson (130) for excellent reviews of Bayesian approaches to model selection.) As Brame et al. (131) discuss, BIC-driven model specification seeks to identify the model with the largest (least negative) BIC value, based on:

$$BIC = \log(L) - 0.5 \cdot r_m \cdot \log(N)$$

where log(L) is the natural log of the likelihood obtained from the model's maximum likelihood estimation, r_m is a distribution-specific term based on the number of model parameters, and log(N) is the natural log of the sample size. For a zero-inflated Poisson model with J groups, $r_m=(4 \cdot J)-1$. BIC thus encourages parsimony by invoking a penalty for additional model parameters, and the penalty imposed is proportional to the sample size. From among a set of models being evaluated, the model with the largest (least negative) BIC is viewed as the most likely model.

Regardless of the criterion is used to guide model selection, it is important to understand that the trajectory groups identified in the group-based modeling approach are only approximations. In the extreme case, the number of unique groups that could potentially be identified by the model is equal to the total number of individuals in the

sample. With large samples, BIC may point to more groups being defined than are necessary to capture the meaningful variability present in the data, despite the penalty extracted for extra parameters. For this reason, Nagin (35) strongly recommends that modeling decisions be grounded in substantive considerations specific to the measures being studied, rather than relying solely on statistical criteria such as BIC. In addition, Nagin further recommends several other diagnostic criteria which can be used to help distinguish the best model to fit the data, as outlined below.

The posterior probability of membership in each group is a key model output which is calculated for each individual in the sample. Using a maximum posterior assignment rule, PROC TRAJ assigns each individual to the group for which they exhibited the highest calculated probability of membership, and also provides the calculated probabilities of the individual's membership in each of the *J* groups defined for the model. It is important to evaluate individuals' final assigned group membership against their probabilities of membership in the other available groups, because the degree to which group membership assignments are unambiguous represents another important way in which the model fit adequacy can be assessed. Diagnostic criteria recommended by Nagin (35) and employed in this study include:

1. Average posterior probability of assignment ($AvePP_j$). If group assignments are completely unambiguous, then the average posterior probability for members of a group would be 1.0. A general recommended rule of thumb is that the average posterior probabilities for each group in the model should at least exceed 0.70 (35).
2. Comparison of estimated group probabilities with the proportion of the sample assigned to the group. Two measures of the probability of group membership are

obtained from PROC TRAJ. The first estimate,, $\hat{\pi}_j$, is provided by the likelihood-maximized parameters. The second measure is the final proportion of persons assigned to each group, based on the maximum posterior assignment rule described above. While no specific threshold for similarity is provided, Nagin (35) recommends confirming that each group *J* shows reasonable similarity between the estimated value of $\hat{\pi}_j$ and the final percentage of persons assigned to the group.

3. Odds of correct classification (OCC_j). Larger values of OCC_j indicate that the model's group assignments are superior to random group assignment. This measure is computed as:

$$OCC_j = \frac{AvePP_j/1 - AvePP_j}{\hat{\pi}_j/1 - \hat{\pi}_j}$$

If individual group assignments were no better than chance, then OCC_j would be equal to 1.0. As a general rule of thumb, Nagin (35) recommends that OCC_j should exceed 5.0 for all groups.

In addition to BIC and the above-listed posterior probability criteria, a final important strategy for model selection is the visual inspection of the trajectory shapes, i.e., the graphed relationship between the model's predicted value of *y* and time for each of the trajectory groups identified by each model. Visual inspection of the graphed trajectories for each group, and comparison of the graphs across models varying in their number of groups, is critical in deciding whether additional groups uncover important features of the data or if the new groups are largely duplicative of other groups.

Based on these guidelines, the present study took the approach – for each of the three morbidity measures studied – to test a series of quadratically-specified models ranging from one to eight groups. Changes in BIC were tabled and reviewed, along with

other selected model statistics. In addition, the mean observed and predicted values of measure *y* over time for each group were graphed for each model using a SAS GRAPH macro written by Jones (121) , and were reviewed alongside the tabled statistical results. Based on this review, a final quadratic model was selected based on the general principle of identifying the most parsimonious model which yielded a favorable BIC relative to competing models, performed well for each of the other model adequacy criteria, and produced substantively-interpretable graphed trajectories that minimized "noise" (that is, minimized the appearance of extraneous groups that appeared to differ little from other groups in their trajectories). Taken together, the diagnostics facilitated the selection of a single credible, final trajectory model for each morbidity measure. Individuals' group membership assignments for the final models – based on the maximum posterior probability rule – were then saved in a SAS data set as categorical variables for use in the survival analysis phase of the study.

Phase 2: Survival Analysis

Overview of survival analytic methods employed. The second broad phase of analysis involved the analysis of survival among the widowed cohort as a function of each widowed person's predeceased spouse's trajectory pattern, their own health trajectory pattern during the year before their spouse died, and other covariates. Up to three years of post-widowhood survival data were included in the survival analysis.

Linear regression methods are not appropriate for modeling the impact of covariates on survival due to fact that a considerable number of widowed individuals did not die during the study period (termed "right censoring"). While logistic regression could be used to model the binary outcome of dying vs. not dying at any time during the

3-year follow-up period, such an analysis would not enable the assessment of whether the exposure measure affects how soon a bereaved person died during the 3-year period. A logistic regression approach also would not accommodate the inclusion of persons who disenrolled from PACE or were otherwise lost to follow-up before the end of the three-year study period. In contrast to linear regression and logistic regression, survival analysis methods are appropriate for analyzing the impact of covariates on survival duration, while appropriately accounting for censoring due either to the event of death not occurring during the study period, or because the person was lost to follow-up before the end of the study. The present study employed two different survival methodologies: Kaplan-Meier analysis of survival curves, and Cox proportional hazards regression.

As the first step of the survival analysis, the crude mortality risk (cumulative number of deaths/total persons) for the 3-year follow-up period and the crude mortality rate (cumulative number of deaths/100 person-years of follow-up) were computed for the entire sample, as well as for groups defined by the predeceased comorbidity trajectory pattern and the widowed comorbidity trajectory pattern. Due to the variable follow-up times of censored individuals in this study, the mortality rate – which incorporates person-time in the denominator – is a more appropriate measure of mortality incidence than is the mortality risk (132).

In order to compare the mortality experience of the bereaved study cohort to that of the overall PACE population, crude mortality rates for the general PACE population were obtained from the PACE program, both for the entire program population and by 5-year age group. To make the rate computation analogous to the present study's procedures, PACE's computation of crude rates for the general enrollment population

was limited to a three-year period of follow-up, beginning with each PACE enrollee's earliest eligibility date during the time period of 2000 to 2006. As for the present study, persons disenrolling from PACE before they died or reached the end of the three-year computation period had their follow-up time censored as of the point of disenrollment.

To facilitate the comparison of the bereaved cohort and general PACE mortality rates, age-adjusted mortality rates were computed for both the study cohort and for the total PACE population using the method of direct standardization to the 2000 U.S. population (133, 134), but considering only groups aged 65 or older. Five-year U.S. reference populations for ages 65-69, 70-74, 75-79, 80-84, and 85 years and older published by the National Center for Health Statistics were used for the standardization (134). Considering only the elderly (65 and older) population, the proportion of the U.S. elderly population falling within each 5-year age group was used to weight the crude PACE-enrolled and study cohort age-specific rates described above, and the resulting weighted age-specific rates were then summed to yield the age-adjusted mortality rates.

Kaplan-Meier analysis of the survivor functions for each categorized trajectory group was next conducted. Using the SAS LIFETEST procedure, survival curves of the bereaved sample were generated for each predeceased trajectory group. The equivalence of the survival curves across the categorical health trajectory groups or across other covariate strata was tested using the log-rank test, and cumulative survival and failure statistics were tabulated.

The second phase of the survival analysis employed multivariate Cox proportional hazards models to examine the association between the morbidity exposure variables, other defined predictors, and survival time (135). The dependent variable for the survival

analyses was the duration of time from the index date until either the widowed person's censoring date (described above) or their own death date. The Cox proportional hazards model estimates the hazard of an event as the product of two components: 1) a baseline hazard which is an unspecified function of time (the lack of specification differentiates the Cox model from parametric survival models such as Weibull or exponential models), and 2) an time-free exponential function of a set of covariates, (136). Specifically, the model formulation states:

$$h(t,\mathbf{X}) = h_0(t) \bullet e^{\sum \beta i Xi}$$

In the above formulation, the first component $h_0(t)$ is the unspecified baseline function of time, and the second component includes the exponentiated set of covariate parameter estimates, which do not depend on time. For the present study, the SAS PHREG procedure was used to conduct the Cox proportional hazards survival analysis, and to identify potential effect modification and confounding involving other predictor variables.

Collinearity considerations. Before proceeding to the survival modeling, the distributions of all potential predictor variables were examined to identify possible outliers and/or small frequencies for individual levels of categorical variables. For continuous variables, categorical groupings were based on the consideration of prior relevant research and the distribution of values in the study sample.

Prior to conducting Kaplan-Meier and Cox proportional hazards survival analyses, additional data screening which incorporated the trajectory patterns described above was conducted. One key area of concern is the potential interdependency among morbidity, hospice use, and place of death. When predictor variables are strongly

associated with and can be predicted by other predictor variables in a model, collinearity is present, which can increase the model's standard errors and produce unreliable regression coefficients (137). For example, it is possible that the predeceased spouse's use of hospice and their place of death could be at least partially caused by the predeceased spouse's morbidity trajectory. Individuals who receive diagnoses for diseases recognized as terminal within a short period, for example, are likely to receive hospice benefits, in contrast to individuals who do not receive such diagnoses. In this case we would not want to view hospice use as a confounder of morbidity, since it appears logical that hospice benefits could be a direct *consequence* of worsening morbidity. In turn, hospice use is also expected to influence the place of death to the extent that hospice services enable individuals to die at home. To explore these potential interdependencies, cross-tabulations and chi-square analyses were first conducted.

Following the cross tabulation and chi-square analyses, the extent of collinearity among all of the study's proposed predictor variables was formally evaluated based on inspection of condition indices (CNIs) and variance decomposition proportions (VDPs), as recommended by Kleinbaum and Klein (137) To obtain CNI and VDP tables from SAS, the COLLIN model option in PROC REG was applied to a linear regression model which predicting survival time from dummy variables corresponding to *k-1* levels of each categorical predictors (i.e., no dummy variable was entered for a categorical variable's proposed reference category). In addition to the CNI and VDP diagnostic tables, variance inflation factors and tolerance values were also obtained for each dummy variable in the regression model by specifying the VIF and TOL options in PROC REG. (PROC REG is the only SAS procedure which provides these collinearity diagnostics.)

The rationale for using linear regression procedures to detect collinearity, even though the study's main analyses employ proportional hazards survival models, is that collinearity describes relationships existing among predictor variables, rather than the relationship between a predictor and the outcome (138). Following generally-accepted guidelines, collinearity was diagnosed as being present if the largest CNI exceeded 30.0 and two or more VDPs exceeded 0.50 (137).

Cox model selection procedures. The Cox modeling strategy followed the "E,V,W" modeling strategy for assessing exposure-disease relationships proposed by Kleinbaum and Klein (137) and taught by Dr. Kevin Sullivan in Emory course AEPI 536D (139). Although originally proposed within the context of logistic regression, the E,V,W model is equally applicable to other regression-based applications, including survival analysis (137). The E,V,W strategy requires the following variable specifications:

- ***D*** = disease outcome (mortality among widowed spouses)
- ***E*** = the primary exposure variable. There are three potential *E* variables assessed independently in this study: the predeceased spouse's Combined Comorbidity trajectory group, the predeceased spouse's Inpatient Days trajectory group, and the predeceased spouse's Ambulatory Visits trajectory group. Each of these measures represents a different way of summarizing underlying morbidity in the predeceased spouse during the year prior to their death. The three morbidity measures are assessed as *E* variables in three separate model series.
- ***C*** = a set of control variables ($C_1, C_2, \ldots C_p$) which may act as either confounders or effect modifiers. The *C* variables identified for this study include gender, age,

race, the widowed spouse's own morbidity pattern, place of death of the predeceased spouse, and use of hospice benefits by the predeceased spouse.

- $\boldsymbol{V}$ = a set of potential confounders ($V_1, V_2, \ldots V_p$) which are either functions of the *C* variables or are the *C* variables themselves.
- $\boldsymbol{W}$ = a set of potential effect modifiers ($W_1, W_2, \ldots Wp$) which are product interactions terms of the *E* and *V* variables, expressed as *E* x *V*. Only two-way *W* interaction effects are evaluated in the present study.

The modeling sequence used hierarchical backward selection procedures, as recommended by Kleinbaum and Klein (137) and Sullivan (139). All models tested were hierarchically well-formulated; that is, for each *W* effect modifier included in the model, all lower-order components (e.g., the main effect term for the *V* variable involved in each *E* x *V* interaction) were also included (137). The initial full model tested included all *E* and *V* variables and all two-way *E* x *V* interactions. Prior to addressing confounding, potential effect modification was first evaluated. To do so, *E* x *V* interaction terms were evaluated by dropping non-significant interactions ($p \geq 0.05$) one at a time, beginning with the term having the highest p-value. The reduced full model included all *V* variables and any remaining significant *E* x *V* interactions. The morbidity *E* variable's hazard ratio from the reduced full model was viewed as the "gold standard" against which confounding would next be assessed (139).

Confounding was assessed using non-statistical criteria, in keeping with the view that confounding is an issue of validity and as such reflects systematic error, not random error (137). To evaluate confounding, the least-significant *V* which was not also involved in a significant *E* x *V* interaction was first removed from the model, and the change in the

hazard ratio from the gold standard was assessed. Hazard ratio changes of more than 10% from the gold standard hazard ratio were considered to be indicative of confounding (132). If a variable was identified as a confounder based on the 10% rule, it was retained in the model. The confounding status of all *V* variables not involved in an *E* x *V* interaction was assessed iteratively using these procedures. A reduced parsimonious model was identified for each morbidity exposure analytic series. The parsimonious model included the *E* exposure variable, all *V* variables identified as confounders or involved in significant *E* x *V* interactions, any additional non-confounder *V* variables showing independent associations with survival duration, and all significant *E* x *V* interaction terms.

Evaluation of the Cox proportional hazards assumption. A key feature of the Cox model is that hazards are proportional – meaning that for any individual in the analysis, the hazard is proportional to the hazard for any other individual in the analysis (140). An important assumption of the Cox model is that the first model component – the baseline hazard -- is a function of time, but does not involve covariates. A corollary assumption is that the second model component – the exponentiated expression of the covariate vector – does not involve time (136). Although the Cox model does not assume a specific form for the survival function over time for an individual, it assumes that hazard functions for any two subjects remain proportional over time (141). If the baseline covariates are correlated with survival time, then the proportional hazards assumption is violated and the validity of the model results could be questionable.

The viability of the proportional hazards assumption for the present study analysis was evaluated for each morbidity measure's parsimonious model described above. This

evaluation was conducted using the Schoenfeld residual goodness-of-fit method outlined by Kleinbaum and Klein (136). Schoenfeld residuals were output from PROC PHREG to a separate dataset by using the OUTPUT statement and RESSCH option. Using an alpha of 0.05, a significant Pearson correlation between a model variable's Schoenfeld residual and ranked failure time was considered indicative of assumption violation (137).

For variables exhibiting significant Schoenfeld residual correlations with ranked failure time, the final survival model was modified to employ an extended Cox model specification (136). The extended Cox model included a variable x time specification to account for the dependence of the affected variable(s) with time. To aid in interpretation of the resulting hazard ratios, the specific time expression chosen for this interaction term was a binary indicator distinguishing the first half of the follow-up period from the second half (e.g., the first 1.5 years vs. the second 1.5 years after bereavement).

Study Limitations and Delimitations

This retrospective observational study has a number of potential limitations and delimitations that should be considered. An important delimitation of the study is that the study cohort includes only persons who were widowed. There is no comparison group of persons who were not widowed. The reason for this delimitation is that the primary objective of the study is to evaluate the context of the predeceased spouse's death on the subsequent survival of the bereaved spouse. Specifically, the study seeks to evaluate the importance of the predeceased spouse's place of death, hospice use, and end-of-life health trajectory pattern. These variables can only be assessed for decedents. A consequence of this delimitation is that this study cannot compare the survival of married and widowed persons to evaluate the main effect of bereavement itself on survival.

The study may also be subject to some degree of selection bias due to the nature of the PACE population from which the study cohort was drawn. The PACE sample is limited only to elderly Pennsylvania residents, so the results of this study may not be generalizable to younger persons or to those living in other geographic regions. The PACE population is also not representative of the general U.S. elderly population, because, due to PACE's income eligibility requirements, PACE cardholders have lower incomes and are older on average than the general non-Medicaid elderly population enrolled in Medicare. A large body of research has demonstrated that individuals with poorer socioeconomic resources over their life course are more likely to have poorer health (142). In addition, individuals who choose to enroll in PACE may be more likely to have high medication needs and thus may be sicker or more frail than persons who are income-eligible but who choose not to enroll in the program, reflecting adverse selection into the program. A related limitation is that the study sample includes only persons who were enrolled in the Medicare Fee-for-Service program, and excludes individuals if either they or their spouse were enrolled in a Medicare Advantage managed care plan during the pre-index baseline period. Prior research has demonstrated a historical pattern of favorable risk selection of healthier Medicare beneficiaries into Medicare Advantage plans (143). Although recent research suggests that changes in Medicare's risk adjustment methods since 2004 have reduced the selection of healthier elderly into Medicare managed care plans (144), to the extent that this bias existed during the time period covered by the present study it may limit the generalizability of the findings.

Other threats to validity relate to the accuracy of information recorded on Medicare claims and on death certificates. Some diagnoses recorded on Medicare claims

may not be accurate and as a result individuals may be misclassified with respect to their true comorbidity levels. However, the comorbidity indices utilized in this study – which rely on Medicare diagnosis data – have been shown to have high predictive validity in prior studies, in that they have been shown to predict future health outcomes such as mortality, hospitalization, and health care utilization. In contrast, the validity of some of the other information used for this study, such as the place of death recorded on U.S. death certificates, has not explicitly been evaluated in prior published studies.

This observational study may also be limited by confounding due to unmeasured variables. For example, the use of hospice services by the predeceased spouse may be confounded with unmeasured variables such as education, the functional status of the bereaved spouse, or the availability of support from other relatives, all of which may also influence the survival of the surviving spouse. The study is also limited by a lack of available data on other relevant measures on the predeceased spouse, such as disabilities and functional limitations (i.e., limitations in the ability to conduct activities of daily living). Prior trajectory-based research suggests that functional limitations may provide more meaningful information about end-of-life health-related decline than medical diagnoses alone can provide (106).

CHAPTER IV: RESULTS

A total of 10,289 married couples met the study's initial enrollment criteria of continuous Medicare fee-for-service program enrollment for both spouses during the 24 months preceding the index date and an active PACE enrollment status for the widowed spouse on the index date. However, 20 individuals (10 married couples) were

subsequently excluded because both spouses died on the same day, and an additional 624 individuals (312 married couples) were excluded because the bereaved spouse resided in a nursing home or personal care home at baseline, yielding a final sample of 9,967 married couples.

Characteristics of the 9,967 bereaved spouses in the study sample are shown in Table 1. Over two-thirds of the bereaved sample was female, with a median age of 79. Nearly 21% of the bereaved spouses were aged 85 or older, and most (96.4%) were white. The majority (72.9%) resided in a home that they owned and 18.1% rented a home or apartment; the remainder of the sample reported living with relatives or other arrangements.

In addition to presenting characteristics of the bereaved spouses, Table 1 also presents information on the place of the predeceased spouse's death (based on the death certificate) and their use of hospice. Nearly half of decedents died in a hospital setting – 41.3% as inpatients and another 7.0% in hospital outpatient or emergency room settings. About a quarter (24.1%) of decedents died in a nursing home or other institutional setting, and 22.4% died at home. Over a quarter (27.5%) of the predeceased spouses had received hospice benefits in the final months before their death.

The last portion of Table 1 provides information on the mortality status of the bereaved sample. Overall, 1,686 persons (16.9%) died during the three-year follow-up period. An additional 2,392 individuals (24.0%) were censored prior to the end of the study, and the remaining 5,889 persons (59.1%) were censored at the end of the study. Among the 1,686 individuals who died, the median survival time was 472 days (in addition, the 25th percentile was 209 days and the 75th percentile was 762 days).

Table 2 provides an overview of the morbidity status of the predeceased and bereaved spouses for the three morbidity measures used in the study: the Combined Comorbidity Score, monthly hospitalization inpatient days, and monthly ambulatory visits. Descriptive statistics, including the mean, standard deviation, median, first and third quartiles, and percentage of subjects having values of zero are presented for each measure. For the Combined Comorbidity Score, descriptive statistics for four time points are shown in Table 2, based on Combined Comorbidity Score calculations preformed 365 days before the index date, 183 days before the index date, 31 days before the index date, and 1 day before the index date. For the two monthly morbidity measures, results are shown for 12 months before the index date, six months before the index date, and the final month preceding the index date.

Health Trajectory Analysis

Results of group-based trajectory models are presented separately for each of the three morbidity measures (the Combined Comorbidity Score, inpatient days, and ambulatory visits) and widowhood group (predeceased vs. widowed spouses). These results are tabulated in Tables 3 through 5, with accompanying graphical displays provided in Figures 2 through 7, and are discussed below. Special attention to detail is provided in the discussion of the first morbidity measure – the Combined Comorbidity Score – in order to illustrate the model selection process.

Combined Comorbidity Score Trajectories

Predeceased Spouses. Section A of Table 3 provides the BIC-based model fit parameters and assignment accuracy diagnostics for the Combined Comorbidity Score trajectory models for the predeceased sample. As shown in Table 3.A, BIC scores for the

predeceased spouse trajectory models improved with the addition of each new group. However, the percentage gains in BIC were greatest when moving from one to two groups (24.61%), followed by two to three groups (7.96%), three to four (3.43%) groups, and four to five groups (1.99%), with diminishing improvement in fit as more groups were added. The average posterior probability of assignment ($AvePP_j$) exceeded 0.70 for all models and groups, and the calculated odds of correct classification (OCC_j) exceeded 5.0 for all models and groups, as well. Finally, the two measures of the probability of group membership ($\hat{\pi}_j$ and P_j) showed high levels of correspondence for all models.

Based on these results, it appears that the 8-group model might provide the best statistical fit of the predeceased spouses' Combined Comorbidity Score trajectories. However, as described in the Methods section, the relatively large sample available for analysis (N=9,967 predeceased spouses) raises concern that non-essential group distinctions may have been extracted in the modeling process. Careful inspection of the graphed results in Figure 2 was therefore used to guide the final selection of the best trajectory model. Figure 2 illustrates that additional features of the data are uncovered as new groups are added. For example, the two-group model shows a moderately-high comorbidity group and a moderately-low comorbidity group, but the three-group model identifies patterns of relatively stable high, medium but increasing, and low but increasing trajectories. These patterns are parsed further in the four-group solution into what appear to be very low increasing, low increasing, medium increasing, and a moderately stable high group.

It is when we reach the five-group solution that key interesting features of the data emerge – in this solution, we see a stable high comorbidity group, a stable medium

comorbidity group, a group that starts low but worsens substantially throughout the year, a relatively stable low group, and a final group with zero to very low comorbidity for most of the year, followed by a late increase. The six-group model shows even more interesting features. In the six-group solution, we see once again a stable high comorbidity group, a stable medium comorbidity group, and a stable low comorbidity group. However, three distinct patterns now emerge from individuals who started the year with very low comorbidity – of these, one group remains near zero for the year; another group starts out very low and then increases steadily to a moderately high level, and the last group remains at low levels until the final five or six months, at which point it increases to a moderate level. It is not clear that the next solution -- the seven-group model -- adds essential distinguishing features beyond the six-group model. For the seven-group model, it appears that the further partitioning is mainly occurring among those with stable medium to high levels of comorbidity. This illustrates the importance of reviewing the modeled trajectories within the context of the study's substantive research questions. For example, trajectory groups that differ on the basis of clearly high vs. clearly low mean comorbidity, or increasing vs. stable comorbidity change, are arguably the most salient considerations for addressing the present study's research questions. Further parsing of some patterns, such as medium stable vs. medium-to moderately-high stable, is not as critical. For this reason, the six-group model, rather than the seven-group model, was selected as the most parsimonious model which yielded substantively-interpretable patterns meaningful to the research questions, and which also displayed good assignment accuracy diagnostics. The final groups identified for the predeceased sample's Combined Comorbidity are:

Group 1: Very low with late increase (11.9%)

Group 2: Stable low (23.4%)

Group 3: Late onset (8.0%)

Group 4: Stable medium (26.4%)

Group 5: Chronic high (19.5%)

Group 6: Steadily worsening (10.8%).

Widowed Spouses. Section B of Table 3 provides the BIC-based model fit parameters and assignment accuracy diagnostics for the Combined Comorbidity Score for the sample of widowed spouses. The steps followed for the widowed model identification parallel those detailed above for the predeceased sample. The results shown in Table 3.B indicate that improvements in BIC were obtained with each sequential increase in the number of groups modeled, up to the last model (eight groups). However, the improvements in BIC dropped off substantially after the first few models. Moving from one to two groups yielded a 36.46% improvement in BIC, with subsequent additions yielding improvements of 13.70% (three groups), 4.19% (four groups), 2.09% (five groups), and 1.92% (six groups). Adding more groups beyond six yielded very small improvements in BIC, ending with only a 0.48% improvement at the eighth group addition. Based on the assignment accuracy diagnostics, all groups display acceptable levels of $AvePP_j$ and OCC_j, although $AvePP_j$ levels decline below 0.90 for the eight group solution. In addition, the correspondence between $\hat{\pi}_j$ and Pj appears highest for models with up to six groups, and declines thereafter.

Figure 3 provides the graphed trajectory patterns associated with each widowed Combined Comorbidity model with between one and eight groups. On average, widowed

spouses had lower mean comorbidity than the predeceased spouses during the year before the index date. However, to allow direct visual comparison with the graphed solutions for the predeceased sample, trajectories for the widowed sample are graphed using the same y-axis maximum value that was needed to accommodate the predeceased spouses' data. Therefore some of the trajectories appear somewhat compressed in the widowed group in Figure 3. It is clear from Figure 3 that patterns of worsening comorbidity are not nearly as salient for the widowed group, compared with the predeceased patterns that were seen in Figure 2. Most of the patterns identified for models two through six appear relatively stable, with the primary distinctions among groups being based on mean comorbidity levels. A potential problem with the two and three group solutions is that medium and high levels of comorbidity are averaged together. Beginning with the four group solution, a core "very low or zero" group emerges which remains fairly constant across the four-group, five-group, and six-group models. In addition to the zero group (making up 41.5% of the sample in the 4-group model), the 4-group model identifies a medium to high group (9.1%), a medium group (21.9%), and a low group (27.6%).

The five-group model appears to carve out two new groups from the "low" group identified in the four-group solution – these additions correspond to a low but increasing group (20.6%) and a low and decreasing group (8.2%). A key difference in this model is that the low to medium groups are repartitioned, yielding a new stable low group which is distinguished from the low-and-decreasing and the low-but-increasing trajectories. Models beyond the five-group solution partition the higher comorbidity groups further, and carve out additional low groups. Selecting the five-group solution appears to offer the best compromise between parsimony and detail. The five-group model allows low

versus high comorbidity levels to be clearly distinguished, and yet would also allow the later consolidation of two or more of the low comorbidity groups in subsequent analyses, if desired. The five widowed Combined Comorbidity groups can be described as:

Group 1: Low and decreasing (8.2%)

Group 2: Zero (41.1%)

Group 3: Very low but moderately increasing (20.6%)

Group 4: Stable low-medium (21.1%)

Group 5: Chronic medium to high (8.9%)

Inpatient Hospitalization Days

Predeceased Spouses. Approximately 83% of the predeceased spouse sample experienced an inpatient hospitalization stay of at least one day sometime during the year prior to their death. Section A of Table 4 provides the BIC-based model fit parameters and assignment accuracy diagnostics for the predeceased sample's monthly Inpatient Hospitalized Days trajectory models. Models with one to four groups were successfully fit using quadratic specifications for all groups. However, models containing five and six groups failed to converge (i.e., produced a false convergence error in PROC TRAJ) unless a simpler intercept only and/or a linear specification was substituted for one or two of the quadratic components. Models containing seven or eight groups failed to converge regardless of the parameter specifications provided; as a result, only models with six or fewer groups were considered further. Figure 4 shows the trajectory patterns for all groups obtained from the one-group through six-group model solutions. The two-group solution fit the data well, as evidenced by the high assignment accuracy – the $AvePP_j$ exceeds 98% for both groups, there is close correspondence between π_j and P_j, and OCC_j

has values of 59.1 and 106.7. The two groups identified in this model include one group showing low levels of hospitalization days until the last three months of the year, at which point the mean values increase, and a second group which displays acceleration in the mean monthly hospitalization days throughout the course of the year.

The three-group solution appears to split out the higher-level group from the prior model into two distinct – but closely parallel – groups corresponding to moderately increasing and somewhat more pronounced increasing levels of hospitalization. It also offers a large improvement in BIC (57.0%) over the two-group solution. However, review of the assignment accuracy diagnostics shown in Table 4.A indicates some potential problems with this model's fit. While the $AvePP_j$ values of 79.7%, 81.6%, and 89.2% exceed Nagin's recommended threshold of 70%, they are well below the values shown for the prior model. There also appears to be lower correspondence between π_j and P_j compared with the two-group model. More importantly, OCC_j falls below 5.0 for one of the three groups, violating Nagin's recommended rules-of-thumb for classification. The four-group model yields only a 1.5% further improvement in BIC, but it displays substantially better diagnostic accuracy for all criteria compared with the three-group solution. This model defines a near-zero group with only a final small increase in the last month (28.3%), a low group with slight increasing utilization over time (35.0%), a group showing substantial acceleration throughout much of the year (11.9%), and a nearly-parallel group to the preceding one, but showing a later and sharper acceleration in hospitalization days (24.9%). The models with five and six groups appear to primarily carve out new groups with largely parallel curves from the above-defined four groups, while adding little additional improvement in BIC (1.34% and 0.54%,

respectively). Based on these results, it appears that the four-group solution provides the best set of trajectories. The predeceased sample's four-group Inpatient Hospital Days solution yields the following groups:

Group 1: Low with gradual increase (35.0%)

Group 2: Sharp acceleration in last 4 months (24.9%)

Group 3: Acceleration in last 6 months (11.9%)

Group 4: Zero or near zero, with very late increase in last month (28.3%)

Widowed Spouses. About a quarter (25.8%) of the widowed sample experienced one or more inpatient hospitalizations during the year preceding the index date. BIC-based model fit parameters and assignment accuracy diagnostics for the widowed sample's Inpatient Days models are shown in Table 4.B. Models with one to three groups were fit successfully using only quadratic components. The four, five, six, and seven group models failed to converge until linear specifications were applied to one or more groups, and models with eight groups failed to converge regardless of the polynomial orders specified. Further consideration was therefore limited to models containing seven or fewer groups, and the results are graphed in Figure 5.

For the widowed sample, all models displayed good diagnostic accuracy performance. Improvements in BIC were greatest going from one to two (31.03%), two to three (10.23%), and three to four (6.84%) groups; however, unlike the other outcomes discussed above, improvements of at least 2% were obtained for each additional group tested beyond four. Based on Figure 5, the two-group solution shows a relatively stable low group accounting for about a quarter of the sample, versus a stable very-low or zero group (76% of the sample). The three-group solution appears to carve out two separate

groups from among those experiencing any hospitalization during the year: a low-but--increasing group, and a low-but-decreasing group. The assignment accuracy diagnostics for the three-group solution were almost as high as for the two-group model, and BIC improved by 10% with the addition of the third group.

Comparing Figures 4 and 5, it appears that the higher trajectories identified in the widowed samples have much lower mean values than the widowed trajectories, reflecting the lower occurrence and duration of hospitalization stays among the widowed compared with the predeceased sample. For this reason, carving out additional groups beyond three in the widowed sample may offer little utility, since the additional groups appear to identify clusters of individuals representing only very small proportions (two to four percent) of the widowed sample. The three-group solution was therefore selected as the best-fitting model for the widowed sample. The final three hospitalization days groups identified for the widowed sample are:

Group 1: Zero or near-zero (75.6%)

Group 2: Low and decreasing (12.5%)

Group 3: Low but increasing (11.9%)

Ambulatory Visits

Predeceased Spouses. Section A of Table 5 provides the BIC-based model fit parameters and assignment accuracy diagnostics for the trajectories of Ambulatory Visits among the predeceased spouse sample. The tabled results indicate that BIC improved with the sequential addition of up to eight groups; however, greatest percentage gains in BIC occurred moving from one to two groups (14.82%) and two to three groups (3.50%). BIC gains for subsequent models were 1.05% (moving from three to four groups) and

declined to below a 1% improvement for each addition beyond the fourth group. Using Nagin's rules of thumb, the assignment accuracy diagnostics were reasonable for all models tested. The trajectory patterns obtained from the models are displayed graphically in Figure 6. Beginning with the four-group model, there appears to be a clear group of "chronic high" ambulatory care utilizers, and a second group of consistently-zero or near-zero utilizers, as well as two other groups with intermediate levels. With the addition of a fifth group, a new pattern emerges for persons whose utilization appears to increase steadily throughout the year. The six-group model uncovers another pattern of persons who begin the pre-index year low, but then increase to higher levels during the last six months of the year. Beyond the six-group model, it appears from visual inspection that the new groups formed are largely parallel of existing groups with only modest differences in mean levels. Based on these considerations, it appears that a six-group model may therefore be the most parsimonious model which uncovers meaningful ambulatory visit change patterns, and which also fits the data well. The six ambulatory visit trajectory groups identified in the predeceased sample are:

Group 1: Stable zero or near-zero (32.2%)

Group 2: Stable low (29.7%)

Group 3: Stable medium (17.0%)

Group 4: Late increase (12.4%)

Group 5: Steady increase (4.7%)

Group 6: Chronic high (4.0%)

Widowed Spouses. The ambulatory visit trajectory model fit parameters and diagnostics for widowed spouses are presented in Section B of Table 5, and the trajectory

patterns from all models are graphed in Figure 7. Model fit improvements, based on BIC, are apparent when moving from one to two groups (13.0% improvement) and two to three groups (2.4%), but then fall to below 1% when moving from three to four groups (0.71%) and thereafter. The model assignment accuracy diagnostics shown in Table 5.B suggest good levels of assignment accuracy for the two and three group solutions, although the correspondence between π_j and P_j does not appear to be as impressive as that seen for the morbidity models previously discussed. The highest-group model tested – eight groups -- does not meet Nagin's criteria for acceptable assignments because AvePP falls below 0.70 for one group. The fits of models with five or more groups appear to be marginal, as well, due to relatively-low OCC values and greater deviation observed for some π_j and P_j pairs. These results suggest that models with two, three, or four groups appear to fit the best. Visual inspection of the groups shows that the two-group solution distinguishes only low and intermediate trends. The three group solution shows what appear to be a stable zero or near-zero group (53.5%), a stable low group (37.6%), and a stable medium (8.8%) group. The four-group model yields a stable medium-high group, a stable medium-low group, a low group, and a stable zero. Given the compressed range of the widowed ambulatory visit data compared with the predeceased sample, it is not clear that a four-group solution describes the sample's variability more meaningfully than the three-group solution does, and the proportion of the sample falling into the medium-high group in the four-group model is only 2.3%. The three-group solution was therefore chosen as the best model for the widowed sample. The final three ambulatory visit groups identified in the widowed sample, therefore, are:

Group 1: Stable zero or near-zero (53.5%)

Group 2: Stable low (37.6%)

Group 3: Stable medium (8.8%)

Survival Analysis

Collinearity Assessment

As described in the Methods section, particular attention was given to potential interdependencies involving the morbidity exposure measures, hospice use, and place of death. Table 6 shows associations between hospice use and place of death in the predeceased sample, and Table 7 presents associations between hospice use and morbidity trajectory patterns for each of the three morbidity exposure variables. The results shown in Table 6 indicate that hospice use and place of death are significantly associated (Chi-square=2,202.10, 4 df, p<.0001). Over half (61.2%) of persons dying at home had received hospice benefits; and persons dying at home accounted for half (49.9%) of all hospice users (1,369 out of 2,741 hospice users). Persons dying in nursing homes accounted for another 29.9% of all hospice users, and 34.1% of all nursing home deaths were accompanied by hospice use. The results shown in Table 7 indicate that hospice use is also significantly associated with morbidity exposure levels. As expected, the prevalence of hospice use was significantly higher among morbidity trajectory groups associated with either chronically high or substantially accelerating morbidity during the last year of life.

Despite these associations, none of the regression-based collinearity assessments suggested problematic levels of collinearity between the E variables and their associated V variables. Variance inflation factors ranged from 1.00 to 1.76 for the Combined Comorbidity model predictor set of E and V variables, from 1.00 to 1.55 for the Inpatient

Days model predictor set, and from 1.00 to 1.55 for the Ambulatory Visit model predictor set. These values are all well below the commonly-applied threshold of 2.5. Similarly, none of the CNI and VDF diagnostics met the threshold (CNI>30.0 and two or more VDFs associated with this CNI exceeding 0.50) for collinearity. The largest CNIs for the Combined Comorbidity, Inpatient Days, and Ambulatory Visits variable sets were 8.23, 6.76, and 7.22, respectively, which are all well below the threshold of 30.0.

Based on these results, it was concluded that although associations exist between the E morbidity measures and several key V variables, the observed patterns of associations are not sufficient to preclude valid multivariate analysis. Therefore all E and V predictor variables were retained for the next phase of the analysis. However, given the temporal and potentially causal pathways involved between morbidity, hospice use, and place of death, hospice use and place of death are primarily of interest as potential effect modifiers, and not as confounders.

Crude Mortality Risks and Rates

The number of events, person-time, crude mortality risk over three years (computed as deaths/number of persons), and crude mortality rates per 100 person-years for the widowed sample, categorized by their predeceased spouses' morbidity trajectory patterns, are summarized in Table 8. During 22,696 total person-years of follow-up of the 9,967 widowed persons in the sample, 1,686 subjects died, yielding a crude mortality risk over three years of 16.92 percent and a crude mortality rate of 7.43 per 100 person-years. Given that 24% of the bereaved sample was censored prior to the study endpoint, the mortality rate is a more appropriate measure of mortality frequency than the mortality

risk because the rate incorporates variable amounts of person-time of follow-up in the denominator.

Across the predeceased Combined Comorbidity Score levels, crude mortality rates range from 6.77 per 100 person-years in the "steadily worsening" group to 7.85 per 100 person-years in the "late onset" group. For Inpatient Hospitalized Days, the crude mortality rates appear to be tightly clustered across all four levels of the predeceased trajectory pattern, with the lowest rate in the "acceleration over last 4 months" group (7.22 per 100 person-years) and highest rate in the "acceleration over last 6 months" group (7.63 per 100 person-years). Somewhat greater variability is suggested by the Ambulatory Visit data – the crude mortality rate is lowest for the "chronic high" ambulatory visit group (4.6 per 100 person-years) and highest in the "stable zero/near-zero" group (rate=8.38 per 100 person-years).

Table 9 again presents the crude mortality risks and rates for the widowed spouses, this time categorized by the widowed subjects' own morbidity trajectory patterns. Greater variability across morbidity levels is suggested by the pattern of results shown in Table 9, compared with Table 8. Considering the Combined Comorbidity Score trajectory groups, the crude mortality rate is highest in the "chronic medium to high" widowed trajectory group (22.70 per 100 person-years), and lowest for the "zero" Combined Comorbidity group (3.90 per 100 person-years). Considering the Inpatient Hospital Days widowed trajectory groups, the crude mortality rate is lowest for the "zero or near zero" group (rate=5.83 per 100 person-years) and highest for the "low but increasing" group (rate=15.59 per 100 person-years). Differences are also apparent across the levels of the widowed Ambulatory Visit Trajectory Groups, with the lowest

crude rate in the "stable zero or near-zero" group (6.51 per 100 person-years) and highest in the "stable medium" group (14.24 per 100 person-years).

Comparison of Mortality Rates to Other PACE Data

As described in the Methods section, age-specific crude mortality rates for the general PACE population were obtained from the PACE program; age-adjusted mortality rates per 100 person-years were then computed for both the study cohort and the general PACE population using direct standardization to the 2000 U.S. elderly population.

For the entire PACE 2000-2006 population followed for a maximum of three years (398,462 persons and 914,790 person-years of follow-up), 60,930 deaths were reported, yielding a crude mortality rate of 6.66 per 100 person-years (95% CI: 6.61, 6.71; this rate is based on unpublished data provided by PACE). The corresponding crude mortality rate for the bereaved study cohort based on 1,686 deaths over 22,696 person-years of follow-up was 7.43 per 100 person-years (95% CI: 7.08, 7.79). However, the age distribution of the study cohort differs from the general PACE population, due at least in part to the present study's requirement of 24 months of continuous enrollment in the Medicare Fee-for-Service program prior to widowhood. For example, only 5.7% of the bereaved sample was aged 65-69 at baseline, compared with 15.7% of the general PACE population. Following direct standardization of the age-specific crude rates, the bereaved sample's age-adjusted rate was 6.14 per 100 person-years (95% CI: 5.75, 6.53), compared with the age-adjusted rate of 5.83 per 100 person-years (95% CI: 5.79, 5.88) observed in the general PACE-enrolled population. It should be noted, however, that the members of the bereaved cohort would also have been included in the general PACE population rate computation; in addition, the general

PACE mortality data provided are not stratified by marital status, limiting our ability to evaluate differences in mortality rates between bereaved and non-bereaved elderly.

Kaplan-Meier Analysis Results

The results of Kaplan-Meier analyses are presented in Table 10 and in Figures 8 through 18. These analyses evaluated the survivor distribution functions for widowed subjects by group, separately for each study measure. The analysis is therefore univariate rather than multivariate, and results for a given variable do not control for the effects of other variables.

The Kaplan-Meier results suggest a minimal impact of either the predeceased spouse's Combined Comorbidity Score trajectory or inpatient days trajectory on the subsequent survival of the widowed subject. The survival curves for the separate trajectory groups (shown in Figures 8 and 9) are not clearly distinguishable, and the log-rank test results are had non-significant p-values of 0.5337 and 0.8372, respectively. A greater role is suggested for the predeceased spouse's ambulatory visits trajectory. As shown in Table 10, widowed spouses of decedents with chronic high ambulatory visit patterns show greater survival, compared with spouses of persons having stable zero or near-zero visit patterns; Figure 10 presents the survival curves, which show significant separation (log-rank $p=0.0003$). The Kaplan-Meier results shown in Table 10 and in Figures 11-13 suggest that widowed subjects' own pre-index morbidity trajectory patterns are much stronger predictors of their future survival than are their predeceased spouses' trajectory patterns. For all three morbidity measures, the log-rank results were very highly significant ($p<0.0001$). The Kaplan-Meier curves shown in Figures 11-13

fall in line with the expectation that worse pre-index date morbidity trajectories are associated with lower survival during follow-up.

Figures 14-16 present the Kaplan-Meier curves according to gender, age group, and race. Results indicate that men had significantly poorer survival (log-rank $p<0.0001$). As expected, older age groups also had more steeply-declining survival curves (log-rank $p<0.0001$). However, no significant difference in survival curves was apparent for race (log-rank $p=0.3515$).

Figure 17 presents survival curves by the place of death of the predeceased spouse. The lowest mortality during follow-up is seen for persons whose spouses died at home, while the highest is observed among persons for whom the spousal place of death was unknown (log-rank $p=0.0002$). Finally, Figure 18 shows Kaplan-Meier survivor functions for persons according to whether the predeceased spouse had used Medicare hospice benefits. The two curves appear to be superimposed on each other, and the log-rank test for this comparison was non-significant ($p=0.5355$).

Cox Proportional Hazards Modeling

Exposure 1: Predeceased Spouse's Combined Comorbidity Trajectory

The results of the Cox analytic series with the predeceased spouse's Combined Comorbidity trajectory as the primary exposure are presented in Tables 11 through 14. Table 11 presents the sequence of backward elimination steps followed for this model series. The two-way interactions involved the exposure variable with race, sex, place, widow's own Combined Comorbidity Score trajectory, and age were removed sequentially. The remaining E x V interaction of predeceased Combined Comorbidity

Score by hospice use could not be removed (p=0.0104) and was therefore retained in the model.

Table 12 presents the results of the confounding assessment that was performed for all V variables in the model, beginning with the variable having the lowest Wald chi-square and proceeding iteratively in order of significance. At each step, a variable was dropped and the difference between all hazard ratios involving the exposure measure was evaluated to see if there was a change of 10% or more. Place of death, race, gender, and age group could be dropped without any appreciable change in the HR estimates. However, because sex and age group each significantly predicted survival among the widowed sample (both $p<0.0001$), they were added back into the model.

The final variable tested – the widowed subject's own Combined Comorbidity Score – resulted in a more than 10% change for several of the individual HRs associated with the exposure variable, indicating that the effect of the predeceased spouse's Combined Comorbidity Score was confounded with the widowed subject's own comorbidity trajectory. This measure was also a strong predictor of survival ($p<0.0001$). Following confounding assessment, the resulting parsimonious model included the exposure measure, widow's own Combined Comorbidity trajectory, hospice use, age group, sex, and the interaction of predeceased Combined Comorbidity trajectory with hospice use.

Table 13 presents the results of evaluating the proportional hazards assumption for the Combined Comorbidity Score model series using Schoenfeld residuals. Two of the four dummy variables associated with widow's own Combined Comorbidity Score categorical variable displayed significant Pearson correlations with time ($r = +0.06$,

$p<0.0197$ and $r = -0.08$, $p=0.0014$), indicating that the proportional hazards assumption was violated for this measure. The final Cox model therefore utilized the extended Cox model form, including an interaction of the widow's own comorbidity trajectory pattern with a binary time measure (< 1.5 years vs $\geq$ 1.5 years since bereavement). Results are displayed in Table 14. Male gender was associated with significantly lower survival (HR=1.788, $p<.0001$), and there is a clear dose-response pattern of increasing mortality rates with advancing age ($p<0.0001$). Considering the widow's own pre-index comorbidity trajectory pattern, results vary according to the duration of time since bereavement. Compared with stable zero levels of comorbidity, the impact of chronic medium-to-high comorbidity scores in the year before bereavement is greatest during the first 1.5 years after widowhood (OR=6.002), and this effect was diminished somewhat at 1.5 years or greater after bereavement (HR=3.642).

Sections B and C of Table 14 show the hazard ratios associated with the predeceased Combined Comorbidity Score by hospice use interaction. Section B shows the hazard ratios for Combined Comorbidity Score, using a reference group of "chronic high" comorbidity at both levels of hospice use. Among bereaved persons whose spouses had used hospice, spousal stable low comorbidity or a late onset of comorbidity are both associated with lower survival, compared with persons whose predeceased spouses displayed chronically high patterns of comorbidity throughout the entire the year before their death (HR=1.47 for stable low and HR=1.62 for late onset). This effect is not apparent among those who did not use hospice, however. The pattern of HRs suggests a synergistic effect between hospice use and low/late onset levels of comorbidity before death. Section C of Table 14 presents the hazard ratios for predeceased comorbidity

trajectory pattern and hospice use using a 6 x 2 table format, with the lower right cell (chronic high comorbidity and no hospice use) serving as the reference cell. Comparing all other combinations to this cell, it is again apparent that stable low and late onset patterns of predeceased comorbidity, when accompanied by hospice use, are associated with somewhat greater mortality rates among survivors (HR=1.23 and 1.36, respectively).

In summary, the results of the Cox survival analysis indicated that hospice use modified the impact of the predeceased spouse's Combined Comorbidity Score trajectory pattern on the surviving spouse's hazard of death. Persons whose spouses had used hospice and yet had low or late onset trajectories of comorbidity appeared to experience a somewhat greater mortality rate than other groups. However, the modest effects observed for these predictors were considerably weaker than the survival effects observed for the widowed person's own Combined Comorbidity Score trajectory pattern, sex, and age. In addition, the widowed person's own Combined Comorbidity Score trajectory pattern was a significant confounder of the predeceased comorbidity exposure-survival relationship, and also displayed nonproportional hazards over time.

Exposure 2: Predeceased Spouse's Inpatient Days Trajectory

Analytic results for the model series focusing on the predeceased spouse's inpatient days trajectory as the exposure variable are shown in Tables 15 through 18. As shown in Table 15, all two-way E x V interaction terms were dropped during the backward elimination stage. Table 16 presents the results of the confounding evaluation that was conducted for this exposure measure. Hospice use, place of death, and race were not confounders and were also not significantly associated with survival, so were dropped from the model. While widow's own inpatient days pattern, age group, and sex were all

shown to be non-confounders, each of these measures significantly predicted survival (all $p < 0.0001$), and so were retained in the parsimonious model.

Table 17 presents the Schoenfeld residual correlation analysis that was conducted to evaluate the proportional hazards assumption for this model series. One measure – level 3 of widow's own morbidity pattern (low but increasing inpatient days) – was significantly correlated with time ($r = -0.17$, $p<0.0001$). Given the level of this correlation, the final Cox model took the extended Cox form and included a time interaction term for this measure. The final model results are presented in Table 18. The deceased spouse's inpatient days trajectory did not demonstrate any significant impact on the survival of the widowed spouse ($p=0.7734$). In contrast to this lack of effect, the widow's own pre-index date inpatient days trajectory was significantly associated with their subsequent survival, and this impact was strongest earlier in the bereavement period. Relative to persons with no inpatient days, those who exhibited patterns of either low and decreasing or low and increasing had worse survival (HR=2.12 and 3.16, respectively) during the first 1.5 years. During the second half of the follow-up period, the HRs were lower (1.52 and 1.57, respectively). As for the prior model series, male gender was significantly associated with survival (HR=1.94, $p<0.0001$), as was age group ($p<0.0001$). In particular, compared with widows or widowers aged 65-69, those aged 80-84 had a 66% greater hazard and those aged 85+ had a hazard ratio of 2.87.

Exposure 3: Predeceased Spouse's Ambulatory Visits Trajectory

Tables 19 through 22 present the results of Cox models analyzing the predeceased spouse's ambulatory visit trajectory pattern as the primary exposure. Similarly to what was found for the inpatient days model series, the ambulatory visit interaction screening

process dropped all 2-way E x V interactions, as shown in Table 19. The confounding assessment for this model series is presented in Table 20. Only one measure – the widow's own ambulatory visit trajectory pattern – was shown to be a confounder of the exposure-outcome relationship. In addition to the widow's own ambulatory visit trajectory, age and sex were also retained in the parsimonious model due to their significant associations with survival (both $p<0.0001$). The remaining non-confounders – hospice use, place of death, and race – were not significantly associated with survival and were therefore omitted from the parsimonious model.

The Schoenfeld residual analysis, shown in Table 21, indicated that the widow's own ambulatory visit trajectory variable violated the proportional hazards assumption. Therefore, as was done for the prior two exposure model series, the final Cox model employed the extended Cox form with an interaction term for widow's ambulatory visit trajectory pattern and time. Results from the final model are presented in Table 22. Similarly to the results shown for the prior two model series, male gender and older age were associated with significantly lower survival during follow-up. The pattern of the predeceased spouse's ambulatory visit trajectory in the year before death was significantly associated with the widowed spouse's survival ($p<0.0001$). Using the stable medium pattern as the reference group, a stable zero or near-zero pattern was associated with worse survival (HR=1.319, 95% CI: 1.139, 1.526); in contrast, a chronically high visit pattern was associated with greater survival (HR=0.667, 95% CI: 0.483, 0.921). The other three visit trajectory patterns (stable low, late increase, and steady increase) did not differ significantly from the stable medium group.

As was also seen for the prior two morbidity series, the widow's own ambulatory visit trajectory had a greater bearing on their subsequent survival than their predeceased spouse's trajectory did. As for the prior two morbidity measures, the association of the widow's own ambulatory visit trajectory with their subsequent survival was strongest during the first half of the follow up period. During that period, compared with persons who had a stable zero pattern of ambulatory visits, patterns of either low or medium levels of visits were both associated with lower survival (HR=1.299 for stable low, and HR=2.876 for stable medium). These effects were diminished somewhat in the second half of follow-up, to HR=1.250 for stable low and 1.739 for stable medium. For this measure, as for the other two morbidity measures, incorporating a time-dependent expression for widow's own morbidity pattern in the extended Cox model had a negligible impact on the HRs for the primary exposure variable (the predeceased spouse's morbidity trajectory pattern).

CHAPTER V: DISCUSSION

Introduction

The final chapter of this thesis will provide an overview of the study's findings and implications within the context of the research questions posed. The chapter will begin with a brief summary of the research problem, methodology, and results. A discussion of the study's conclusions, implications, and recommendations will then follow.

Summary of Study

Rationale and Significance

Research spanning many decades has yielded intriguing insights regarding the apparent benefits of marriage on health. In particular, widowhood has been shown to have substantially negative health effects on surviving spouses, with the consensus of many studies suggesting an increase in mortality risk of about 25% following widowhood (9, 68). Yet the mechanisms involved in the bereavement-mortality association are unclear. It appears likely from a number of prior studies that the context of the predeceased spouse's death, including whether their death was expected, may be an important factor. Another relevant factor may be the extent to which the bereaved spouse provided caregiving to their spouse before death. However, translating concepts such as the likely expectedness of death into objective measurement instruments is challenging, and the number of studies that have examined variability in mortality as a function of specified characteristics of the predeceased spouse's death has been fairly limited.

The trajectory of health change before death has long been recognized in the gerontological literature as a concept that is important to studies of aging. In their 1968 book entitled "Time for Dying," Barney Glaser and Anselm Strauss outlined several different trajectories of death, and discussed how heterogeneity in the dying process affects not only the dying person, but others around them (37). Based on this work, a number of gerontological researchers have used various methods to identify patterns of health decline or functional decline before death. Important work in this area was conducted by Lunney et al. (39), who theorized that four common end-of-life trajectories are relevant: 1) sudden death, with no obvious health decline before death, 2) terminal

illness, with sharp decline occurring over an approximate 6-week period before death, 3) organ or systemic failure, characterized by gradually declining function with periodic sharp exacerbations, and 4) frailty, characterized by a slow decline from a steadily progressing illness or disability.

Understanding the health trajectories that are followed prior to death is important, because it provides information about the dying process. Furthermore, in the context of examining bereavement effects, trajectory patterns represent an important element of the context of death. It appears reasonable that varying trajectory shapes of decline before death might be associated with both the expectedness of death and the likely caregiving burden or other distress placed on spouses before the death occurs. Gaining a better understanding of common end-of-life trajectories and their impact on surviving bereaved spouses may therefore advance our understanding of how spousal loss affects widows' and widowers' own subsequent health and mortality risk.

A key impetus for the present study is the increasing application of group-based trajectory modeling methods across a variety of research settings (35, 36). These methods enable clusters of individuals to be identified who share a common pathway of change over time in some measure. No known published studies to date have applied group-based trajectory modeling to examine the end-of-life trajectories in married decedents and their impact on the decedents' surviving spouses. The goal of the present study was to apply group-based trajectory modeling to morbidity data obtained on a sample of married decedents, and to examine the potential impact of these end-of-life morbidity trajectories on the mortality rate of bereaved surviving spouses.

Study Sample and Research Questions

The sample used for this study was drawn from the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE), a state-funded program which provides prescription assistance to income-eligible Pennsylvania elderly aged 65 and older. A sample of 9,967 elderly married couples were identified who met study eligibility criteria related to their enrollment in both PACE and the Medicare Fee-for-Service program. Medicare claims data for inpatient and outpatient services were available for all participants, as was mortality information obtained from CMS and the Pennsylvania Department of Health.

Using the sample of 9,967 elderly married couples, the present study sought to address the following research questions:

- What are the discernible patterns of health trajectory among decedents and their spouses?
- Does the health trajectory pattern of the predeceased spouse affect the survival of the bereaved spouse, after adjustment for potential confounding variables?
- Does the bereaved spouse's own health trajectory pattern confound or modify the effect of spousal health trajectory pattern on survival?
- Do demographic characteristics – including gender, age, or race -- confound or modify the effect of spousal health trajectory pattern on the survival of bereaved spouses?
- Do other circumstances surrounding the predeceased spouse's death – specifically, the place of death and the use of hospice before death – modify the effect of spousal health trajectory pattern on the bereaved spouse's survival?

Methodology Used

To address the first research question, we applied group-based trajectory modeling analyses, using a user-written SAS routine ("PROC TRAJ") provided by Jones et al. (124). The following three morbidity measures were analyzed:

- The Combined Comorbidity Score developed by Gagne et al. (107), which blends Charlson and Elixhauser comorbidity scoring into a single validated measure;
- The monthly number of inpatient days spent in the hospital; and
- The monthly number of ambulatory health care visits.

Trajectory patterns were examined separately for the predeceased spouses' morbidity measures and the widowed spouses' own corresponding pre-widowhood measures. Using the widowhood date as the index date for both widowed and deceased members of each married pair, trajectories of change over time in the year before the index date were evaluated.

Group membership for each of the three morbidity measures – based on each bereaved subject's predeceased spouse's trajectory pattern – comprised the exposure measures for the second part of the study, which examined the impact of these patterns on the subsequent survival of the bereaved spouse. The bereaved person's own trajectory pattern for each measure was treated as a potential confounder and effect modifier, as were age group, sex, and race. Place of death and hospice use were also examined for their confounding associations with the exposure measures. However, their primary conceptual focus for this study was in effect modification, not confounding, due to the potential causal pathways going from the predeceased spouse's morbidity pattern to hospice use and place of death.

The impact of each exposure or control variable on the bereaved sample's survival experience over the first three years after widowhood was evaluated using Kaplan-Meier and Cox proportional hazards survival models. First, the association of each measure with bereaved persons' survival was examined univariately by inspecting Kaplan-Meier survival summaries and survival curves, and by applying the log-rank test to evaluate differences in the survival curves across strata of each variable of interest. Next, Cox proportional hazards models were tested for each morbidity measure, using the E-V-W modeling strategy outlined by Kleinbaum and Klein (137). Effect modification was tested using two-way E x V interaction terms. Following the dropping of non-significant E x V terms, hazard ratios from the resulting reduced model were used as the "gold standard" with which to compare hazard ratios when potential confounders were dropped, one at a time, from the model. Control variables which were identified as confounders – based on a 10% change in the hazard ratio (132, 137) – were retained in the final parsimonious model, along with any additional variables which significantly predicted survival time. As part of the modeling process, multicollinearity and violation of the Cox proportional hazards assumption were also evaluated using methods provided by Kleinbaum and Klein (136, 137)

Conclusions, Implications, and Recommendations

Key findings, conclusions, and implications are summarized below within the context of the original research questions and objectives formulated for the study.

<u>Research Question 1</u>: What are the discernible patterns of health trajectory among decedents and their spouses?

Multiple clear trajectories emerged from each of the group-based trajectory model undertaken. Because one important goal of the study was to explicitly evaluate end-of-life trajectories, trajectories were constructed separately for the deceased and bereaved samples. For each measure, the trajectory patterns observed among decedents appear to have greater heterogeneity than those observed among bereaved spouses.

For the Combined Comorbidity Score, six trajectories were identified among the predeceased spouses: 1) very low with late increase, 2) stable low, 3) late onset, 4) stable medium, 5) chronic high, and 6) steadily worsening. The corresponding trajectory set for widowed spouses included: 1) low and decreasing, 2) stable zero, 3) very low but moderately increasing, 4) stable low-medium, and 5) chronic medium-high.

For inpatient hospital days in the predeceased sample, four trajectories were identified: 1) low with gradual increase, 2) sharp acceleration in last 4 months, 3) acceleration over last 6 months, 4) zero or near zero, with a very late increase in the last month. Inpatient utilization among the widowed sample was much lower than among the deceased sample. Three bereaved inpatient days trajectory patterns were identified for the widowed sample: 1) zero or near-zero, 2) low and decreasing, and 3) low but increasing.

Six ambulatory visit trajectory groups identified in the predeceased sample, including: 1) stable zero or near-zero, 2) stable low, 3) stable medium, 4) late increase, 5) steady increase, and 6) chronic high. Lower mean utilization and less overall variability was seen in the bereaved sample, compared with the predeceased group. For the bereaved group, the following trajectories were observed: 1) stable zero or near-zero, 2) stable low, and 3) stable medium.

Although a great deal of complexity was apparent in the trajectories identified, particularly for the predeceased sample, each model's assignment accuracy diagnostics indicated that the identified groups were clearly distinguished from one another. The resulting trajectories appeared for the most part to be theoretically meaningful and interpretable. Comparing the results obtained from this study with the trajectories operationalized by other researchers, it appears that our defined trajectories do not map onto, but are generally consistent with, the patterns Lunney et al. (39) proposed. For example, our trajectory patterns reflecting stable zero or stable very low levels of morbidity would in general be consistent with Lunney et al.'s "sudden death" pattern, in which there is no apparent forewarning in terms of diagnosed serious illness or rising health care utilization. Similarly, group-based trajectories which we have described as showing a late onset or final acceleration are consistent with Lunney et al.'s pattern of "terminal illness." Other trajectories such as the chronic medium to high patterns are consistent with what Lunney et al. described as "frailty," and patterns showing steady worsening throughout the year before death are consistent with Lunney et al.'s description of "organ system failure." Despite these broad consistencies, the group-based approach did not map completely onto the four Lunney et al. groups. In general, more groups were identified which showed somewhat greater complexity than the groups that Lunney et al. conceptualized. In addition, despite the powerful maximum likelihood approach used by the group-based trajectory modeling methodology, subjectivity remains because -- particularly with large samples -- extraneous or duplicative groups may be identified. Thus, despite the availability of multiple assignment accuracy diagnostics, an

unavoidable subjective element still remains in deciding which particular solution should be selected to describe the data.

Research Question 2: Does the health trajectory pattern of the predeceased spouse affect the survival of the bereaved spouse, after adjustment for potential confounding variables?

Results of the Kaplan-Meier and Cox proportional hazards models suggest a limited role for some but not all spousal morbidity trajectory measures. The effect of spousal Combined Comorbidity appeared to mainly be limited to two trajectory groups and was modified by hospice use. Persons whose spouses had used hospice and yet had stable low or late onset trajectories of comorbidity appeared to experience a higher mortality rate than other groups. In the second analytic series, no significant effect of spousal pre-death inpatient days trajectory was apparent. However, for the third morbidity measure – ambulatory visits – some differences in widows' and widowers' survival according to spousal ambulatory visit trajectory were apparent ($p<0.0001$). Using stable medium as the reference group, a stable zero or near-zero pattern was associated with lower survival (HR=1.319); in contrast, a chronically high pattern was associated with greater survival (HR=0.667). The other three patterns (stable low, late increase, and steady increase) did not differ significantly from the stable medium group.

In the aggregate, the associations of the three morbidity exposure variables were not consistent. The significant findings, however, may be interpretable in view of the potential stress posed by deaths that have little forewarning. For both the Combined Comorbidity Score analysis and the ambulatory visit analysis, there is some suggestion that lower morbidity prior to death in the predeceased spouse may be associated with

worsened survival for the bereaved spouse. This could potentially be related to the unexpectedness of death, and would be consistent with prior research by Smith and Zick (18) and by Carr et al. (30) finding that unexpected deaths are frequently associated with worse post-bereavement health outcomes among survivors, which may reflect processes related to anticipatory grief (84) occurring in expected, but not unexpected, deaths.

Research Question 3: Does the bereaved spouse's own health trajectory pattern confound or modify the effect of spousal health trajectory pattern on survival?

Results for all three morbidity measures indicated that widows' and widowers' own morbidity trajectory patterns were more significant predictors of their future survival than were their spouses' patterns. This is not surprising, given the strong prognostic significance of the Combined Comorbidity Score and claims-based utilization measures such as inpatient days and ambulatory visits. Each of these three morbidity measures also showed significant correlations with time, resulting in violation of the Cox proportional hazards assumption and requiring the addition of a morbidity-time interaction in the final extended Cox model. For each of the three morbidity measures, the adverse impact of having a worse trajectory pattern was greatest during the first 1.5 years of follow-up, and was reduced in the second 1.5 years. Future research strategies might address this finding by incorporating time-varying measures of comorbidity which make use of updated diagnostic measurements at specific points during the follow-up period.

For the Combined Comorbidity Score and ambulatory visit trajectory analyses, the effect of the predeceased spouse's trajectory on the widowed spouse's survival was

confounded with the widowed spouse's own trajectory pattern. This suggests that spouses may have similar health trajectories, and this is particularly of interest given prior research on health concordance among spouses (145). Thanks to recent advances in group-based trajectory modeling which enable the estimation of joint trajectories (121, 146), an important avenue for future research would be to simultaneously model the joint morbidity trajectories of spouses to evaluate their concordance.

Extending this line of research to explore health concordance in spouses should also consider the complex pathways through which concordance may occur. Similarity in spousal trajectories may reflect shared demographic or socioeconomic backgrounds, assortative mating for risk-associated characteristics or behaviors, or other shared exposures of spouses to similar environmental factors that affect morbidity. Another relevant area which has received increasing attention is the concept of social control of health behaviors within marriage. Research on health-related social control has shown that married spouses are an important source of health-related support, and spouses may both directly and indirectly influence each other's health-related behaviors and health care access (21-24, 147). The concept of social control of health within marriage has roots in social cognitive theory, which has established the importance of self-efficacy and social interactions in determining health behaviors (19, 148). Within the context of marriage, the concept of self-efficacy has also been expanded to "collective efficacy" whereby spouses augment each other's ability to address many different types of situations, including health issues (22). Future research should therefore consider the complexity of pathways through which spouses may not only share certain risks for disease, but may also directly influence each other's health.

<u>Research Question 4</u>: Do demographic characteristics – including gender, age, or race -- confound or modify the effect of spousal health trajectory pattern on the survival of bereaved spouses?

Race did not appear to confound or modify the exposure-survival time association for any of the three morbidity measures, nor was it an independent significant predictor of survival time in this sample. However, the sample available for study was largely homogeneous for race (96.4% white) which limited our ability to explore differences. Future research in settings other than PACE would enable more meaningful analysis of racial and ethnic differences.

In keeping with most epidemiologic studies of mortality in the elderly, male gender and older age were strongly associated with worse survival during the three-year follow-up period. However, sex and age did not emerge as either confounders or effect modifiers of any of the morbidity exposure-outcome associations. Existing research on mortality following bereavement suggests that, in general, post-bereavement rate elevations are greater in men than in women (9, 68). However, the limited number of studies that have examined widowhood effects by specific causes of death or hospitalization of the predeceased spouse have not found consistent sex differences in these effects. For example, Christakis and Allison (82) found similar patterns of mortality rate elevations in men and women as a function of specific spousal illnesses, suggesting that certain diseases consistently increase the hazard of death for the other spouse, regardless of gender. On the other hand, a related study by Elwert and Christakis (28) concluded that the specific cause of death may be more salient for bereaved husbands than for bereaved wives. Similarly, using data from the Changing Lives of

Older Couples Study, Lee and Carr (91) examined the effects of serious illness in predeceased spouses on the post-bereavement functional limitations of their surviving spouses, and found stronger effects in men than women. Given these inconsistent findings, more research is needed on how the specific patterns of spousal illness before death may affect men and women differently.

Research Question 5: Do other circumstances surrounding the predeceased spouse's death – specifically, the place of death and the use of hospice before death – modify the effect of spousal health trajectory pattern on the bereaved spouse's survival?

Using information recorded on death certificates, we examined widows' and widowers' survival according to whether their predeceased spouses died at home, in the hospital, in a nursing facility, or at another (or unknown) location. Controlling for other factors, there is little evidence in this study that the place that the predeceased spouse's death occurred has a large bearing on their surviving spouse's future survival. Most prior studies have examined the impact of place of death in the context of palliative care and terminal illness, for which deaths at home are viewed as preferred by many patients (102). For the present study, one research hypothesis was that deaths at home might be associated with worse outcomes for bereaved persons if their spouses had died suddenly, with little or no forewarning. However, multivariate Cox proportional hazards analyses did not reveal any increase in the hazard for surviving spouses if their predeceased spouses died at home, regardless of the pre-death health trajectory experienced by the decedent. The results therefore do not indicate that that dying at home – regardless of the morbidity trajectory followed before death – is associated with worse outcomes for the

surviving spouse. Regardless of the degree of expectedness of the death, it may be that deaths at home are viewed by survivors as having been associated with less suffering for the decedent, which may help the bereaved spouse cope with the loss even in the case of unexpected death.

We also examined the potential effect modification of any hospice use by the predeceased spouse prior to their death. Our results indicate that hospice use modified the effect of the decedent's Combined Comorbidity Score trajectory, but primarily in the form of augmentation for selected cells. Among hospice users, stable low or late onset morbidity patterns were associated with worse survival, relative to chronic high patterns (HR=1.47 and 1.62, respectively), but no morbidity trajectory effects were apparent in non-hospice users. The worsened survival associated with the specific combination of stable low or late onset Combined Comorbidity and use of hospice is somewhat difficult to understand, especially in view of contradictory results obtained by Christakis and Iwashyna (33), who observed lower mortality among bereaved spouses if hospice had been used. One possible explanation for why our trajectory-based results are different from the work by Christakis and Iwashyna (33) may be that low or late onset Combined Comorbidity levels – when combined with hospice use – could reflect recent diagnosis of a terminal illness which advances rapidly. If so, the pattern of results observed here could suggest that other deaths that are completely sudden and unexpected – i.e., very low comorbidity, low medical utilization, and no hospice use – may still be less stressful on the bereaved than rapidly advancing terminal illness, which is likely to be associated with more interaction with the health care system and with the stress of having to confront a rapidly-deteriorating situation. Although hospice provides critical support to

terminally ill individuals and their families, the presence of hospice may nevertheless contribute in some way to the trauma of confronting a spouse's impending death.

An implication of the present findings is that spouses of elderly who die following the rapid onset of illness that is accompanied by hospice use may be especially vulnerable following the spousal loss. The stress of rapidly-advancing illness combined with hospice use may be associated not only with a lack of forewarning, but also with special burdens related to caregiving during the dying process. The present results may therefore support the use of stress management interventions for caregivers of elderly receiving Medicare hospice benefits. Bereavement counseling and family-based interventions designed for elderly spouses of hospice recipients, especially for the spouses of elderly whose illness advanced rapidly, may also be useful in identifying distressed widowed elderly who may be at heightened risk of death.

It is also possible that hospice use may be confounded with other unmeasured variables related to the amount of pain, suffering, and loss of functional capacity that a dying spouse is experiencing – factors which cannot be captured by morbidity trajectory pattern alone. To understand these associations further, future research should attempt to examine the timing and specific types of diagnoses associated with hospice use, as well as the degree of pain and functional limitations experienced during the dying process, in order to understand the relative impact of these factors on widows' and widowers' subsequent health outcomes. The present study's parallel finding that low levels of ambulatory visits before death appear to be related to higher bereaved mortality rates suggests another area for further research and potential intervention on the part of health care providers or family members. Further research is needed to gain a better

understanding of the degree to which low levels of ambulatory visits before death may be associated with a lack of forewarning of the death, or whether a generalized lack of ambulatory care may affect health outcomes for both spouses.

The present study has a number of strengths and weaknesses that should be considered when evaluating the findings. One key weakness is that the study cohort includes only persons who were widowed. As discussed in the Methods section, this study delimitation was a result of the focus on the context of the predeceased spouse's death using information that would only be available or meaningful for decedents. Future studies should seek to examine health trajectories in a general married cohort, rather than only a deceased/widowed cohort, in order to examine the general effect of one spouse's morbidity trajectory on subsequent health outcomes for the other spouse.

As previously discussed in the Methods section, the study may also be subject to selection bias due to the nature of the PACE population from which the study cohort was identified. PACE cardholders have lower incomes and are older on average than the general Medicare population, so the results may not be generalizable to all elderly or to non-elderly. In addition, individuals who choose to enroll in PACE may be more likely to have high medication needs and thus may be sicker or more frail than persons who are income-eligible but who choose not to enroll in the program, reflecting adverse selection into the program. Other threats to validity relate to the accuracy of information recorded on Medicare claims and on death certificates. For example, the validity of some of the information used for this study, such as the place of death recorded on the death certificate, has not explicitly been evaluated in prior published studies.

This observational study may also be limited by confounding due to unmeasured variables. For example, the use of hospice services by the predeceased spouse may be confounded with unmeasured variables such the suffering or functional status of the bereaved spouse, or the availability of support from other relatives, all of which may also influence the survival of the bereaved spouse.

Despite these weaknesses and limitations, the study also has a number of strengths. One strength is its robust sample size and the comprehensive Medicare utilization data available for all participants. A second strength is the availability of mortality data obtained via linkage, which enabled us to define the timing of widowhood as well as the subsequent mortality of the bereaved spouses in the study with a high degree of accuracy, and to also examine place of death as a potential effect modifier.

In conclusion, this study makes use of a powerful methodology – group-based trajectory modeling – to identify common trajectories of morbidity in both the bereaved and non-bereaved spouses during the year before widowhood. The study results appear to validate the utility of group-based trajectory modeling in identifying meaningful end-of-life trajectory groups. Although the association of these end-of-life trajectories with bereaved spouses' subsequent survival was not consistent across all groups and measures, some of the study's findings suggest that lower levels of spousal morbidity before death may be associated with worse post-widowhood survival among the bereaved. Future research is needed to understand the complex pathways through which spouses are affected by each other's health, and to understand how other factors – such as hospice use – interact with these pathways.

TABLES

Table 1
Characteristics of Bereaved Spouses (N=9,967)

Characteristic	Number	Percent
Index Year *(median index year=2004)*		
2000	1,430	14.4
2001	1,163	11.7
2002	1,042	10.4
2003	1,198	12.0
2004	1,835	18.4
2005	1,755	17.6
2006	1,544	15.5
Age *(median age=79)*		
65-69	568	5.7
70-74	1,729	17.4
75-79	2,814	28.2
80-84	2,794	28.0
85+	2,062	20.7
Gender		
Female	6,870	68.9
Male	3,097	31.1
Race		
White	9,604	96.4
Black	180	1.8
Other Race	183	1.8
Residence		
Own	7,261	72.9
Rent	1,806	18.1
Live with relative	588	5.9
Other/missing	312	3.1
Spouse's place of death		
Hospital	4,862	48.8
Nursing home	2,403	24.1
Decedent's home	2,236	22.4
Other/unknown	466	4.7
Spouse's use of hospice		
No use	7,226	72.5
Any use	2,741	27.5
Mortality during follow-up		
Died during follow-up	1,686	16.9
Censored before end of study	2,392	24.0
Censored at end of study	5,889	59.1

Table 2
Morbidity of Predeceased and Bereaved Spouses

Morbidity Measure	Range	% with Zero Score	Mean	S.D.	Q1 (P25)	Q2 (Median)	Q3 (P75)
A. Predeceased Spouses (N=9,967)							
Combined Comorbidity Score							
Index date-365 days	0-17	26.5%	2.91	2.89	0	2	5
Index date-183 days	0-18	21.9%	3.39	3.09	1	3	5
Index date-31 days	0-20	12.6%	4.91	3.55	2	5	7
Index date-1 day	0-20	6.5%	6.16	3.62	3	6	9
Monthly Inpatient Hospitalization Days							
Index month-12	0-30	92.4%	0.56	2.43	0	0	0
Index month-6	0-30	88.4%	0.88	3.23	0	0	0
Index month-1	0-30	39.0%	6.36	7.86	0	4	10
Monthly Ambulatory Visits							
Index month-12	0-16	60.3%	0.72	1.21	0	0	1
Index month-6	0-26	57.1%	0.83	1.37	0	0	1
Index month-1	0-20	44.6%	1.10	1.50	0	1	2
B. Widowed Spouses (N=9,967)							
Combined Comorbidity Score							
Index date-365 days	0-16	55.9%	1.15	1.83	0	0	2
Index date-183 days	0-16	53.7%	1.25	1.92	0	0	2
Index date-31 days	0-17	50.7%	1.44	2.13	0	0	2
Index date-1 day	0-17	50.0%	1.47	2.18	0	1	2
Monthly Inpatient Hospitalization Days							
Index month-12	0-30	97.4%	0.16	1.25	0	0	0
Index month-6	0-29	96.6%	0.21	1.39	0	0	0
Index month-1	0-30	95.0%	0.35	2.00	0	0	0
Monthly Ambulatory Visits							
Index month-12	0-12	71.9%	0.42	0.84	0	0	1
Index month-6	0-11	72.4%	0.41	0.82	0	0	1
Index month-1	0-10	73.0%	0.41	0.86	0	0	1

Table 3
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of the Combined Comorbidity Score

Model (Classes)	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
A. Predeceased Spouses								
1	-364,330.50	—	—	1	1.000	1.000	1.000	—
2	-274,657.39	89,673.11	24.61%	1	0.472	0.472	0.991	119.1
				2	0.528	0.528	0.991	96.8
3	-252,789.32	21,868.07	7.96%	1	0.252	0.253	0.984	182.3
				2	0.426	0.426	0.977	57.6
				3	0.321	0.322	0.980	104.4
4	-244,128.65	8,660.68	3.43%	1	0.153	0.152	0.987	415.2
				2	0.286	0.286	0.965	68.4
				3	0.340	0.340	0.956	42.3
				4	0.220	0.221	0.964	95.6
5	-239,266.26	4,862.39	1.99%	1	0.161	0.158	0.991	602.9
				2	0.226	0.228	0.947	60.7
				3	0.116	0.115	0.931	102.5
				4	0.297	0.299	0.946	41.7
				5	0.201	0.200	0.965	108.5
6	-235,859.62	3,406.64	1.42%	1	0.119	0.119	0.980	364.0
				2	0.234	0.234	0.956	70.6
				3	0.080	0.079	0.950	219.1
				4	0.264	0.264	0.937	41.5
				5	0.195	0.195	0.961	102.5
				6	0.108	0.109	0.917	91.3
7	-232,935.48	2,924.14	1.24%	1	0.110	0.109	0.987	595.7
				2	0.190	0.190	0.945	73.9
				3	0.071	0.072	0.945	222.3
				4	0.102	0.101	0.930	117.1
				5	0.203	0.204	0.917	43.2
				6	0.094	0.093	0.945	165.8
				7	0.230	0.231	0.936	49.2

Table 3 (continued)
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of the Combined Comorbidity Score

Model (Classes)	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
A. Predeceased Spouses (continued)								
8	-231,102.51	1,832.97	0.79%	1	0.101	0.101	0.979	426.2
				2	0.150	0.151	0.932	77.0
				3	0.063	0.063	0.947	265.0
				4	0.097	0.096	0.910	94.5
				5	0.211	0.212	0.924	45.2
				6	0.209	0.211	0.928	48.9
				7	0.092	0.091	0.945	169.4
				8	0.077	0.076	0.909	119.2
B. Widowed Spouses								
1	-248,075.20	—	—	1	1.000	1.000	1.000	—
2	-157,625.06	90,450.14	36.46%	1	0.446	0.449	0.991	136.1
				2	0.360	0.358	0.985	115.5
				3	0.193	0.193	0.982	227.6
3	-136,025.49	21,599.57	13.70%	1	0.446	0.449	0.991	136.1
				2	0.360	0.358	0.985	115.5
				3	0.193	0.193	0.982	227.6
4	-130,324.65	5,700.83	4.19%	1	0.415	0.412	0.997	456.1
				2	0.276	0.279	0.964	70.9
				3	0.219	0.219	0.960	85.0
				4	0.091	0.090	0.970	324.6
5	-127,595.41	2,729.24	2.09%	1	0.082	0.080	0.965	305.8
				2	0.411	0.411	0.995	293.3
				3	0.206	0.209	0.953	78.7
				4	0.211	0.211	0.962	94.6
				5	0.089	0.090	0.967	297.9

Table 3 (continued)
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of the Combined Comorbidity Score

Model (Classes)	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
B. Widowed Spouses (continued)								
6	-125,142.91	2,452.51	1.92%	1	0.081	0.081	0.963	298.1
				2	0.393	0.394	0.997	448.6
				3	0.209	0.210	0.946	65.9
				4	0.099	0.098	0.968	271.2
				5	0.157	0.155	0.949	100.2
				6	0.062	0.062	0.953	305.0
7	-123,467.55	1,675.35	1.34%	1	0.069	0.070	0.948	246.5
				2	0.400	0.403	0.988	120.2
				3	0.200	0.202	0.944	68.0
				4	0.094	0.091	0.970	314.3
				5	0.043	0.040	0.921	259.2
				6	0.136	0.136	0.940	99.4
				7	0.059	0.059	0.956	347.1
8	-122,880.81	586.74	0.48%	1	0.073	0.073	0.954	264.9
				2	0.389	0.389	0.996	376.2
				3	0.056	0.053	0.945	288.1
				4	0.192	0.193	0.943	70.0
				5	0.124	0.123	0.930	94.3
				6	0.064	0.066	0.872	100.7
				7	0.047	0.046	0.886	159.2
				8	0.057	0.057	0.953	337.2

Table 4
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of Hospital Inpatient Days

Model (Classes)	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
A. Predeceased Spouses								
1	-355,014.95	—	—	1	1.000	1.000	1.000	—
2	-290,162.40	64,852.55	18.27%	1	0.657	0.657	0.991	59.1
					0.343	0.343	0.982	106.7
3	-124,833.99	165,328.41	56.98%	1	0.538	0.631	0.797	3.4
				2	0.323	0.265	0.816	9.3
				3	0.139	0.104	0.892	51.2
4	-122,965.60	1,868.39	1.50%	1	0.350	0.334	0.874	12.9
				2	0.249	0.233	0.813	13.1
				3	0.119	0.102	0.890	60.4
				4	0.283	0.332	0.844	13.8
5	-121,323.01	1,642.59	1.34%	1	0.293	0.300	0.816	10.7
				2	0.219	0.199	0.806	14.8
				3	0.127	0.107	0.829	33.3
				4	0.284	0.332	0.845	13.8
				5	0.076	0.062	0.856	72.2
6	-120,672.05	650.96	0.54%	1	0.033	0.023	0.856	176.8
				2	0.257	0.267	0.784	10.5
				3	0.155	0.133	0.810	23.2
				4	0.282	0.332	0.841	13.5
				5	0.193	0.180	0.767	13.8
				6	0.079	0.065	0.805	48.0

(Models with more than six groups failed to converge.)

Table 4 (continued)
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of Hospital Inpatient Days

Model (Classes)	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
B. Widowed Spouses								
1	-113,723.55	—	—	1	1.000	1.000	1.000	—
2	-78,439.66	-35,283.89	31.03%	1	0.767	0.764	0.999	293.0
				2	0.233	0.236	0.986	224.9
3	-70,416.29	8,023.37	10.23%	1	0.756	0.755	0.999	274.6
				2	0.125	0.125	0.971	236.7
				3	0.119	0.120	0.972	256.8
4	-65,598.54	4,817.76	6.84%	1	0.128	0.128	0.981	352.8
				2	0.743	0.743	1.000	1,189.6
				3	0.084	0.085	0.975	416.4
				4	0.045	0.044	0.976	855.2
5	-62,471.11	3,127.43	4.77%	1	0.743	0.743	0.999	583.6
				2	0.024	0.024	0.953	818.2
				3	0.113	0.112	0.982	434.8
				4	0.078	0.078	0.982	631.3
				5	0.043	0.042	0.968	682.0
6	-60,948.36	1,522.75	2.44%	1	0.125	0.125	0.977	304.5
				2	0.742	0.742	0.999	669.5
				3	0.028	0.028	0.987	2,585.5
				4	0.023	0.023	0.957	915.9
				5	0.044	0.043	0.971	714.9
				6	0.038	0.038	0.972	880.4
7	-57,932.91	3,015.46	4.95%	1	0.065	0.064	0.862	90.4
				2	0.742	0.742	0.999	423.6
				3	0.028	0.029	0.952	692.0
				4	0.051	0.049	0.939	286.8
				5	0.037	0.036	0.971	871.2
				6	0.050	0.051	0.917	209.6
				7	0.029	0.029	0.977	1,421.9

(Models with more than seven groups failed to converge.)

Table 5
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of Ambulatory Visits

Model	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
A. Predeceased Spouses								
1	-170,048.70	—	—	1	1.000	1.000	1.000	—
2	-144,848.99	25,199.71	14.82%	1	0.647	0.647	0.979	25.1
				2	0.353	0.353	0.962	46.3
3	-139,778.54	5,070.45	3.50%	1	0.471	0.474	0.952	22.5
				2	0.413	0.412	0.931	19.1
				3	0.116	0.114	0.941	120.7
4	-138,317.11	1,461.44	1.05%	1	0.342	0.347	0.912	19.9
				2	0.381	0.380	0.874	11.2
				3	0.229	0.226	0.900	30.4
				4	0.049	0.047	0.942	319.9
5	-137,066.79	1,250.32	0.90%	1	0.372	0.372	0.864	10.8
				2	0.314	0.321	0.901	19.8
				3	0.056	0.051	0.863	106.9
				4	0.211	0.208	0.893	31.3
				5	0.048	0.046	0.945	343.1
6	-136,475.84	590.95	0.43%	1	0.322	0.338	0.890	17.1
				2	0.297	0.302	0.824	11.1
				3	0.170	0.165	0.879	35.6
				4	0.124	0.110	0.763	22.7
				5	0.047	0.045	0.842	107.1
				6	0.040	0.040	0.923	289.9
7	-135,993.81	482.03	0.35%	1	0.240	0.239	0.762	10.2
				2	0.231	0.240	0.859	20.3
				3	0.247	0.253	0.840	16.0
				4	0.135	0.125	0.771	21.6
				5	0.093	0.089	0.874	67.8
				6	0.019	0.018	0.925	637.0
				7	0.036	0.034	0.856	159.3

Table 5 (continued)
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of Ambulatory Visits

Model	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
A. Predeceased Spouses (continued)								
8	-135,745.90	247.92	0.18%	1	0.149	0.142	0.720	14.6
				2	0.213	0.227	0.848	20.6
				3	0.221	0.221	0.746	10.3
				4	0.059	0.054	0.774	54.5
				5	0.236	0.239	0.843	17.3
				6	0.082	0.079	0.865	71.7
				7	0.024	0.023	0.831	203.6
				8	0.016	0.015	0.928	797.9
B. Widowed Spouses								
1	-108,950.90	—	—	1	1.000	1.000	1.000	—
2	-94,771.86	14,179.04	13.01%	1	0.763	0.773	0.972	11.0
				2	0.237	0.227	0.949	60.5
3	-92,471.56	2,300.30	2.43%	1	0.535	0.551	0.918	9.7
				2	0.376	0.362	0.896	14.3
				3	0.088	0.087	0.919	116.8
4	-91,792.22	679.33	0.73%	1	0.389	0.414	0.851	9.0
				2	0.436	0.418	0.862	8.1
				3	0.152	0.145	0.884	42.6
				4	0.023	0.022	0.913	437.2
5	-91,571.06	221.17	0.24%	1	0.333	0.330	0.864	12.7
				2	0.442	0.457	0.828	6.1
				3	0.172	0.162	0.831	23.7
				4	0.049	0.047	0.864	122.3
				5	0.004	0.004	0.952	4,503.5

Table 5 (continued)
Model Fit and Assignment Accuracy Diagnostics for Trajectory Modeling of Ambulatory Visits

Model	BIC	BIC Difference	% Change in BIC	Group	π_j	P_j	$AvePP_j$	OCC_j
B. Widowed Spouses (continued)								
6	-91,295.55	275.51	0.30%	1	0.443	0.447	0.834	6.3
				2	0.317	0.330	0.842	11.5
				3	0.158	0.150	0.817	23.8
				4	0.030	0.023	0.766	107.3
				5	0.048	0.046	0.864	125.0
				6	0.004	0.004	0.952	4,607.2
7	-91,230.26	65.29	0.07%	1	0.147	0.195	0.738	16.3
				2	0.495	0.480	0.877	7.3
				3	0.229	0.211	0.813	14.7
				4	0.073	0.071	0.860	77.5
				5	0.040	0.027	0.730	65.3
				6	0.010	0.009	0.844	541.6
				7	0.007	0.006	0.926	1,838.0
8	-91,095.03	135.23	0.15%	1	0.295	0.330	0.804	9.8
				2	0.021	0.016	0.686	101.9
				3	0.438	0.423	0.834	6.4
				4	0.155	0.150	0.782	19.5
				5	0.027	0.021	0.737	100.6
				6	0.053	0.050	0.846	99.0
				7	0.007	0.006	0.845	806.4
				8	0.004	0.004	0.944	3,829.7

Table 6
Prevalence of Hospice Use Among Predeceased Spouses by Place of Death

Place of Death	No Hospice Use N	No Hospice Use %	Any Hospice Use N	Any Hospice Use %
Hospital	4,436	91.2	426	8.8
Nursing Home	1,584	65.9	819	34.1
Home	867	38.8	1,369	61.2
Other/unknown	339	72.7	127	27.3
Total	7,226	72.4	2,741	27.5
Chi-square = 2,202.10, 4 df, p<.0001				

Table 7
Prevalence of Hospice Use Among Predeceased Spouses
by Predeceased Morbidity Trajectory Pattern

Morbidity Series and Predeceased Trajectory Group	No Hospice Use N	No Hospice Use %	Any Hospice Use N	Any Hospice Use %
Combined Comorbidity Score				
1: Very low with final increase	1,028	86.5	160	13.5
2: Stable low	1,826	78.4	502	21.6
3: Late onset (6 months)	570	72.0	222	28.0
4: Stable medium	1,930	73.3	703	26.7
5: Chronic high	1,200	62.7	744	38.3
6: Steadily worsening	672	62.1	410	37.9
Chi-square=331.17, 5 df, p<.0001				
Monthly Hospitalized Inpatient Days				
1: Start low with gradual increase	2,208	66.4	1,118	33.6
2: Acceleration in last 4 months	1,685	72.6	635	27.4
3: Acceleration over last 6 months	759	74.9	254	25.1
4: Zero with very late increase	2,574	77.8	734	22.2
Chi-square=112.17, 5 df, p<.0001				
Monthly Ambulatory Visits				
1: Stable zero/near-zero	2,875	85.3	497	14.7
2: Stable low	2,184	72.7	822	27.4
3: Stable medium	1,064	64.6	582	35.4
4: Late increase	585	53.4	511	46.6
5: Steady increase	289	64.4	160	35.6
6: Chronic high	229	57.5	169	42.5
Chi-square=587.06, 5 df, p<.0001				

Table 8
Crude Mortality Risks and Rates
by Predeceased Spouse's Morbidity Trajectory Pattern

Predeceased Morbidity Trajectory Group	No. of Persons	Total Deaths	Total Person-Years of Follow-Up Observed	Crude Mortality Risk Over 3 Years (Deaths/ Persons), as %[1]	Crude Mortality Rate (Deaths/100 Person-Years)[1]	
					Rate	95% CI
Total Widowed Sample	9,967	1,686	22,696.0	16.92	7.43	7.08, 7.79
Combined Comorbidity Score						
1: Very low with final increase	1,188	202	2,668.4	17.00	7.57	6.58, 8.67
2: Stable low	2,328	397	5,342.3	17.05	7.43	6.73, 8.19
3: Late onset (6 months)	792	140	1,783.7	17.68	7.85	6.63, 9.23
4: Stable medium	2,633	469	6,005.2	17.81	7.81	7.13, 8.54
5: Chronic high	1,944	313	4,458.3	16.10	7.02	6.28, 7.83
6: Steadily worsening	1,082	165	2,438.2	15.25	6.77	5.79, 7.86
Inpatient Hospital Days						
1: Start low, gradual increase	3,326	569	7,476.3	17.11	7.61	7.00, 8.26
2: Acceleration last 4 months	2,320	383	5,307.5	16.51	7.22	6.52, 7.97
3: Acceleration last 6 months	1,013	174	2,281.2	17.18	7.63	6.56, 8.83
4: Zero with very late increase	3,308	560	7,631.0	16.93	7.34	6.75, 7.97
Ambulatory Visits						
1: Stable zero/near-zero	3,372	636	7,587.9	18.86	8.38	7.75, 9.05
2: Stable low	3,006	502	6,864.1	16.70	7.31	6.69, 7.98
3: Stable medium	1,646	262	3,811.8	15.92	6.87	6.08, 7.74
4: Late increase	1,096	178	2,458.1	16.24	7.24	6.24, 8.37
5: Steady increase	449	65	1,038.8	14.48	6.26	4.87, 7.93
6: Chronic high	398	43	935.4	10.80	4.60	3.37, 6.14

[1] Due to considerable variability in the follow-up period due to censoring before the end of the study, the crude mortality rate is a better measure of mortality frequency than is the crude mortality risk.

Table 9
Crude Mortality Risks and Rates
by Widowed Subject's Own Morbidity Trajectory Pattern

Widowed Morbidity Trajectory Group	No. of Persons	Total Deaths	Total Person-Years of Follow-Up Observed	Crude Mortality Risk Over 3 Years (Deaths/ Persons), as %[1]	Crude Mortality Rate (Deaths/100 Person-Years)[1]	
					Rate	95% CI
Total Widowed Sample	9,967	1,686	22,696.0	16.92	7.43	7.08, 7.79
Combined Comorbidity Score						
1: Low and decreasing	794	117	1,884.3	14.74	6.21	5.16, 7.41
2: Zero	4,092	393	10,074.4	9.60	3.90	3.53, 4.30
3: Low but increasing	2,080	325	4,733.6	15.63	6.87	6.15, 7.64
4: Stable low-medium	2,107	498	4,448.4	23.64	11.20	10.24, 12.21
5: Chronic medium- high	894	353	1,555.4	39.49	22.70	20.42, 25.16
Inpatient Hospital Days						
1: Zero or near-zero	7,523	1,041	17,861.4	13.84	5.83	5.48, 6.19
2: Low and decreasing	1,247	300	2,621.2	24.06	11.45	10.20, 12.80
3: Low but increasing	1,197	345	2,213.4	28.82	15.59	14.01, 17.30
Ambulatory Visits						
1: Stable zero or near-zero	5,493	827	12,699.8	15.06	6.51	6.08, 6.97
2: Stable low	3,604	612	8,261.4	16.98	7.41	6.84, 8.01
3: Stable medium	870	247	1,734.9	28.39	14.24	12.54, 16.10

[1] Due to considerable variability in the follow-up period due to censoring before the end of the study, the crude mortality rate is a better measure of mortality frequency than is the crude mortality risk.

Table 10
Kaplan-Meier Survival Summary for Study Variables

Variable	Cumulative Survival $\hat{S}(t)$ and Failure $\hat{F}(t)$ Estimates at Selected Study Time Points						Log-Rank Test		
	365 Days		730 Days		1,095 Days				
	$\hat{S}(t)$	$\hat{F}(t)$	$\hat{S}(t)$	$\hat{F}(t)$	$\hat{S}(t)$	$\hat{F}(t)$	χ^2	df	p-value
Total Sample	92.8	7.2	86.1	13.9	80.1	19.9		–	
Age Group									
65-69	97.2	2.8	92.9	7.1	88.9	11.1	400.74	4	<0.0001
70-74	95.8	4.2	91.7	8.3	87.3	12.7			
75-79	95.2	4.8	90.5	9.5	85.7	14.3			
80-84	92.8	7.2	85.4	14.6	79.3	20.7			
85+	85.9	14.1	74.7	25.3	65.0	35.0			
Gender									
Female	94.9	5.1	89.8	10.2	84.8	15.2	301.78	1	<0.0001
Male	88.0	12.0	77.5	22.5	69.0	31.0			
Race									
White	92.8	7.2	86.1	14.0	80.0	20.0	2.09	2	0.3515
Black	94.3	5.7	89.2	10.8	84.6	15.4			
Other Race	90.6	9.4	84.0	16.0	80.3	19.7			
Spouse's place of death									
Hospital	92.9	7.1	86.4	13.6	80.0	20.0	20.22	3	0.0002
Nursing home	91.1	8.9	84.4	15.6	78.5	21.5			
At home	94.7	5.3	88.2	11.8	82.8	17.2			
Other/unknown	91.7	8.3	81.0	19.0	75.3	24.7			
Spouse's use of hospice									
No use	92.5	7.5	85.9	14.1	80.0	20.0	0.38	1	0.5355
Any use	93.6	6.4	86.7	13.3	80.3	19.7			
Deceased Spouse's Combined Comorbidity Trajectory									
1: Very low, late incr.	92.3	7.7	85.5	14.5	79.7	20.3	4.11	5	0.5337
2: Stable low	93.1	6.9	86.0	14.0	80.0	20.0			
3: Late onset	92.7	7.3	86.1	13.9	79.0	21.0			
4: Stable medium	92.4	7.6	85.4	14.6	79.2	20.8			
5: Chronic high	92.8	7.2	86.5	13.5	81.2	18.8			
6: Steadily worsening	94.0	6.0	88.0	12.0	81.5	18.5			

Table 10 (continued)
Kaplan-Meier Survival Summary for Study Variables

	Cumulative Survival $\widehat{S}$(t) and Failure $\widehat{F}$(t) Estimates at Selected Study Time Points								
	365 Days		730 Days		1,095 Days		Log-Rank Test		
Variable	$\widehat{S}$(t)	$\widehat{F}$(t)	$\widehat{S}$(t)	$\widehat{F}$(t)	$\widehat{S}$(t)	$\widehat{F}$(t)	χ^2	df	p-value
Deceased Spouse's Inpatient Days Trajectory									
1: Low gradual increase	92.6	7.4	85.6	14.4	79.7	20.3	0.85	3	0.8372
2: Sharp acceleration last 4 months	93.0	7.0	86.3	13.7	80.5	19.5			
3: Acceleration over last 6 months	92.8	7.2	85.7	14.3	79.5	20.5			
4: Zero, very late incr.	92.9	7.1	86.6	13.4	80.2	19.8			
Deceased Spouse's Ambulatory Visits Trajectory									
1: Stable zero or near zero	92.1	7.9	84.4	15.6	77.8	22.2	23.08	5	0.0003
2: Stable low	92.6	7.4	86.2	13.8	80.3	19.7			
3: Stable medium	93.0	7.0	87.1	12.9	81.5	18.5			
4: Late increase	93.2	6.8	86.9	13.1	80.5	19.5			
5: Steady increase	95.2	4.8	88.7	11.3	82.6	17.4			
6: Chronic high	96.2	3.8	90.9	9.1	87.0	13.0			
Widowed Subject's Combined Comorbidity Trajectory									
1: Low and decreasing	95.7	4.3	89.6	10.4	82.5	17.5	745.84	4	<0.0001
2: Zero	97.0	3.0	93.2	6.9	88.7	11.3			
3: Low but increasing	92.8	7.2	86.8	13.2	81.5	18.5			
4: Stable low-medium	89.7	10.3	79.5	20.5	71.5	28.5			
5: Chronic med.- high	77.8	22.2	62.9	37.1	52.1	47.9			
Widowed Subject's Inpatient Days Trajectory									
1: Zero or near-zero	95.2	4.8	89.4	10.6	83.7	16.3	315.67	2	<0.0001
2: Low and decreasing	88.1	11.9	78.9	21.1	71.3	28.7			
3: Low but increasing	82.2	17.8	71.9	28.1	65.0	35.0			
Widowed Subject's Ambulatory Visits Trajectory									
1: Stable zero/near-zero	93.9	6.1	87.9	12.1	82.2	17.8	122.25	2	<0.0001
2: Stable low	93.1	6.9	86.1	13.9	80.0	19.9			
3: Stable medium	84.5	15.5	74.4	25.6	66.6	33.4			

Table 11
Sequence of Backward Elimination of E x V Interactions for Predeceased Combined Comorbidity Cox Model Series

Initial Full Model:

Exposure (E Variable): DCC6GRP *(Spouse's Combined Comorbidity Trajectory Group)*

Control Variables (V Variables):

WCC5GRP *(Widowed Subject's Own Combined Comorbidity Trajectory Group)*
DAGE *(Age Group)*
SEX *(Gender)*
RACE *(Race)*
PLACE *(Place of Predeceased Spouse's Death)*
SANYHOSPICE *(Predeceased Spouse's Use of Hospice)*

E x V Interactions: DCC6GRP*WCC5GRP, DCC6GRP*DAGE, DCC6GRP*SEX, DCC6GRP*RACE, DCC6GRP*PLACE, DCC6GRP*SANYHOSPICE

⇩

Backward Elimination of ExV Interactions:

Step 1: Remove DCC6GRP*RACE (Wald χ^2=2.68, 10 df, p=0.9880)

Step 2: Remove DCC6GRP*SEX (Wald χ^2=1.74, 5 df, p=0.8833)

Step 3: Remove DCC6GRP*PLACE (Wald χ^2=12.63, 15 df, p=0.6307)

Step 4: Remove DCC6GRP*WCC5GRP (Wald χ^2=18.21, 20 df, p=0.5738)

Step 5: Remove DCC6GRP*DAGE (Wald χ^2=21.16, 20 df, p=0.3879)

⇩

Reduced Full Model Variable Set (Gold Standard):

E: DCC6GRP
V: WCC5GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE,
E x V: DCC6GRP*SANYHOSPICE (Wald χ^2=14.98, 5 df, p=0.0104)

Table 12
Confounding Assessment for Predeceased
Combined Comorbidity Cox Model Series

Reduced Full Model (Gold Standard):
E: DCC6GRP
V: WCC5GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE,
E x V: DCC6GRP*SANYHOSPICE

Deceased Combined Comorbidity Trajectory Group by Hospice Use	Hazard Ratio	95% CI	± 10% Boundaries
No Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	–
Group 1: Very low, late increase	1.170	0.953, 1.435	1.053, 1.287
Group 2: Stable low	0.962	0.803, 1.153	0.866, 1.058
Group 3: Late onset	1.094	0.856, 1.397	0.985, 1.203
Group 4: Stable medium	1.106	0.929, 1.315	0.995, 1.217
Group 6: Steadily worsening	1.060	0.838, 1.339	0.954, 1.166
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	–
Group 1: Very low, late increase	1.287	0.844, 1.961	1.158, 1.416
Group 2: Stable low	1.487	1.136, 1.947	1.338, 1.636
Group 3: Late onset	1.626	1.149, 2.301	1.463, 1.789
Group 4: Stable medium	1.057	0.814, 1.373	0.951, 1.163
Group 6: Steadily worsening	0.961	0.698, 1.323	0.865, 1.057

Step 1: Drop Place of Death (*PLACE*, Wald χ^2=5.00, 3 df, p=0.1718)

Deceased Combined Comorbidity Trajectory Group by Hospice Use	New Hazard Ratio	95% CI	Is PLACE a Confounder?
No Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	No - none of the HR point estimates change by more than 10% from their corresponding gold standard HR point estimates. Therefore PLACE is not a confounder and is removed from the model.
Group 1: Very low, late increase	1.174	0.958, 1.439	
Group 2: Stable low	0.962	0.803, 1.152	
Group 3: Late onset	1.100	0.861, 1.405	
Group 4: Stable medium	1.105	0.929, 1.314	
Group 6: Steadily worsening	1.061	0.840, 1.341	
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.282	0.841, 1.954	
Group 2: Stable low	1.478	1.130, 1.934	
Group 3: Late onset	1.620	1.145, 2.292	
Group 4: Stable medium	1.056	0.813, 1.371	
Group 6: Steadily worsening	0.958	0.696, 1.319	

Table 12 (continued)
Confounding Assessment for Predeceased
Combined Comorbidity Cox Model Series

Step 3: Drop Race (*RACE*, Wald χ^2=3.74, 2 df, p=0.1540)

Deceased Combined Comorbidity Trajectory Group by Hospice Use	New Hazard Ratio	95% CI	Is RACE a Confounder?
No Hospice Use			No - none of the HRs change by more than 10% from their corresponding gold standard HRs. Therefore RACE is not a confounder and is removed from the model.
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.179	0.962, 1.446	
Group 2: Stable low	0.970	0.811, 1.162	
Group 3: Late onset	1.099	0.860, 1.404	
Group 4: Stable medium	1.112	0.935, 1.322	
Group 6: Steadily worsening	1.062	0.840, 1.342	
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.285	0.843, 1.959	
Group 2: Stable low	1.473	1.126, 1.928	
Group 3: Late onset	1.622	1.147, 2.295	
Group 4: Stable medium	1.060	0.816, 1.376	
Group 6: Steadily worsening	0.953	0.692, 1.311	

Step 4: Drop Gender (*SEX* , Wald χ^2=134.35, 1 df, p<0.0001)

Deceased Combined Comorbidity Trajectory Group by Hospice Use	New Hazard Ratio	95% CI	Is SEX a Confounder?
No Hospice Use			No - none of the HRs change by more than 10% from the gold standard. However, given the significant association between sex and the outcome variable (p<0.0001), sex will be kept in the model.
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.278	1.043, 1.566	
Group 2: Stable low	1.025	0.856, 1.227	
Group 3: Late onset	1.166	0.913, 1.490	
Group 4: Stable medium	1.123	0.945, 1.336	
Group 6: Steadily worsening	1.085	0.858, 1.371	
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.306	0.857, 1.991	
Group 2: Stable low	1.435	1.097, 1.878	
Group 3: Late onset	1.614	1.141, 2.283	
Group 4: Stable medium	1.043	0.803, 1.354	
Group 6: Steadily worsening	0.951	0.691, 1.309	

(SEX added back into model)

Table 12 (continued)
Confounding Assessment for Predeceased
Combined Comorbidity Cox Model Series

Step 5: Drop Age Group (*DAGE*, Wald χ^2=206.44, 4 df, p<0.0001)			
Deceased Combined Comorbidity Trajectory Group by Hospice Use	**New Hazard Ratio**	**95% CI**	**Is DAGE a Confounder?**
No Hospice Use			No - none of the HRs change by more than 10% from the gold standard. However, given the significant association between DAGE and the outcome variable (p<0.0001), it will be kept in the model.
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.171	0.955, 1.435	
Group 2: Stable low	1.017	0.850, 1.217	
Group 3: Late onset	1.124	0.880, 1.436	
Group 4: Stable medium	1.187	0.999, 1.411	
Group 6: Steadily worsening	1.084	0.858, 1.370	
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	1.392	0.913, 2.121	
Group 2: Stable low	1.548	1.183, 2.025	
Group 3: Late onset	1.547	1.094, 2.188	
Group 4: Stable medium	1.117	0.861, 1.450	
Group 6: Steadily worsening	0.976	0.709, 1.344	

(DAGE added back into model)

Step 6: Drop Widowed Combined Comorbidity (*WCC5GRP*) (Wald χ^2=484.76, 4 df, p<0.0001)			
Deceased Combined Comorbidity Trajectory Group by Hospice Use	**New Hazard Ratio**	**95% CI**	**Is WCC5GRP a Confounder?**
No Hospice Use			Yes, multiple cells have HRs that have changed more than 10% from their corresponding gold standard HR. Therefore WCC5GRP is a confounder and must be kept in the model.
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	0.985	0.805, 1.207	
Group 2: Stable low	0.852	0.712, 1.019	
Group 3: Late onset	0.942	0.738, 1.202	
Group 4: Stable medium	1.027	0.864, 1.221	
Group 6: Steadily worsening	0.957	0.758, 1.209	
Any Hospice Use			
Group 5: Chronic high (Reference)	1.000	–	
Group 1: Very low, late increase	0.987	0.648, 1.503	
Group 2: Stable low	1.283	0.981, 1.678	
Group 3: Late onset	1.411	0.998, 1.995	
Group 4: Stable medium	1.002	0.771, 1.300	
Group 6: Steadily worsening	0.917	0.666, 1.262	

(WCC5GRP added back into model)

Parsimonious Model includes: DCC6GRP, WCC5GRP, SANYHOSPICE, DAGE, SEX, and DCC6GRP*SANYHOSPICE

Table 13
Schoenfeld Residual Correlations with Ranked Failure Time
For Parsimonious Combined Comorbidity Cox Model Predictors

Residual No.	Residual Variable	Pearson Correlation with Ranked Failure Time	p-value
1	DCC6GRP - 1	0.007	0.7602
2	DCC6GRP - 2	0.004	0.8801
3	DCC6GRP - 3	0.010	0.6758
4	DCC6GRP - 4	-0.004	0.8812
5	DCC6GRP - 6	0.025	0.3035
6	SANYHOSPICE - 1	0.047	0.0550
7	WCC5GRP - 1	0.057	0.0197
8	WCC5GRP - 3	-0.036	0.1426
9	WCC5GRP - 4	-0.013	0.5852
10	WCC5GRP - 5	-0.078	0.0014
11	DAGE 70-74	-0.009	0.7231
12	DAGE 75-79	0.021	0.3878
13	DAGE 80-84	0.003	0.9155
14	DAGE 85+	-0.025	0.3024
15	SEX M	-0.033	0.1764
16	DCC6GRP - 1*SANYHOSPICE - 1	0.041	0.0895
17	DCC6GRP - 2*SANYHOSPICE - 1	0.043	0.0784
18	DCC6GRP - 3*SANYHOSPICE - 1	0.001	0.9629
19	DCC6GRP - 4*SANYHOSPICE - 1	0.040	0.1008
20	DCC6GRP - 6*SANYHOSPICE - 1	-0.018	0.4623

Table 14
Final Extended Cox Proportional Hazards Model Results Predicting Survival from Predeceased Spouse's Combined Comorbidity Trajectory Group

Adds a Time-Dependent Covariate for Widow's Combined Comorbidity Trajectory

A. Variables Not Involved in E x V Interaction

Variable	HR	95% CI	Wald p-Value	Effect Modifier/ Confounder
Gender			<0.0001	–
Female (ref)	1.000	–		
Male	1.788	1.620, 1.973		
Age Group			<0.0001	–
65-69 (ref)	1.000	–		
70-74	1.059	0.774, 1.449		
75-79	1.128	0.838, 1.519		
80-84	1.526	1.139, 2.045		
85+	2.548	1.903, 3.411		
Widowed Subject's Combined Comorbidity Trajectory:			<0.0001	*confounder*
< 1.5 Years Since Bereavement:				
2: Zero (ref)	1.000	–		
1: Low and decreasing	1.382	1.016, 1.880		
3: Very low but increasing	1.935	1.579, 2.370		
4: Stable low-medium	2.707	2.246, 3.262		
5: Chronic medium to high	6.002	4.942, 7.289		
< 1.5 Years Since Bereavement:				
2: Zero (ref)	1.000	–		
1: Low and decreasing	1.626	1.230, 2.149		
3: Very low but increasing	1.344	1.082, 1.669		
4: Stable low-medium	2.195	1.812, 2.660		
5: Chronic medium to high	3.642	2.892, 4.586		

B. Variables Involved in E x V Interaction

Hospice Use	Deceased Combined Comorbidity Trajectory Group by Hospice Use	HR	95% CI
No Hospice	5: Chronic high (Ref)	1.000	–
	1: Very low, late increase	1.177	0.961, 1.443
	2: Stable low	0.969	0.810, 1.160
	3: Late onset	1.097	0.859, 1.401
	4: Stable medium	1.110	0.933, 1.320
	6: Steadily worsening	1.059	0.838, 1.338
Any Hospice	5: Chronic high (Ref)	1.000	–
	1: Very low, late increase	1.286	0.844, 1.960
	2: Stable low	1.471	1.124, 1.924
	3: Late onset	1.624	1.148, 2.297
	4: Stable medium	1.063	0.818, 1.379
	6: Steadily worsening	0.956	0.694, 1.316

Table 14 (continued)
Final Cox Proportional Hazards Model Results Predicting Survival from Predeceased Spouse's Combined Comorbidity Trajectory Group

C. Hazard Ratios and 95% CIs for Predeceased Combined Comorbidity and Hospice Use, Using No Hospice and Chronic High Comorbidity as Reference Group

Predeceased Spouse's Combined Comorbidity Trajectory Group	Hospice Use: Any Hospice	Hospice Use: No Hospice
Group 1: Very low with late increase	1.079 (0.721-1.614)	1.177 (0.961-1.443)
Group 2: Stable low	1.234 (0.972-1.565)	0.969 (0.810-1.160)
Group 3: Late onset	1.362 (0.986-1.883)	1.097 (0.859-1.401)
Group 4: Stable medium	0.891 (0.709-1.121)	1.110 (0.933-1.320)
Group 6: Steadily worsening	0.802 (0.597-1.076)	1.059 (0.838-1.338)
Group 5: Chronic high	0.839 (0.665-1.058)	1.000 (reference)

Table 15
Sequence of Backward Elimination of E x V Interactions for Predeceased Inpatient Days Cox Model Series

Initial Full Model:

Exposure (E Variable): DID4GRP *(Spouse's Inpatient Days Trajectory Group)*

Control Variables (V Variables):

WID3GRP *(Widowed Subject's Own Inpatient Days Trajectory Group)*
DAGE *(Age Group)*
SEX *(Gender)*
RACE *(Race)*
PLACE *(Place of Predeceased Spouse's Death)*
SANYHOSPICE *(Predeceased Spouse's Use of Hospice)*

E x V Interactions: DID4GRP*WID3GRP, DID4GRP*DAGE, DID4GRP*SEX, DID4GRP*RACE, DID4GRP*PLACE, DID4GRP*SANYHOSPICE

⇩

Backward Elimination of ExV Interactions:

Step 1: Remove DID4GRP*SEX (Wald χ^2=1.22, 3 df, p=0.7471)

Step 2: Remove DID4GRP*PLACE (Wald χ^2=7.51, 9 df, p=0.5842)

Step 3: Remove DID4GRP*WID3GRP (Wald χ^2=7.64, 6 df, p=0.2658)

Step 4: Remove DID4GRP*DAGE (Wald χ^2=16.26, 12 df, p=0.1797)

Step 5: Remove DID4GRP*SANYHOSPICE (Wald χ^2=5.40,3 df, p=0.1450)

Step 6: Remove DID4GRP*RACE (Wald χ^2=10.15,6 df, p=0.1184)

No E x V interactions remain

⇩

Reduced Full Model Variable Set (Gold Standard):

E: DID4GRP
V: WID3GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE

Table 16
Confounding Assessment for Predeceased
Inpatient Days Cox Model Series

Reduced Full Model (Gold Standard):			
E: DID4GRP			
V: WID3GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE			
Deceased Inpatient Days Trajectory Group	**Hazard Ratio**	**95% CI**	**± 10% Boundaries**
Group 1: Low gradual increase (Ref)	1.000	–	–
Group 2: Sharp acceleration last 4 months	0.930	0.817, 1.059	0.837, 1.023
Group 3: Acceleration over last 6 months	0.956	0.806, 1.133	0.860, 1.052
Group 4: Zero with very late increase	0.974	0.866, 1.096	0.877, 1.071

Step 1: Drop Any Hospice (SANYHOSPICE, Wald χ^2=0.1139, 1 df, p=0.7357)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is SANYHOSPICE a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – none of the HRs changed by more than 10%. SANYHOSPICE can be removed.
Group 2: Sharp acceleration last 4 months	0.931	0.817, 1.060	
Group 3: Acceleration over last 6 months	0.956	0.806, 1.134	
Group 4: Zero with very late increase	0.976	0.868, 1.098	

Step 2: Drop Place of Death (PLACE, Wald χ^2=4.39, 3 df, p=0.2228)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is PLACE a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – none of the HRs changed by > 10% from gold standard. PLACE can be removed.
Group 2: Sharp acceleration last 4 months	0.937	0.823, 1.066	
Group 3: Acceleration over last 6 months	0.967	0.815, 1.146	
Group 4: Zero with very late increase	0.980	0.872, 1.102	

Step 3: Drop Race (RACE, Wald χ^2=3.15, 2 df, p=0.2066)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is RACE a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – none of the HRs changed by > 10% from gold standard. RACE can be removed.
Group 2: Sharp acceleration last 4 months	0.935	0.821, 1.064	
Group 3: Acceleration over last 6 months	0.964	0.813, 1.143	
Group 4: Zero with very late increase	0.983	0.875, 1.105	

Table 16 (continued)
Confounding Assessment for Predeceased
Inpatient Days Cox Model Series

Step 4: Drop Widow's Inpatient Days Group (WID3GRP, Wald χ^2=235.04, 2 df, p=<0.0001)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is WID3GRP a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – no HRs changed by >10% from gold standard. However, WID3GRP will be kept in the model as a significant survival predictor (p<0.0001).
Group 2: Sharp acceleration last 4 months	0.935	0.822, 1.065	
Group 3: Acceleration over last 6 months	0.991	0.837, 1.175	
Group 4: Zero with very late increase	0.970	0.863, 1.090	

(WID3GRP added back into model)

Step 5: Drop Age Group (DAGE, Wald χ^2=278.80, 4 df, p=<0.0001)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is DAGE a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – no HRs changed by >10% from the gold standard. However, given the significant association with survival (p<0.0001), DAGE will be kept in the model.
Group 2: Sharp acceleration last 4 months	0.936	0.822, 1.065	
Group 3: Acceleration over last 6 months	0.937	0.790, 1.110	
Group 4: Zero with very late increase	0.987	0.878, 1.109	

(DAGE added back into model)

Step 6: Drop Gender (SEX, Wald χ^2=178.82, 1 df, p=<0.0001)			
Deceased Inpatient Days Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is SEX a Confounder?**
Group 1: Low gradual increase (Ref)	1.000	–	No – no HRs changed by >10% from the gold standard. However, given the significant association with survival (p<0.0001), SEX will be kept in the model.
Group 2: Sharp acceleration last 4 months	0.952	0.836, 1.083	
Group 3: Acceleration over last 6 months	1.013	0.855, 1.201	
Group 4: Zero with very late increase	0.974	0.867, 1.095	

(SEX added back into model)

Parsimonious Model includes: DID4GRP, WID3GRP, DAGE, SEX

Table 17
Schoenfeld Residual Correlations with Ranked Failure Time
For Parsimonious Inpatient Days Cox Model Predictors

Residual Variable No.	Residual Variable	Pearson Correlation with Ranked Failure Time	p-value
1	DID4GRP - 2	0.007	0.7772
2	DID4GRP - 3	0.013	0.6053
3	DID4GRP - 4	0.011	0.6540
4	WID3GRP - 2	-0.031	0.2055
5	WID3GRP - 3	-0.168	<0.0001
6	DAGE 70-74	-0.008	0.7470
7	DAGE 75-79	0.020	0.4196
8	DAGE 80-84	0.003	0.9100
9	DAGE 85+	-0.026	0.2950
10	SEX M	-0.035	0.1493

Table 18
Results of Final Extended Cox Model Predicting Survival
From Predeceased Spouse's Inpatient Days Trajectory Group

Includes a Time-Dependent Covariate for Widow's Own Inpatient Days Trajectory

Variable	HR	95% CI	Overall Wald P-Value	Effect Modifier/ Confounder Status
Exposure:				
Deceased Spouse's Inpatient Days Trajectory:			0.7734	–
1: Low gradual increase (Ref)	1.000	–		
2: Sharp acceleration last 4 mo.	0.934	0.821, 1.064		
3: Acceleration over last 6 months	0.965	0.814, 1.144		
4: Zero with very late increase	0.983	0.875, 1.105		
Covariates:				
Widowed Subject's Inpatient Days Trajectory:			<0.0001	–
< 1.5 Years Since Bereavement:				
1: Zero or near-zero (Ref)	1.000	–		
2: Low and decreasing	2.121	1.793, 2.509		
3: Low but increasing	3.157	2.711, 3.677		
≥ 1.5 Years Since Bereavement:				
1: Zero or near-zero (Ref)	1.000	–		
2: Low and decreasing	1.523	1.244, 1.863		
3: Low but increasing	1.565	1.263, 1.940		
Gender				
Female (Ref)	1.000	–	<0.0001	–
Male	1.944	1.764, 2.144		
Age Group			<0.0001	–
65-69 (Ref)	1.000	–		
70-74	1.093	0.799, 1.494		
75-79	1.191	0.884, 1.603		
80-84	1.663	1.242, 2.226		
85+	2.871	2.148, 3.839		

Table 19
Sequence of Backward Elimination of E x V Interactions for Predeceased Ambulatory Visits Cox Model Series

Initial Full Model:

Exposure (E Variable): DAV6GRP *(Spouse's Ambulatory Visits Trajectory Group)*

Control Variables (V Variables):

WAV3GRP *(Widowed Subject's Own Ambulatory Visits Trajectory Group)*
DAGE *(Age Group)*
SEX *(Gender)*
RACE *(Race)*
PLACE *(Place of Predeceased Spouse's Death)*
SANYHOSPICE *(Predeceased Spouse's Use of Hospice)*

E x V Interactions: DAV6GRP*WAV3GRP, DAV6GRP*DAGE, DAV6GRP*SEX, DAV6GRP*RACE, DAV6GRP*PLACE, DAV6GRP*SANYHOSPICE

⇩

Backward Elimination of ExV Interactions:

Step 1: Remove DAV6GRP*RACE (Wald χ^2=4.28, 10 df, p=0.9337)

Step 2: Remove DAV6GRP*PLACE (Wald χ^2=9.29, 15 df, p=0.8617)

Step 3: Remove DAV6GRP*SANYHOSPICE (Wald χ^2=0.76, 5 df, p=0.9798)

Step 4: Remove DAV6GRP*SEX (Wald χ^2=2.01, 5 df, p=0.8472)

Step 5: Remove DAV6GRP*WAV3GRP (Wald χ^2=6.34,10 df, p=0.7863)

Step 6: Remove DAV6GRP*DAGE (Wald χ^2=16.16,20 df, p=0.7094)

No E x V interactions remain

⇩

Reduced Full Model Variable Set (Gold Standard):

E: DAV6GRP
V: WAV3GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE

Table 20
Confounding Assessment for Predeceased
Ambulatory Visits Cox Model Series

Reduced Full Model (Gold Standard):			
E: DAV6GRP			
V: WAV3GRP, DAGE, SEX, RACE, PLACE, SANYHOSPICE			
Deceased Ambulatory Visit Trajectory Group	**Hazard Ratio**	**95% CI**	**± 10% Boundaries**
Group 3: Stable medium (Ref)	1.000	–	–
Group 1: Stable zero or near-zero	1.318	1.137, 1.529	1.186, 1.450
Group 2: Stable low	1.084	0.933, 1.259	0.976, 1.192
Group 4: Late increase	1.071	0.884, 1.297	0.964, 1.178
Group 5: Steady increase	0.957	0.729, 1.256	0.861, 1.053
Group 6: Chronic high	0.667	0.483, 0.921	0.600, 0.734

Step 1: Drop Hospice Use (SANYHOSPICE, Wald χ^2=0.3382, 1 df, p=0.5609)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is SANYHOSPICE a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	No – none of the HRs changed by more than 10%. SANYHOSPICE can be removed from the model.
Group 1: Stable zero or near-zero	1.311	1.132, 1.519	
Group 2: Stable low	1.082	0.931, 1.256	
Group 4: Late increase	1.075	0.888, 1.301	
Group 5: Steady increase	0.957	0.729, 1.256	
Group 6: Chronic high	0.668	0.483, 0.923	

Step 2: Drop Place (PLACE, Wald χ^2=3.72, 3 df, p=0.2935)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is PLACE a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	No – none of the HRs changed by more than 10%. Therefore PLACE can be removed from the model.
Group 1: Stable zero or near-zero	1.323	1.143, 1.531	
Group 2: Stable low	1.087	0.936, 1.262	
Group 4: Late increase	1.070	0.884, 1.295	
Group 5: Steady increase	0.959	0.731, 1.259	
Group 6: Chronic high	0.663	0.480, 0.916	

Table 20 (continued)
Confounding Assessment for Predeceased
Ambulatory Visits Cox Model Series

Step 3: Drop Race (RACE, Wald χ^2=2.54, 2 df, p=0.2810)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is RACE a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	No – none of the HRs changed by more than 10%. Therefore RACE can be removed.
Group 1: Stable zero or near-zero	1.320	1.140, 1.528	
Group 2: Stable low	1.085	0.934, 1.260	
Group 4: Late increase	1.069	0.883, 1.294	
Group 5: Steady increase	0.957	0.729, 1.256	
Group 6: Chronic high	0.665	0.482, 0.919	

Step 4: Drop Widowed Subject's Own Ambulatory Visit Trajectory Group (WAV3GRP, Wald χ^2=139.7, 2 df, p<.0001)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is WAV3GRP a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	Yes -- HR for stable zero was reduced by 10.2%. In addition, WAV3GRP is a significant survival predictor so should remain.
Group 1: Stable zero or near-zero	1.184	1.025, 1.367	
Group 2: Stable low	1.048	0.902, 1.216	
Group 4: Late increase	1.017	0.840, 1.230	
Group 5: Steady increase	0.928	0.707, 1.218	
Group 6: Chronic high	0.708	0.513, 0.978	

(WAV3GRP added back into model)

Step 5: Drop Age Group (DAGE, Wald χ^2= 270.30, 4 df, p<.0001)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is DAGE a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	No – the largest HR change is -8.7% (for chronic high), but no HR change exceeds 10%. However, DAGE should remain in model due to significance.
Group 1: Stable zero or near-zero	1.400	1.210, 1.619	
Group 2: Stable low	1.121	0.965, 1.302	
Group 4: Late increase	1.141	0.942, 1.380	
Group 5: Steady increase	0.948	0.723, 1.244	
Group 6: Chronic high	0.609	0.441, 0.841	

(DAGE added back into model)

Table 20 (continued)
Confounding Assessment for Predeceased
Ambulatory Visits Cox Model Series

Step 5: Drop Gender (SEX, Wald χ^2= 196.98, 4 df, p<.0001)			
Deceased Ambulatory Visit Trajectory Group	**New Hazard Ratio**	**95% CI**	**Is SEX a Confounder?**
Group 3: Stable medium (Ref)	1.000	–	No – very little change in HRs and none approach 10%. However, given significant association with survival, SEX should remain in the model.
Group 1: Stable zero or near-zero	1.320	1.140, 1.528	
Group 2: Stable low	1.085	0.934, 1.260	
Group 4: Late increase	1.069	0.883, 1.294	
Group 5: Steady increase	0.957	0.729, 1.256	
Group 6: Chronic high	0.665	0.482, 0.919	

(SEX added back into model)

Parsimonious Model: (Same as Model Obtained from Step 3)

E: DAV6GRP
V: WAV3GRP, DAGE, SEX

Deceased Ambulatory Visit Trajectory Group	**Final Hazard Ratio**	**95% CI**
Group 3: Stable medium (Ref)	1.000	–
Group 1: Stable zero or near-zero	1.320	1.140, 1.528
Group 2: Stable low	1.085	0.934, 1.260
Group 4: Late increase	1.069	0.883, 1.294
Group 5: Steady increase	0.957	0.729, 1.256
Group 6: Chronic high	0.665	0.482, 0.919

Table 21
Schoenfeld Residual Correlations with Ranked Failure Time
For Parsimonious Ambulatory Visit Cox Model Predictors

Residual Variable No.	Residual Variable	Pearson Correlation with Ranked Failure Time	p-value
1	DAV6GRP - 1	0.004	0.8786
2	DAV6GRP - 2	0.005	0.8231
3	DAV6GRP - 4	-0.002	0.9298
4	DAV6GRP - 5	0.026	0.2839
5	DAV6GRP - 6	0.011	0.6532
6	WAV3GRP - 2	0.011	0.6580
7	WAV3GRP - 3	-0.084	0.0005
8	DAGE 70-74	-0.006	0.7995
9	DAGE 75-79	0.021	0.3817
10	DAGE 80-84	0.004	0.8675
11	DAGE 85+	-0.029	0.2276
12	SEX M	-0.036	0.1425

Table 22
Results of Final Extended Cox Model Predicting Survival
From Predeceased Spouse's Ambulatory Visits Trajectory Group

Includes a Time-Dependent Covariate for Widow's Own Ambulatory Visit Trajectory

Variable	HR	95% CI	Overall Wald P-Value	Effect Modifier/ Confounder Status
Exposure:				
Deceased Spouse's Ambulatory Visit Trajectory:			<0.0001	–
Group 3: Stable medium (Ref)	1.000	–		
Group 1: Stable zero or near-zero	1.319	1.139, 1.526		
Group 2: Stable low	1.087	0.936, 1.263		
Group 4: Late increase	1.071	0.885, 1.296		
Group 5: Steady increase	0.959	0.731, 1.258		
Group 6: Chronic high	0.667	0.483, 0.921		
Covariates:				
Widowed Subject's Ambulatory Visit Trajectory:			<0.0001	*confounder*
< *1.5 Years Since Bereavement:*				
1: Stable zero or near-zero (Ref)	1.000	–		
2: Stable low	1.299	1.126, 1.499		
3: Stable medium	2.876	2.407, 3.437		
≥ *1.5 Years Since Bereavement::*				
1: Stable zero or near-zero (Ref)	1.000	–		
2: Stable low	1.250	1.070, 1.461		
3: Stable medium	1.739	1.358, 2.228		
Gender				
Female (Ref)	1.000	–	<0.0001	–
Male	2.011	1.824, 2.218		
Age Group				
65-69 (Ref)	1.000	–	<0.0001	–
70-74	1.054	0.771, 1.442		
75-79	1.178	0.875, 1.585		
80-84	1.666	1.244, 2.232		
85+	2.940	2.198, 3.932		

FIGURES 2 - 18

Figure 2
Group Trajectory Patterns of Predeceased Spouses' Combined Comorbidity Scores

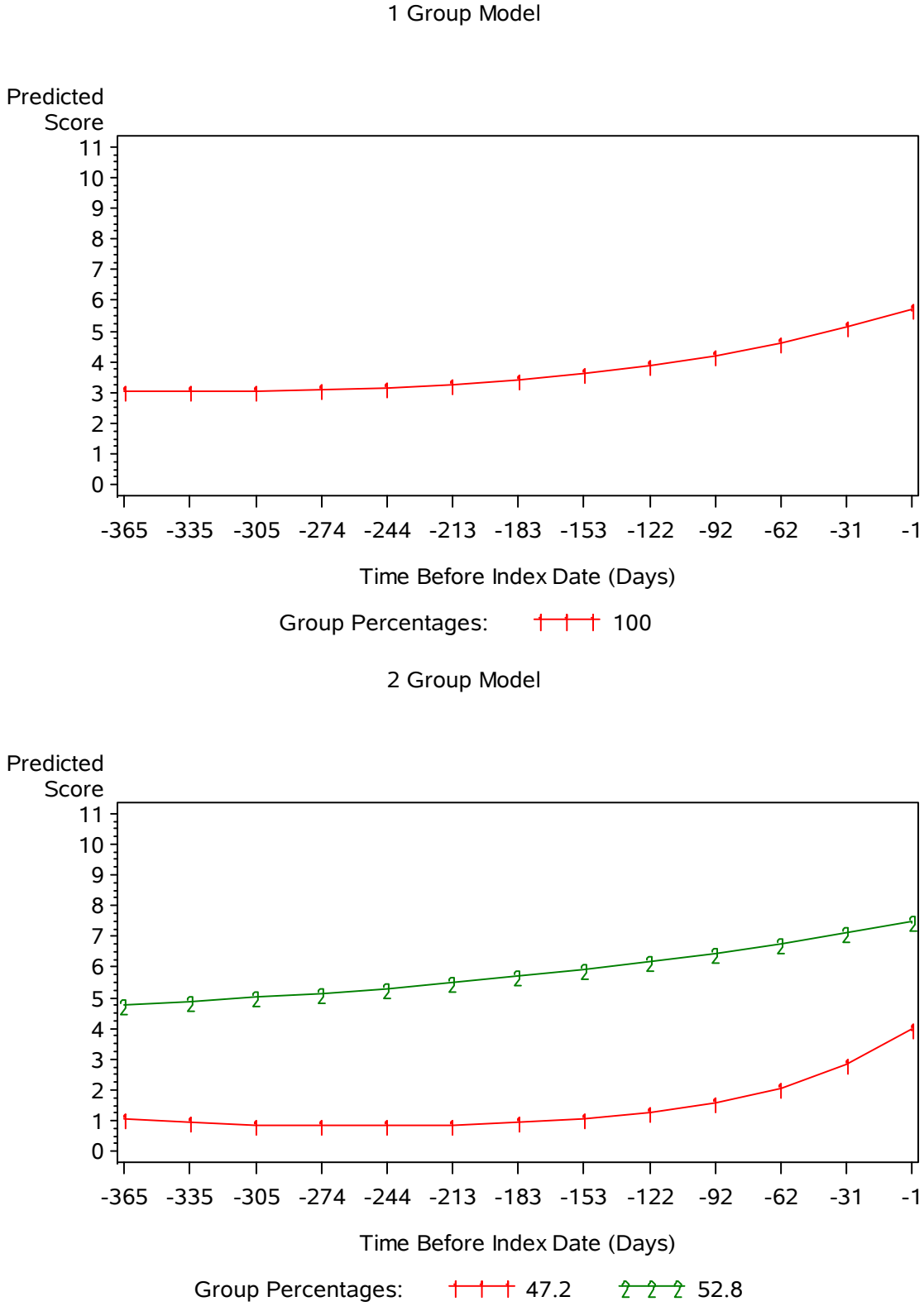


Figure 2 (continued)
Group Trajectory Patterns of Predeceased Spouses' Combined Comorbidity Scores

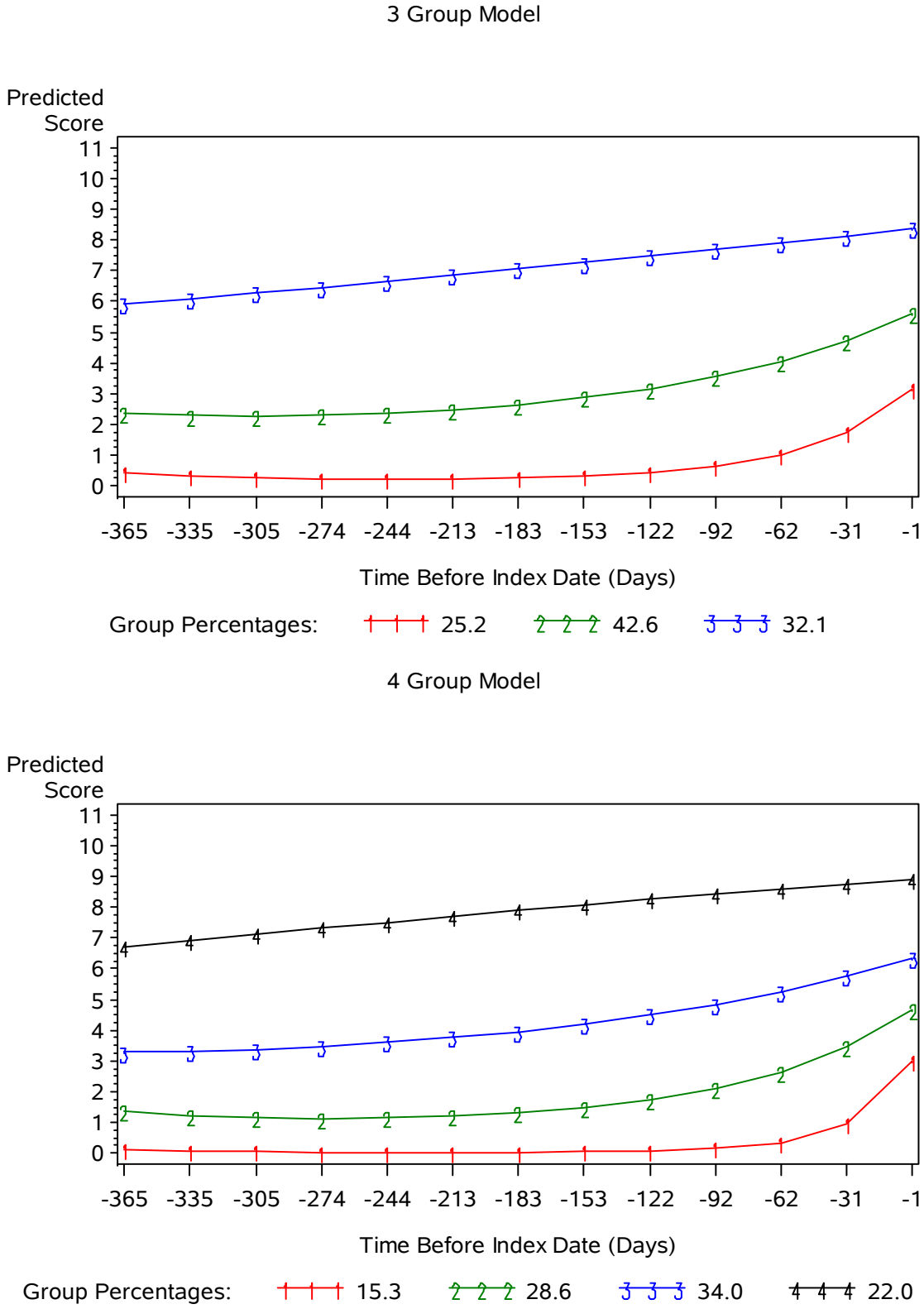
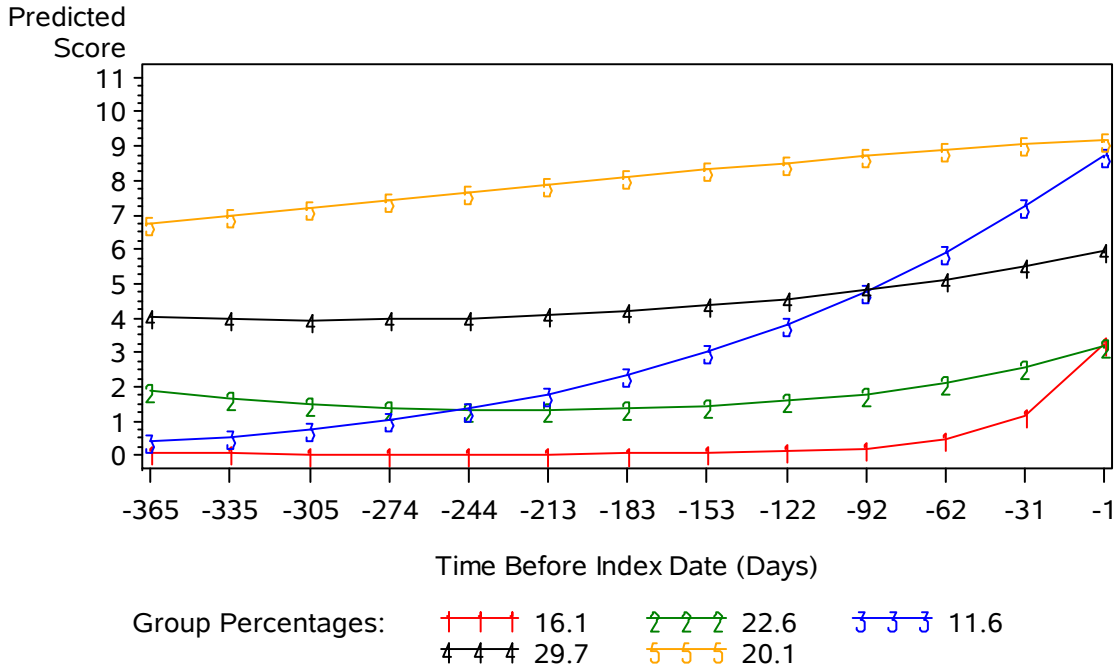


Figure 2 (continued)
Group Trajectory Patterns of Predeceased Spouses' Combined Comorbidity Scores

5 Group Model



6 Group Model

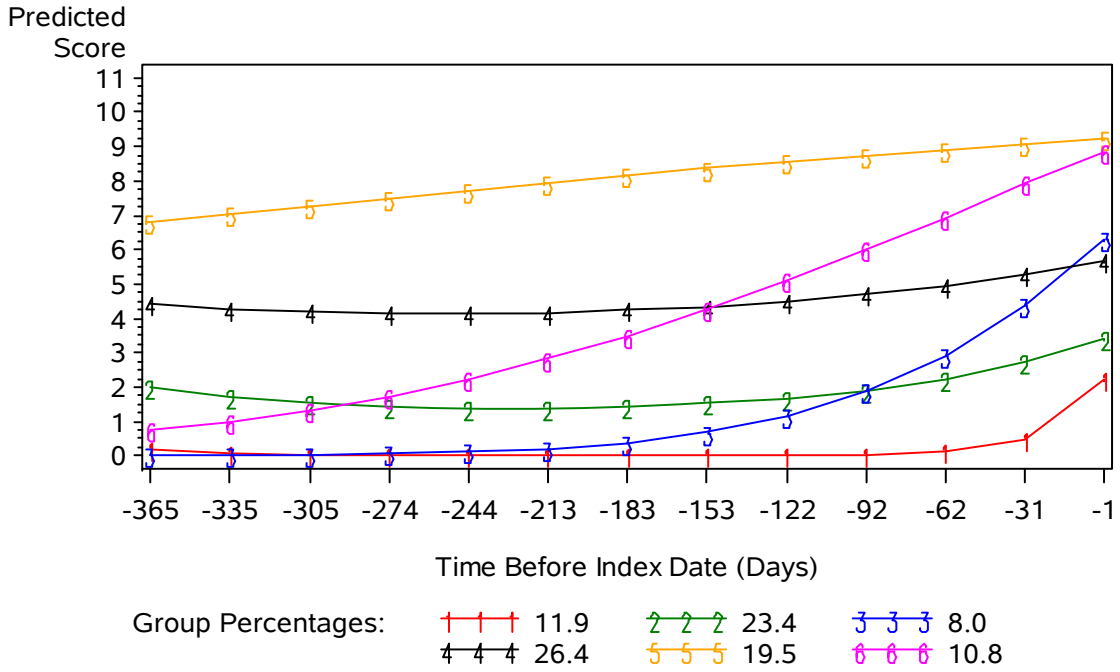


Figure 2 (continued)
Group Trajectory Patterns of Predeceased Spouses' Combined Comorbidity Scores

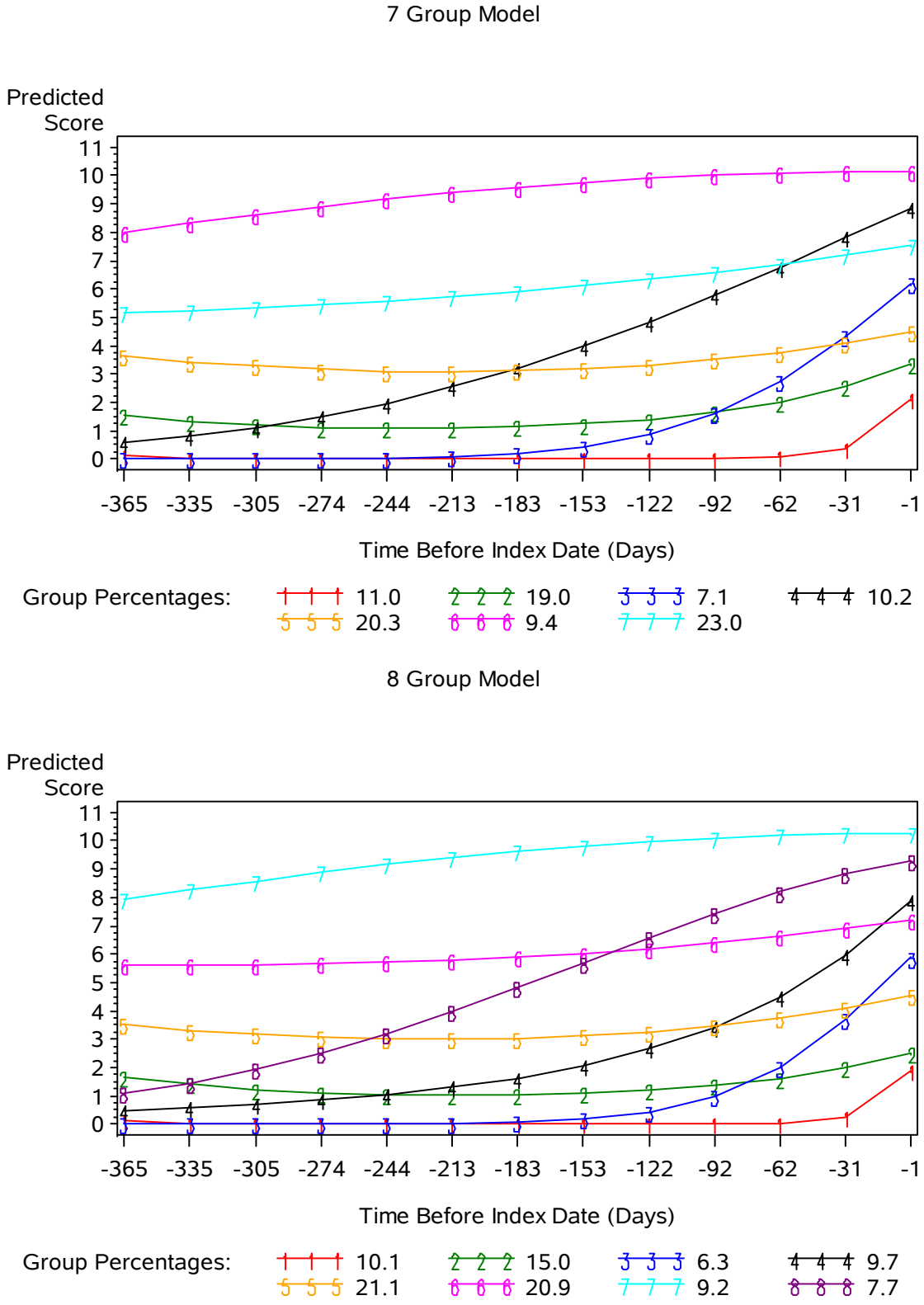


Figure 3
Group Trajectory Patterns of Widowed Spouses' Combined Comorbidity Scores

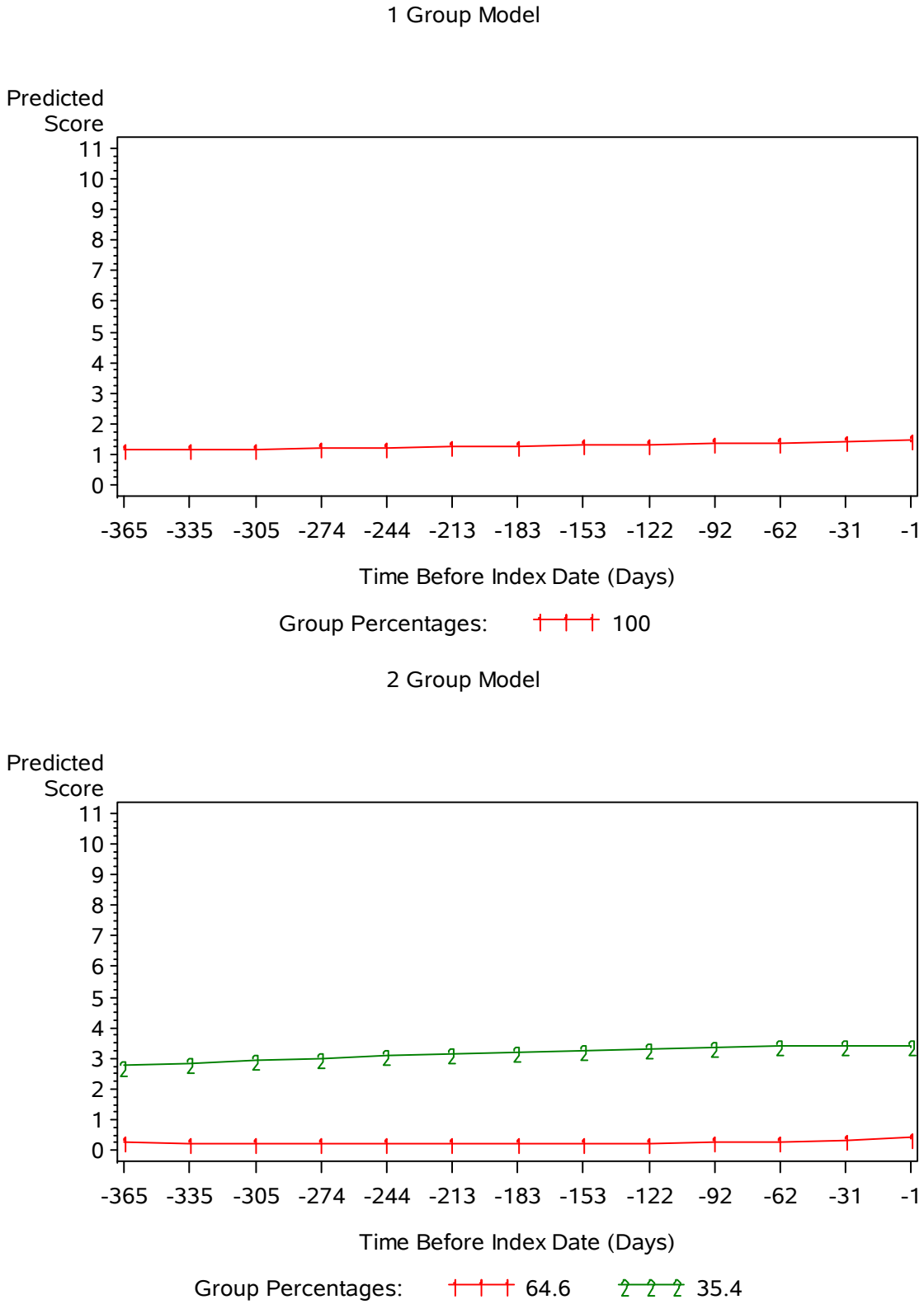


Figure 3 (continued)
Group Trajectory Patterns of Widowed Spouses' Combined Comorbidity Scores

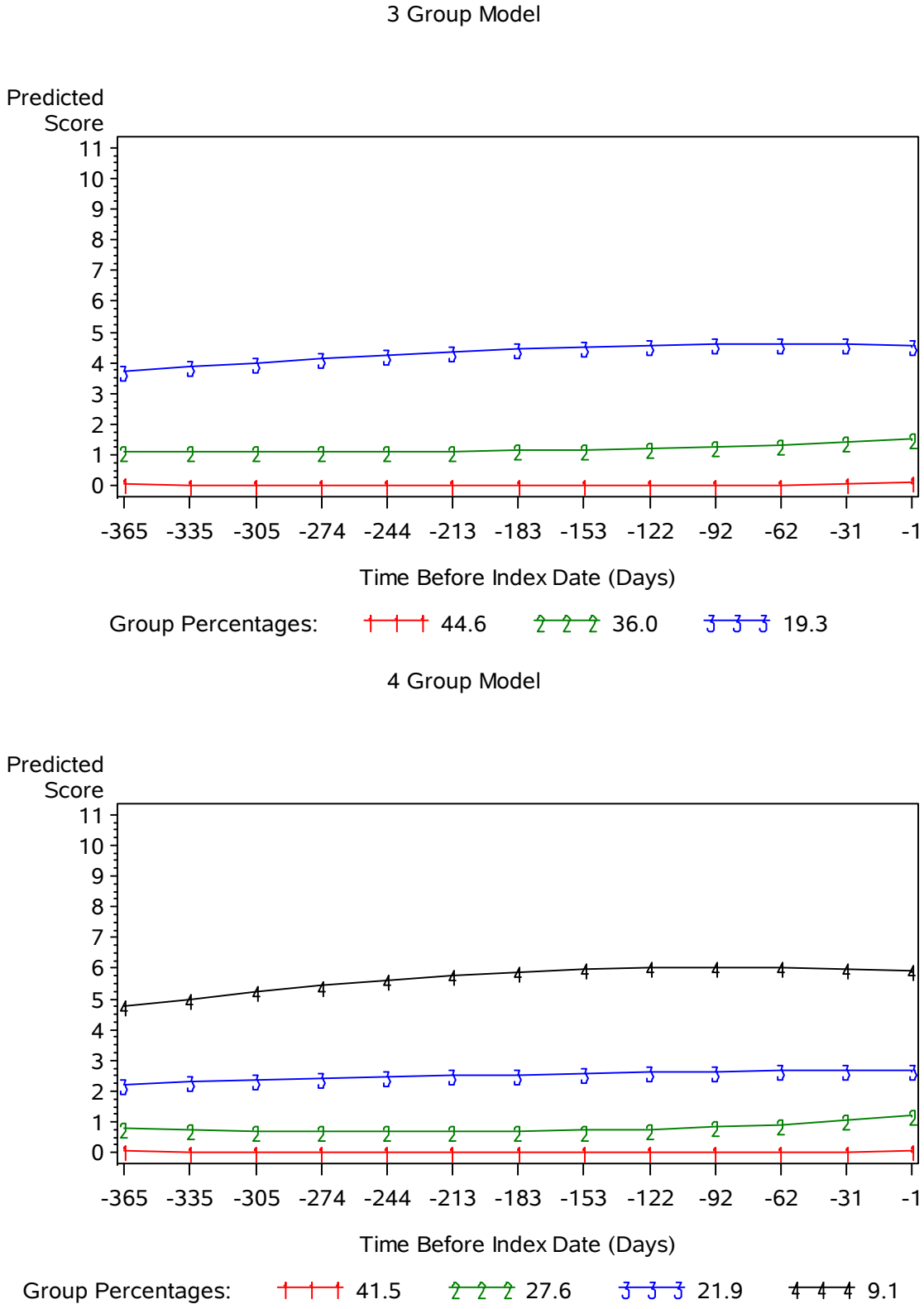


Figure 3 (continued)
Group Trajectory Patterns of Widowed Spouses' Combined Comorbidity Scores

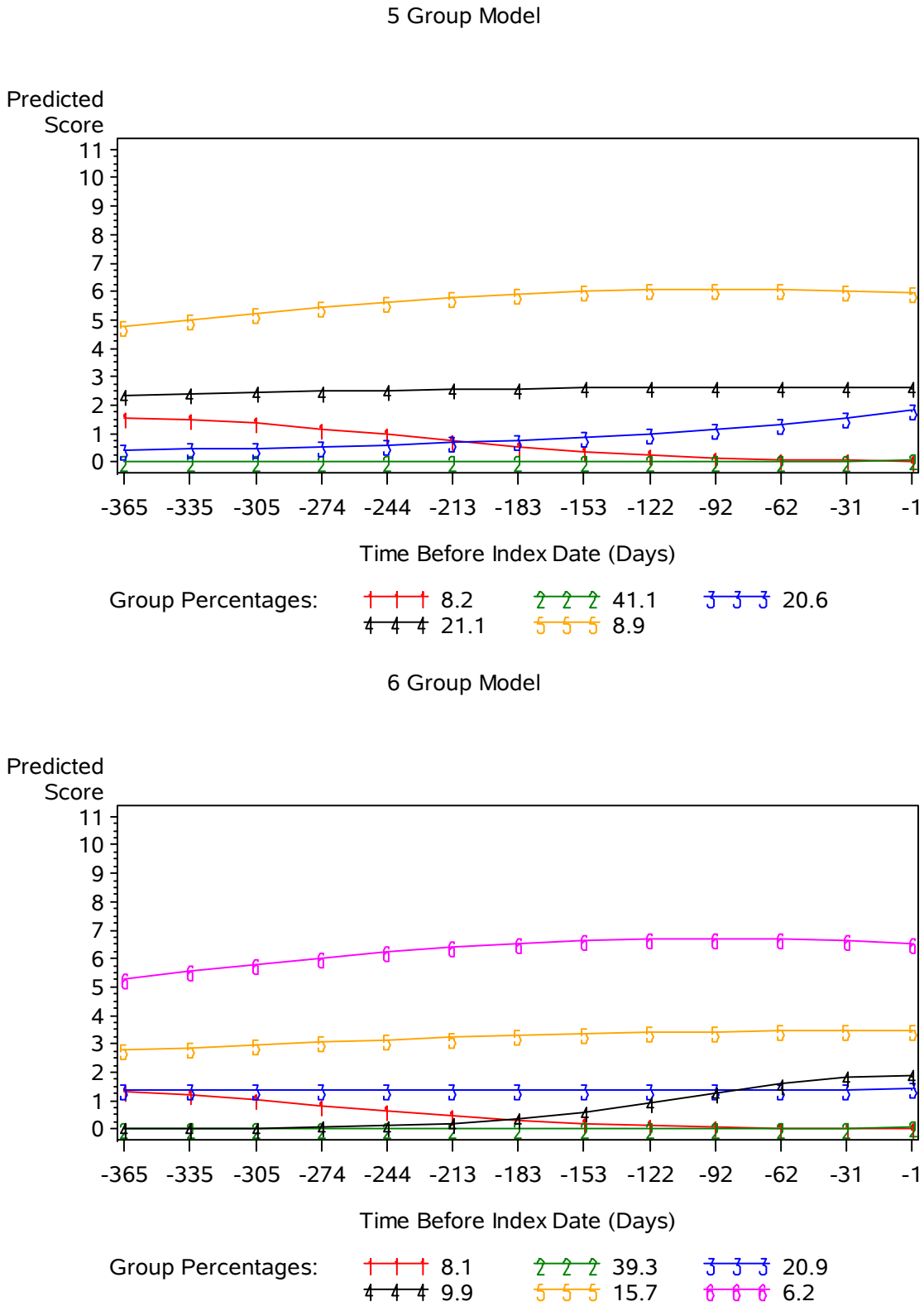


Figure 3 (continued)
Group Trajectory Patterns of Widowed Spouses' Combined Comorbidity Scores

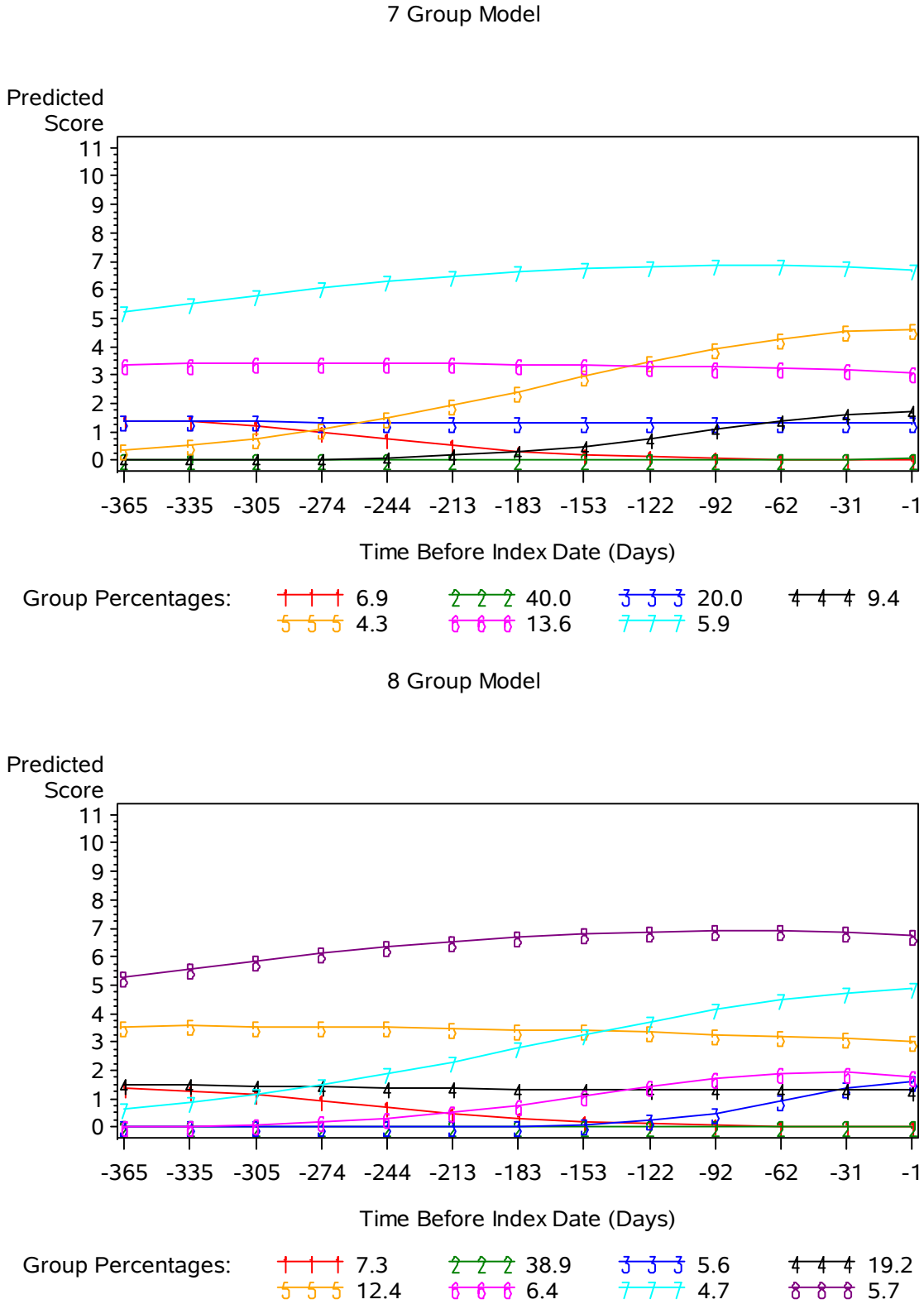


Figure 4
Group Trajectory Patterns of Predeceased Spouses' Monthly Inpatient Days

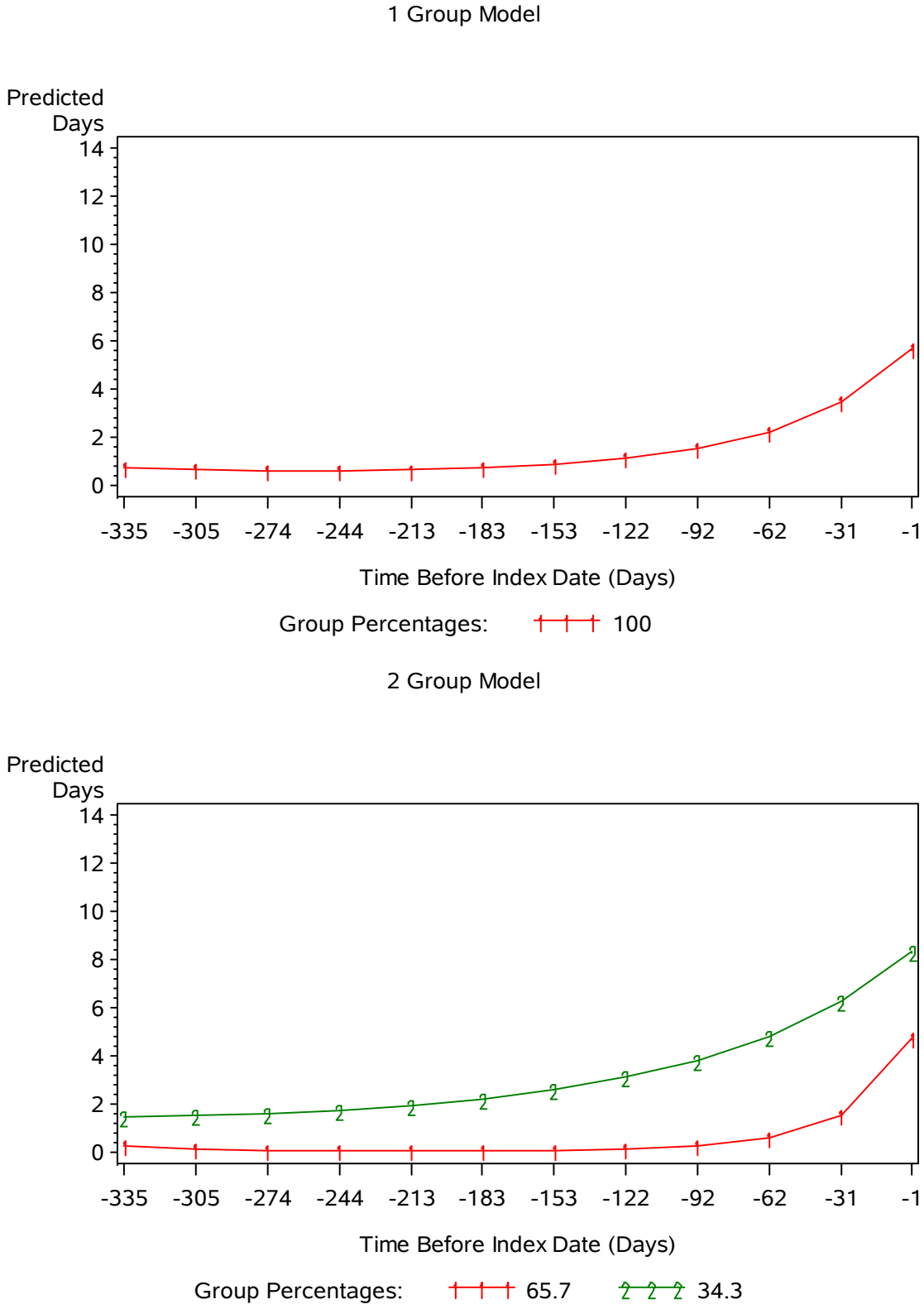


Figure 4 (continued)
Group Trajectory Patterns of Predeceased Spouses' Monthly Inpatient Days

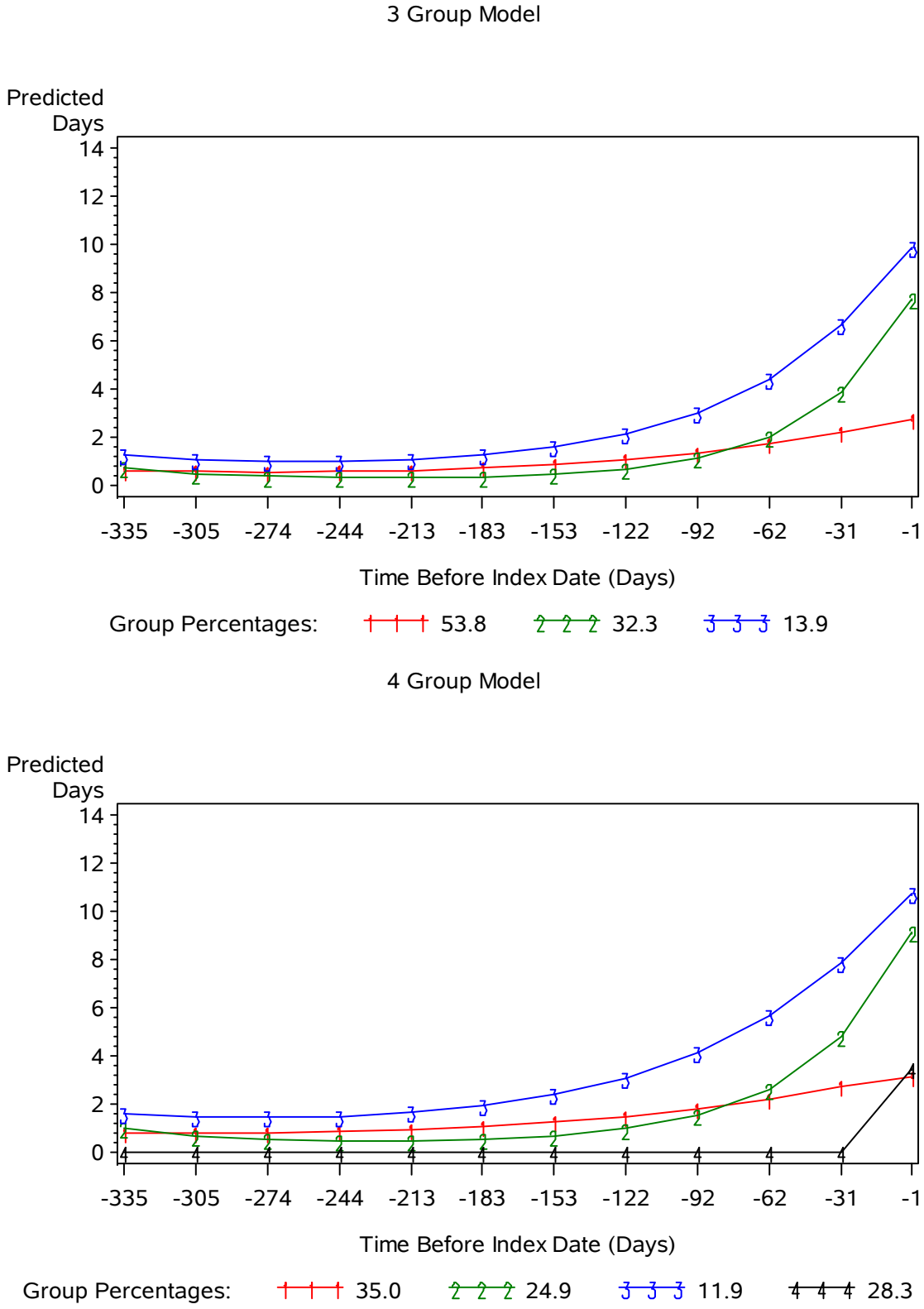
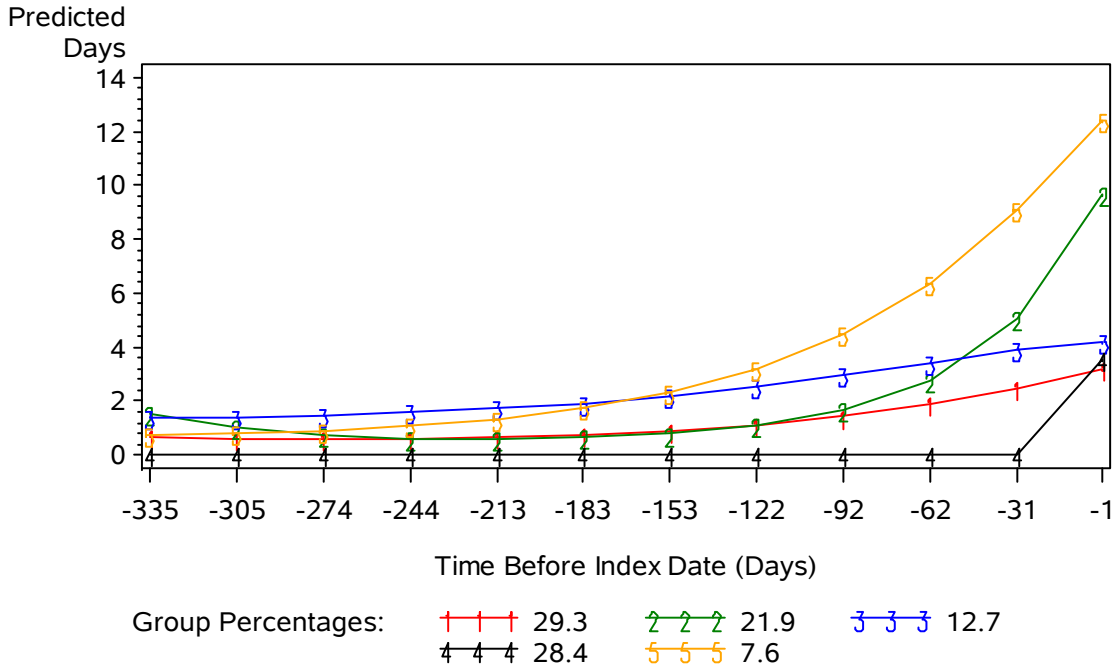


Figure 4 (continued)
Group Trajectory Patterns of Predeceased Spouses' Monthly Inpatient Days

5 Group Model



6 Group Model

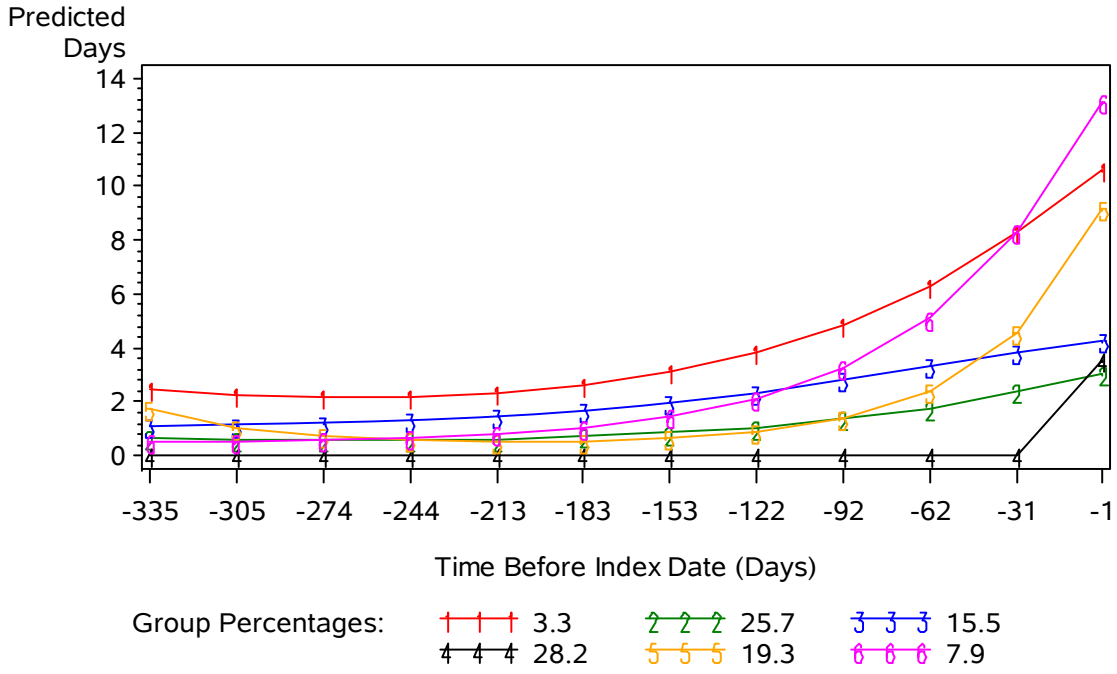


Figure 5
Group Trajectory Patterns of Widowed Spouses' Monthly Inpatient Days

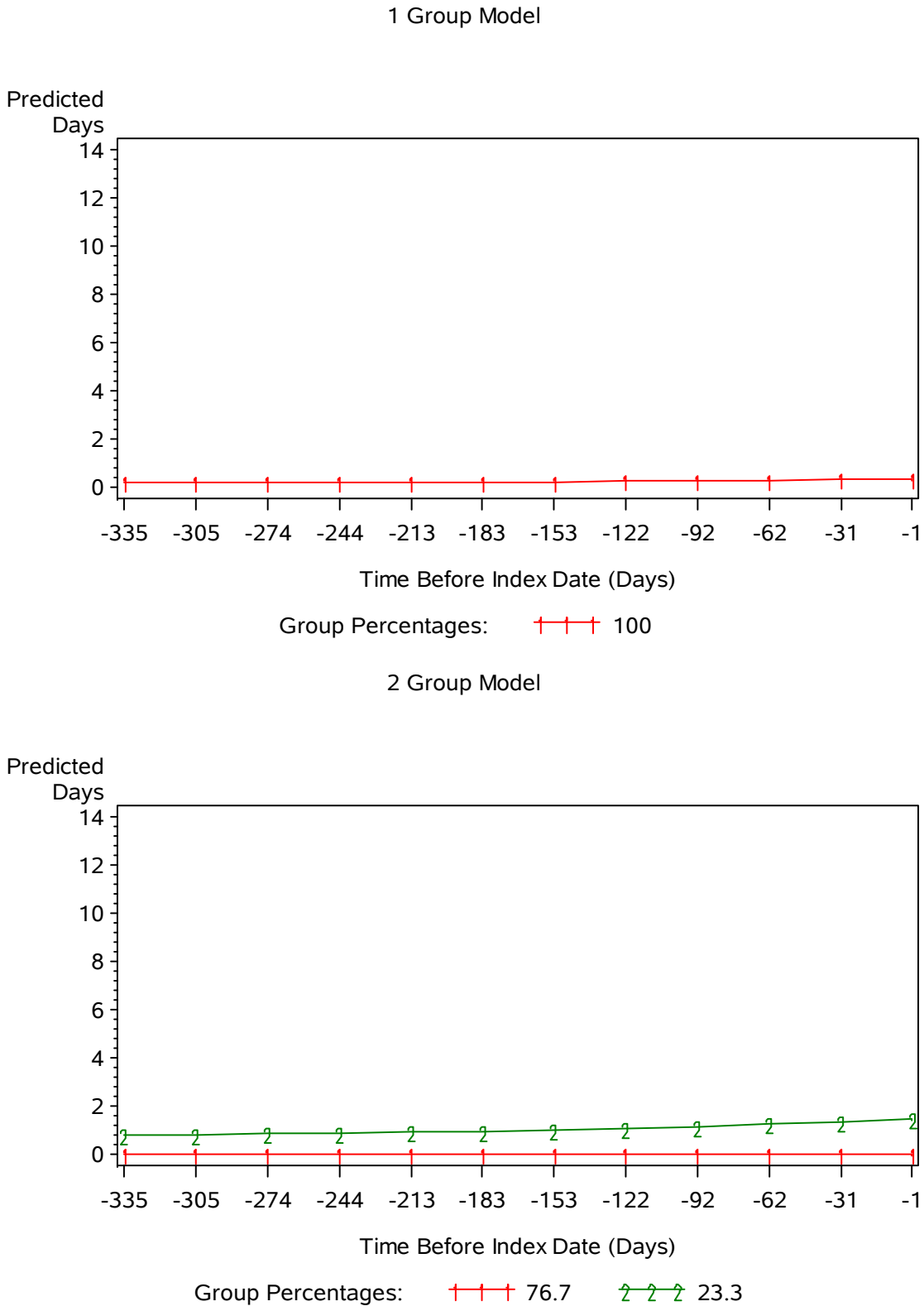
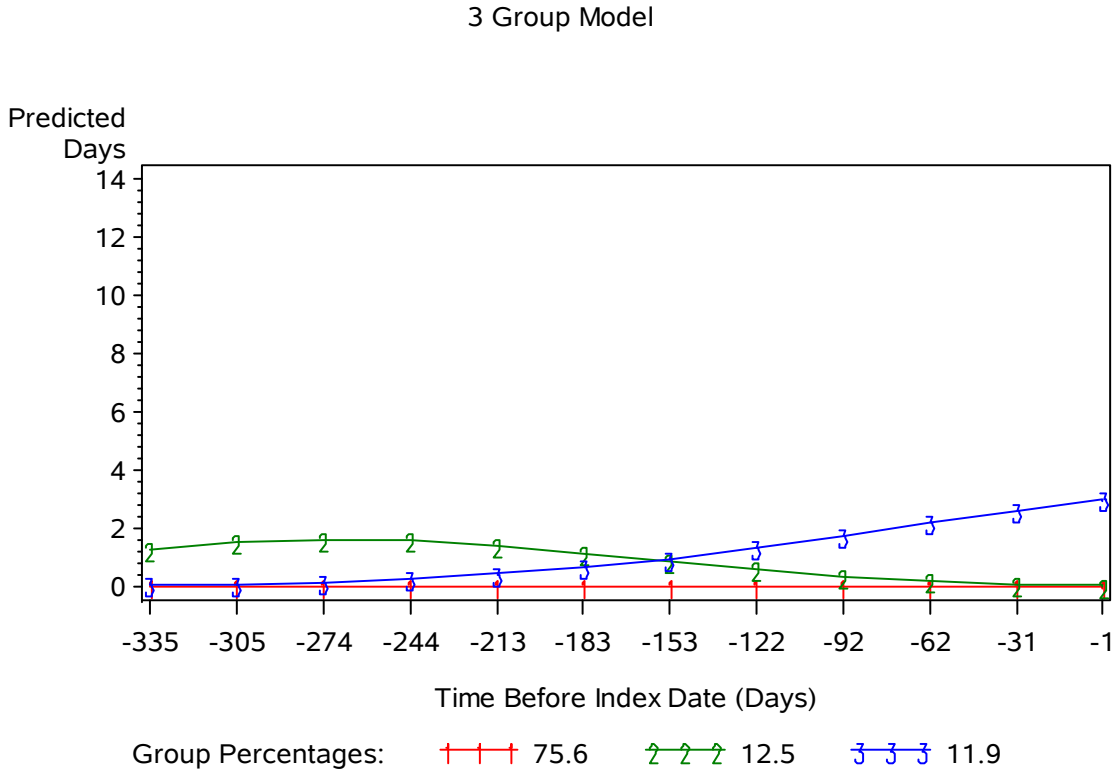
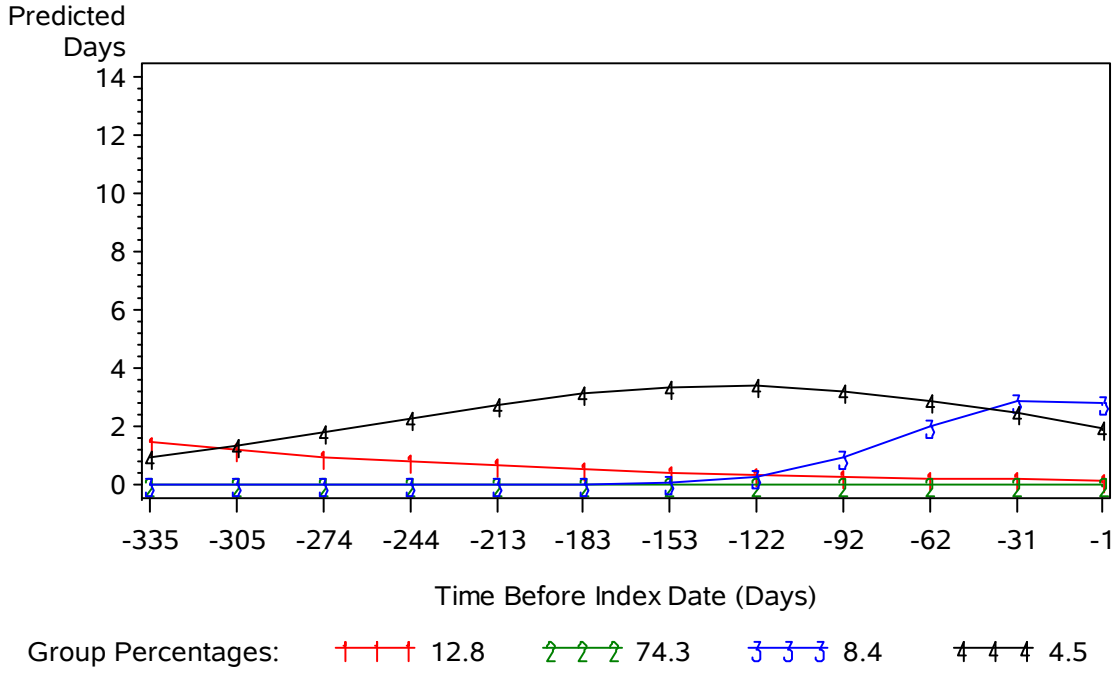


Figure 5 (continued)
Group Trajectory Patterns of Widowed Spouses' Monthly Inpatient Days





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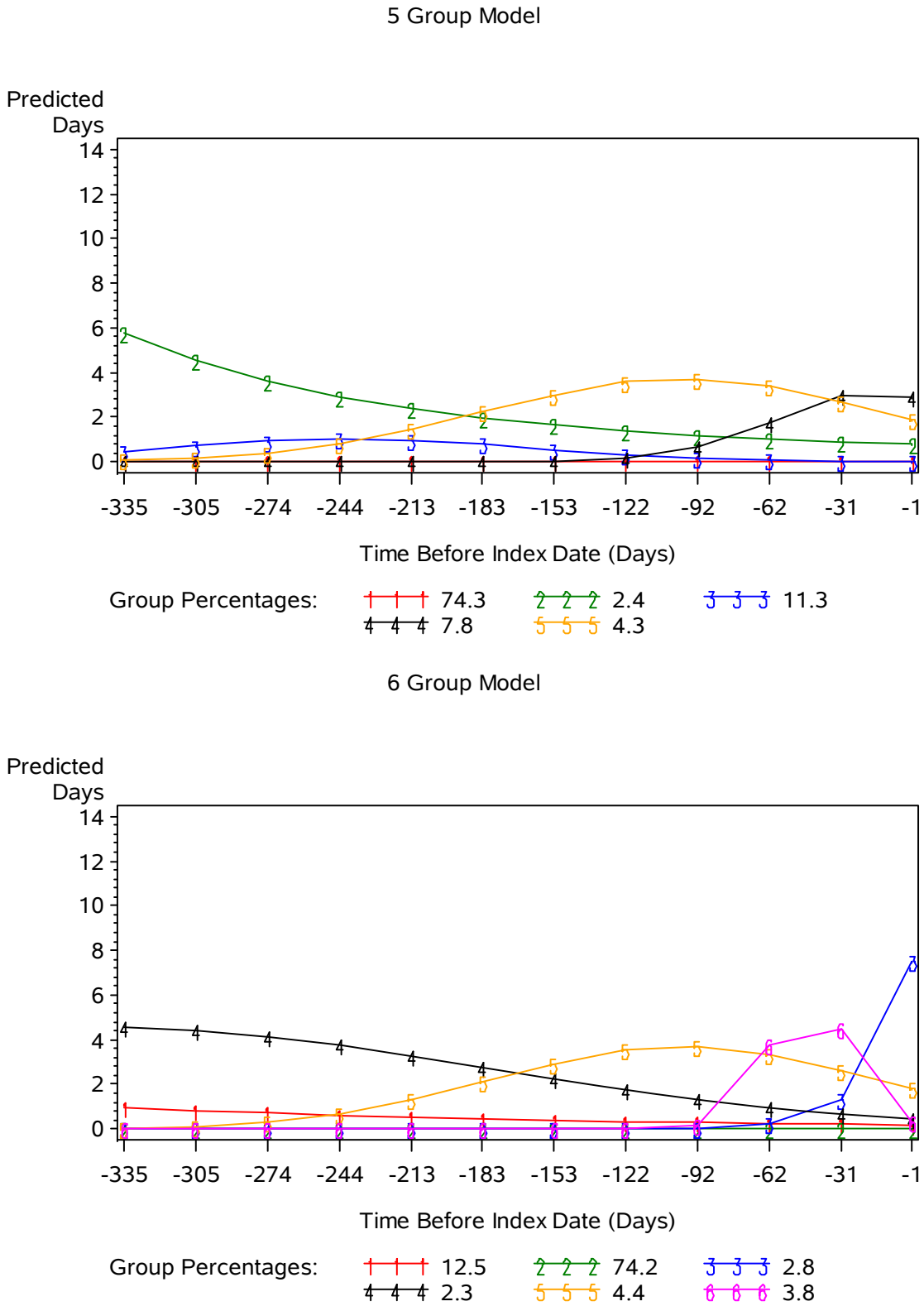
Group Trajectory Patterns of Widowed Spouses' Monthly Inpatient Days



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Group Trajectory Patterns of Widowed Spouses' Monthly Inpatient Days

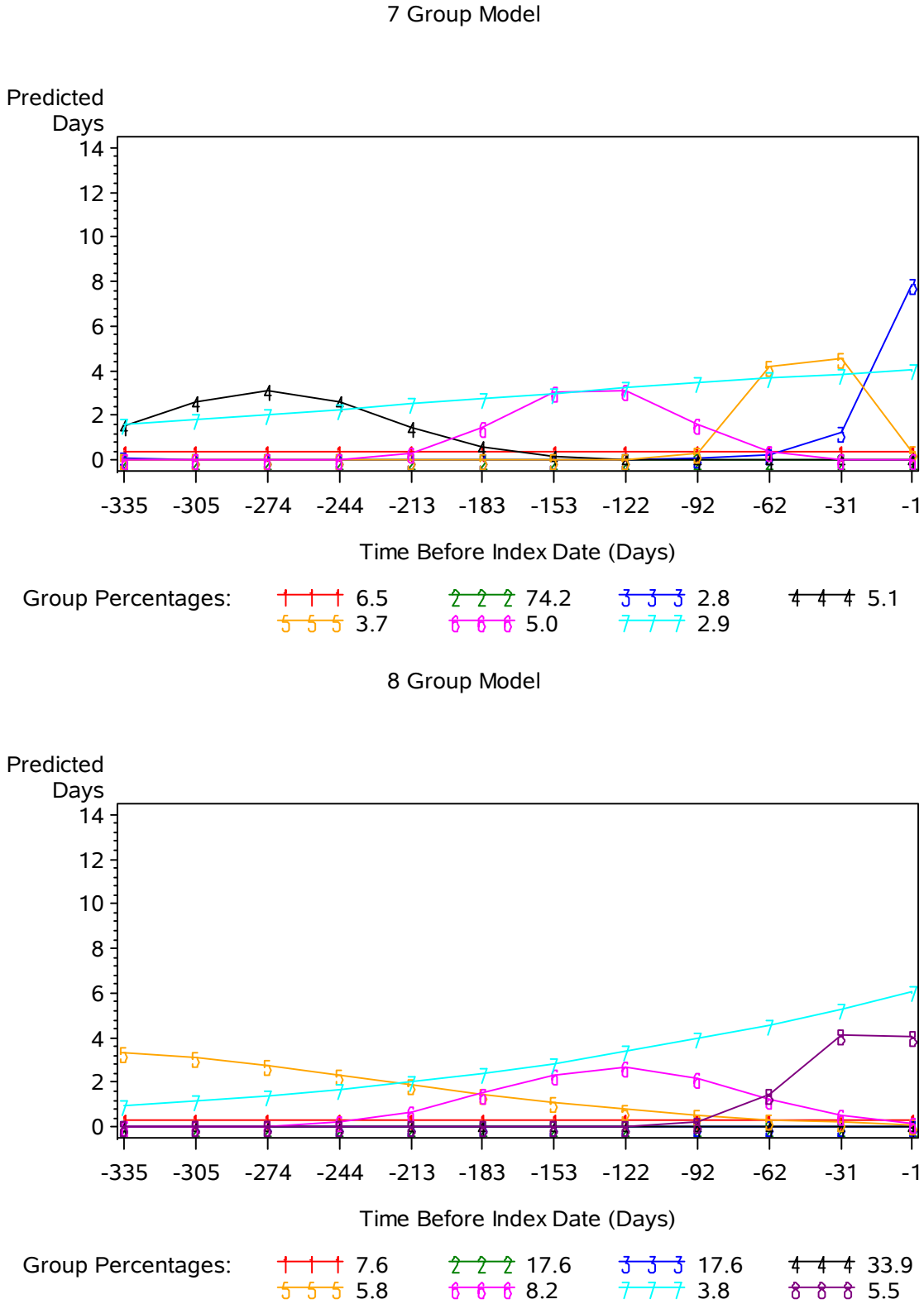
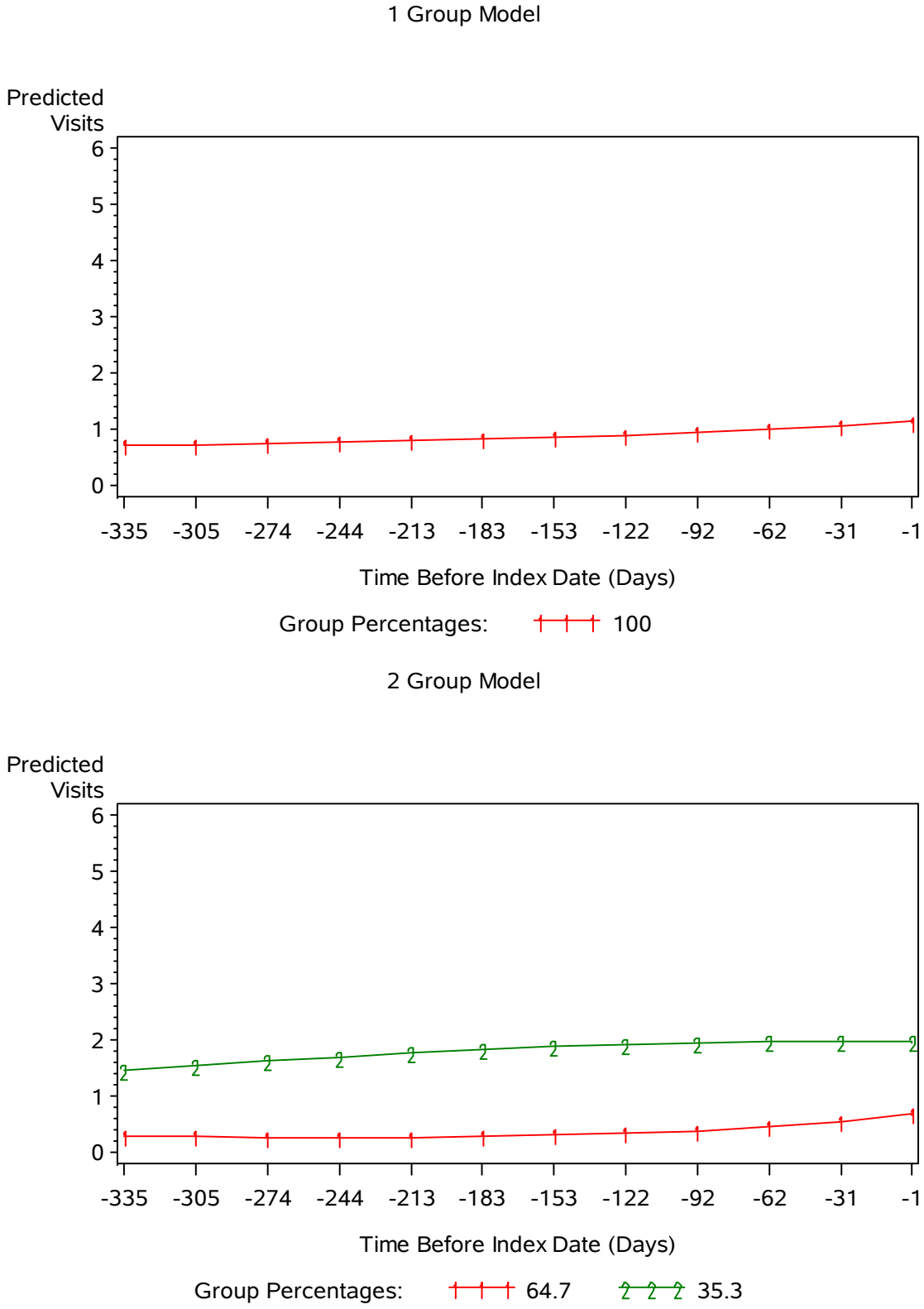


Figure 6
Group Trajectory Patterns of Predeceased Spouses' Monthly Ambulatory Visits



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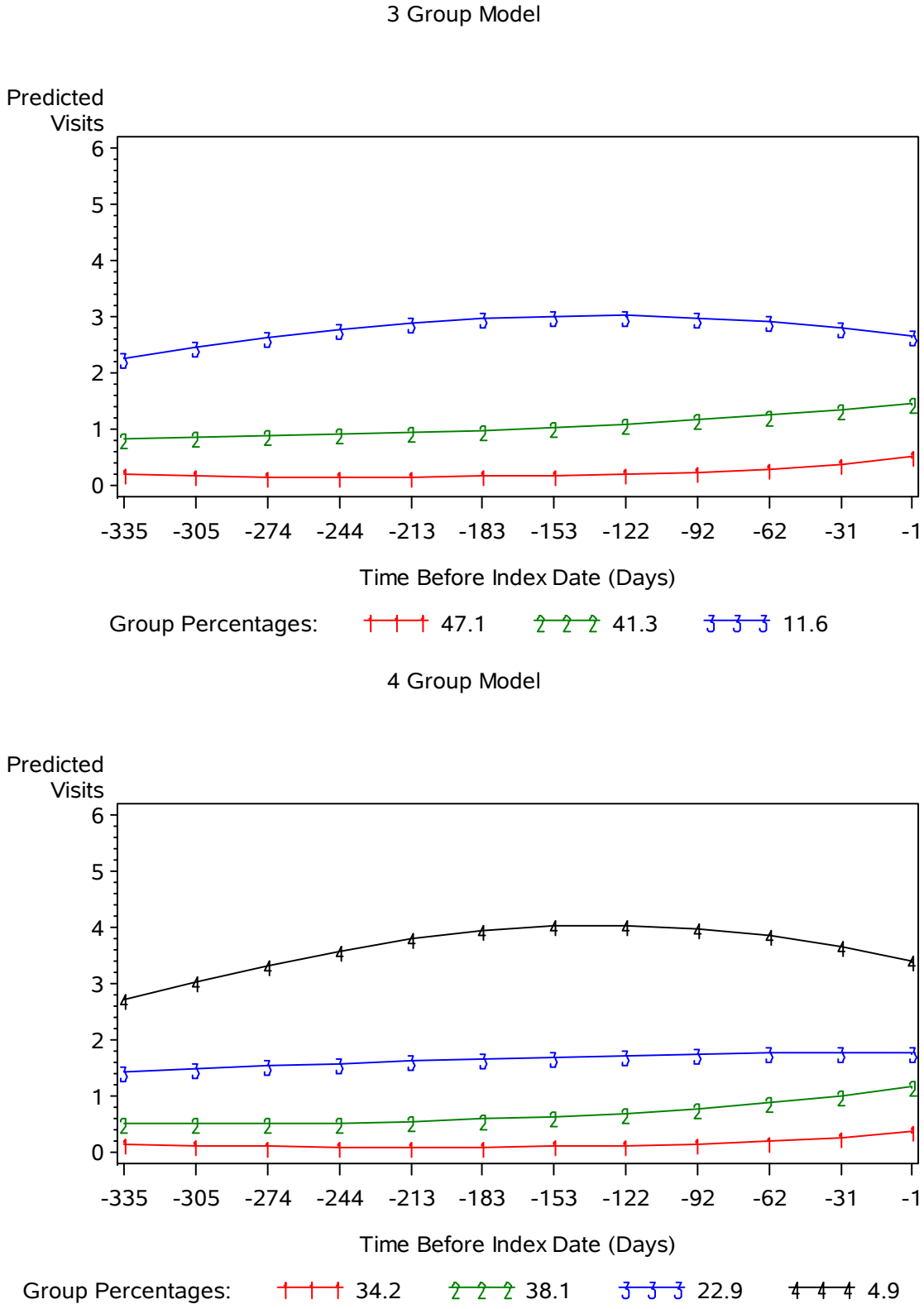
Group Trajectory Patterns of Predeceased Spouses' Monthly Ambulatory Visits



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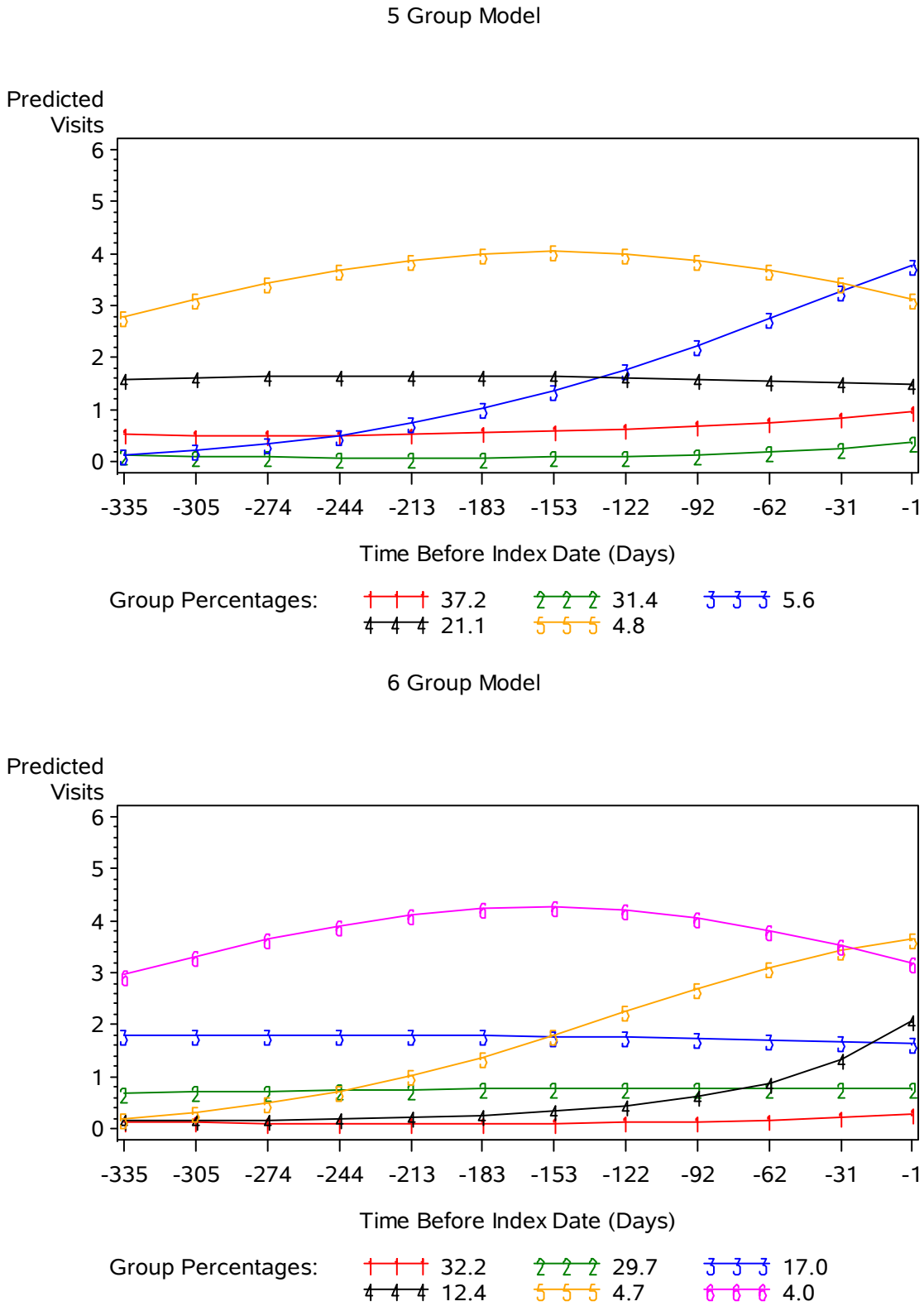
Group Trajectory Patterns of Predeceased Spouses' Monthly Ambulatory Visits



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Group Trajectory Patterns of Predeceased Spouses' Monthly Ambulatory Visits

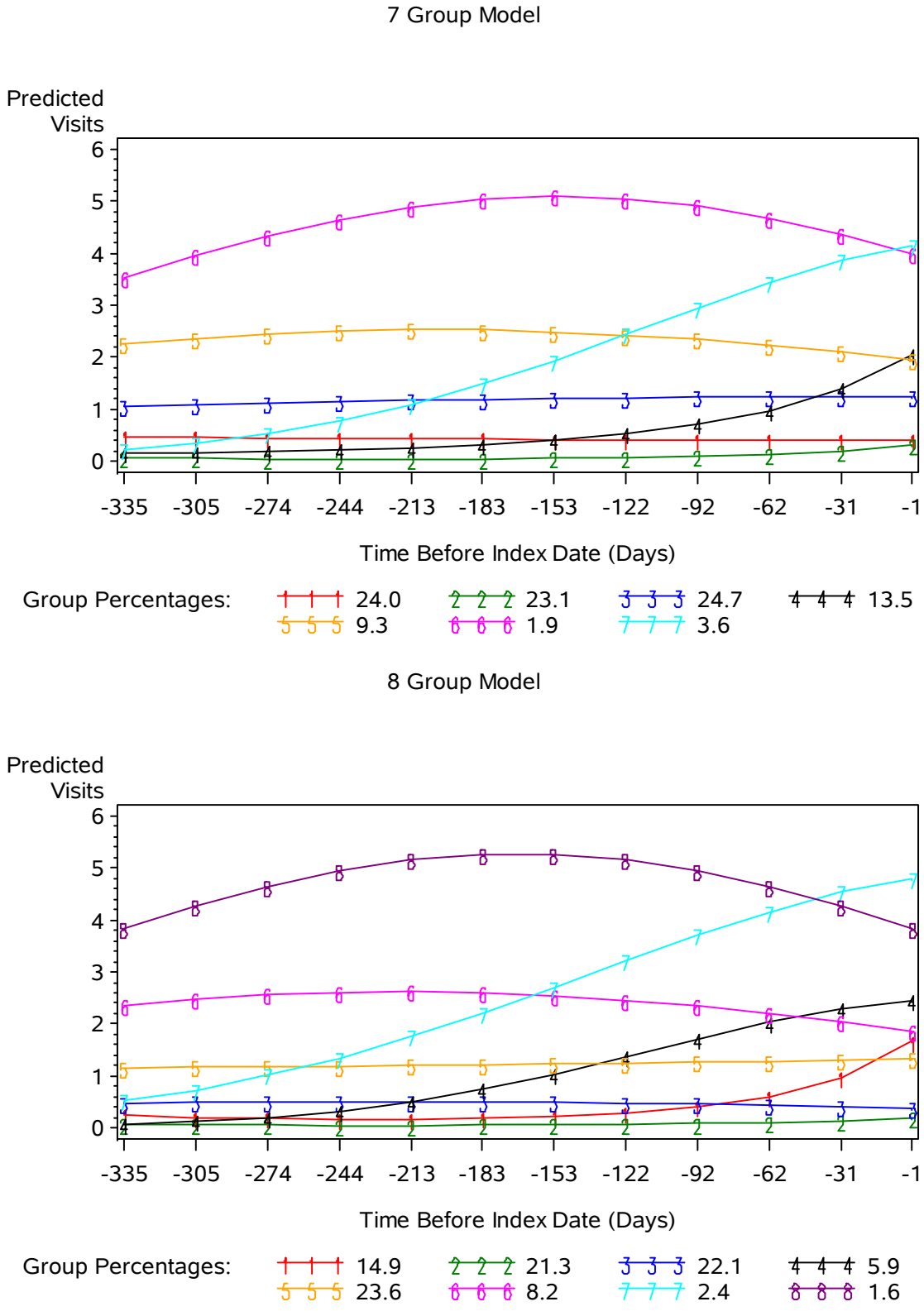


Figure 7
Group Trajectory Patterns of Widowed Spouses' Monthly Ambulatory Visits

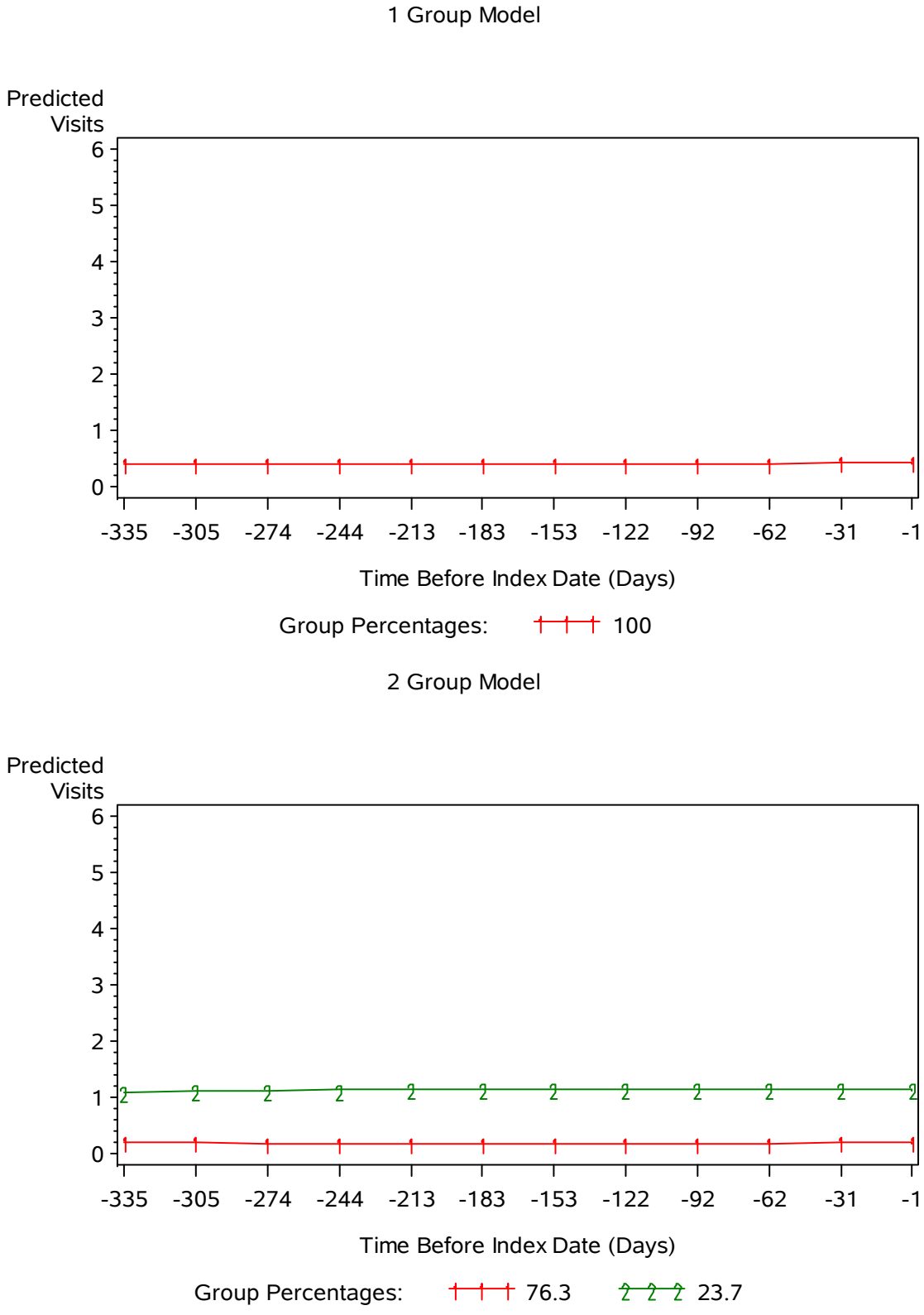
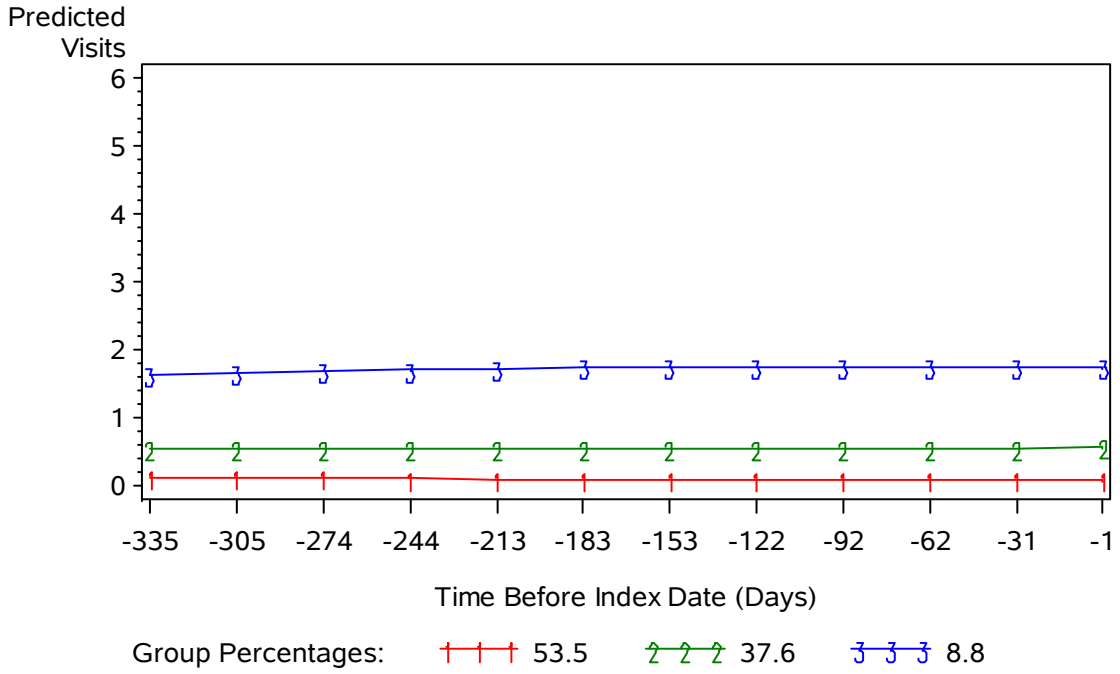
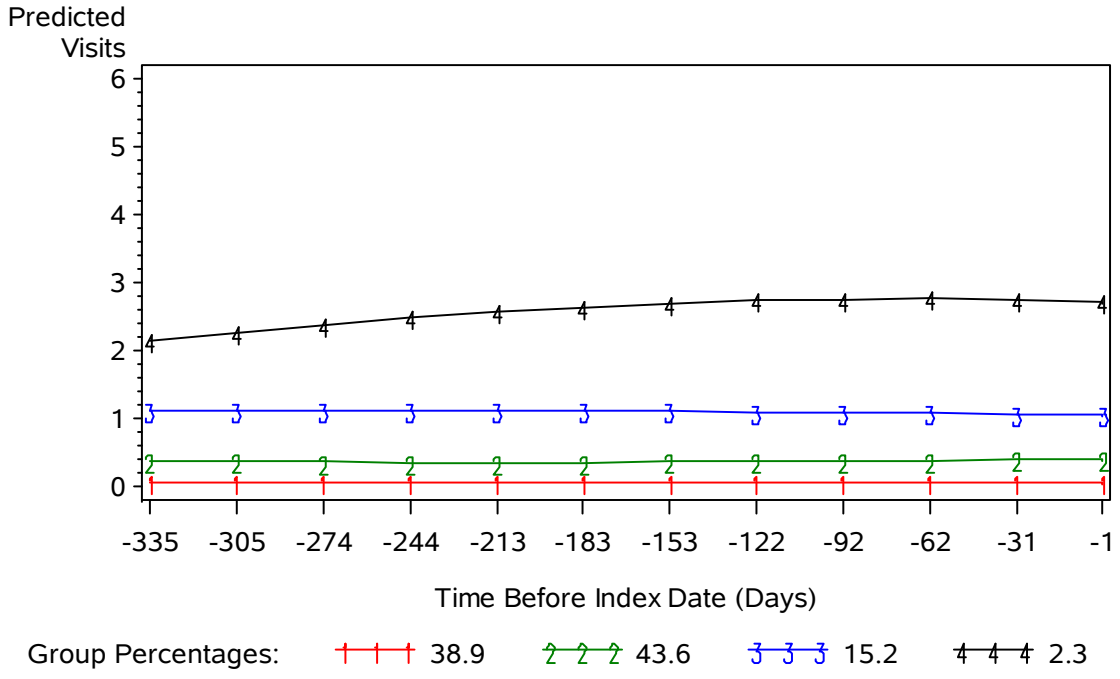


Figure 7 (continued)
Group Trajectory Patterns of Widowed Spouses' Monthly Ambulatory Visits

3 Group Model



4 Group Model



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Group Trajectory Patterns of Widowed Spouses' Monthly Ambulatory Visits

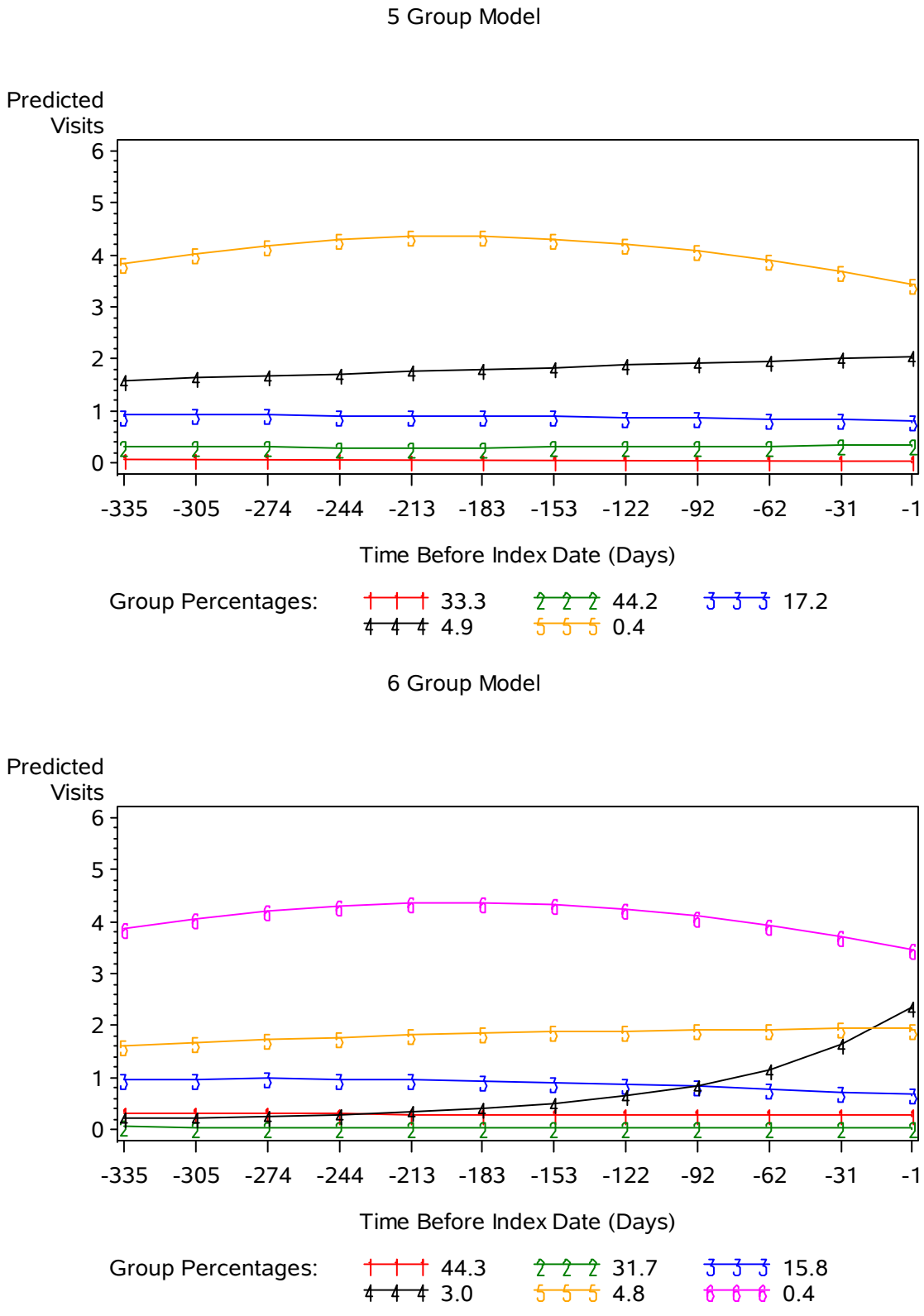


Figure 7 (continued)
Group Trajectory Patterns of Widowed Spouses' Monthly Ambulatory Visits

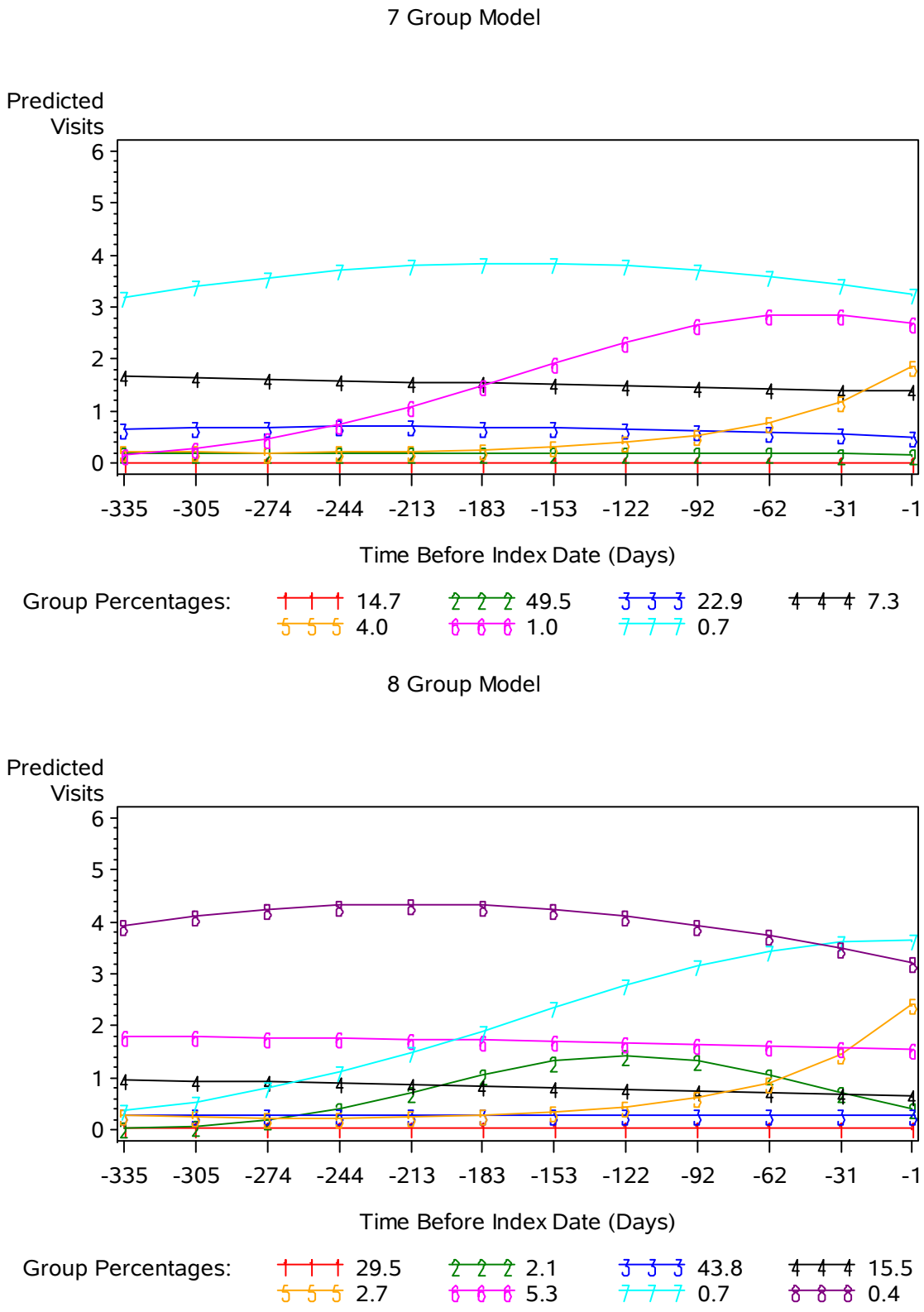
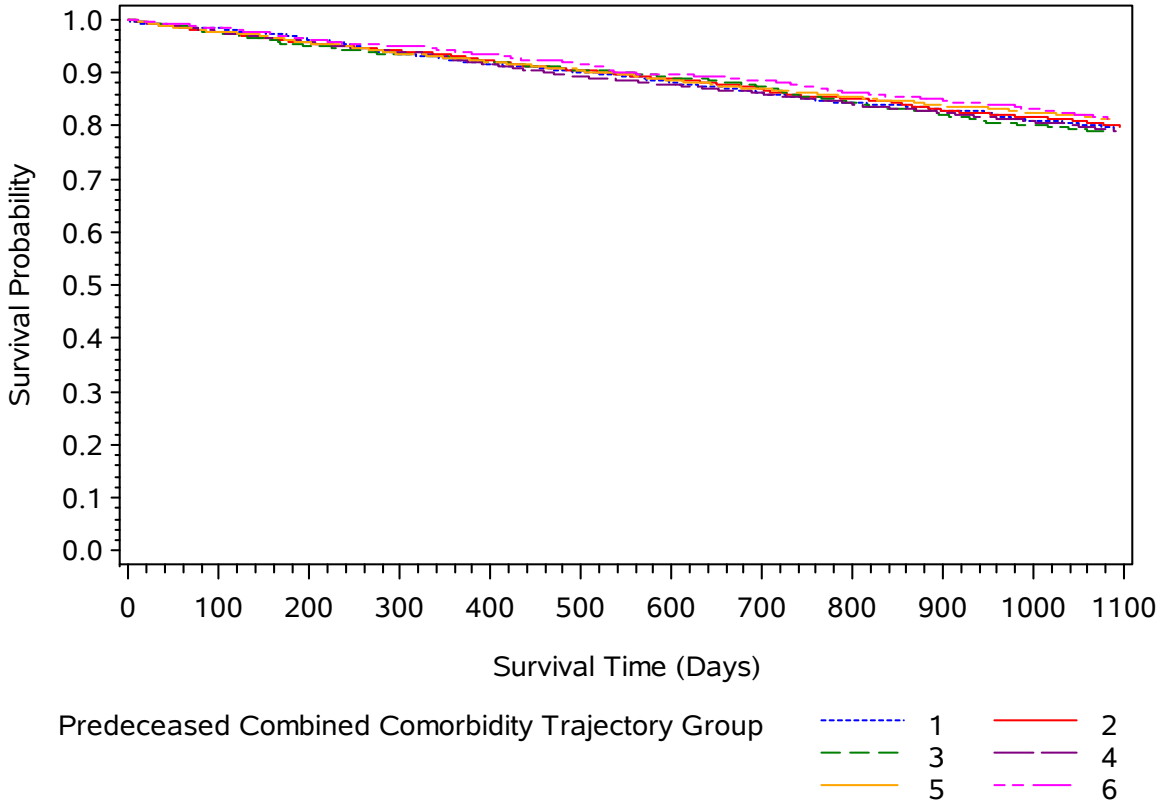


Figure 8
Kaplan-Meier Survival Curves for Widowed Spouses
By Predeceased Combined Comorbidity Trajectory Group



Predeceased Combined Comorbidity Trajectory Group Descriptions:

Group 1: Very low with late increase

Group 2: Stable low

Group 3: Late onset

Group 4: Stable medium

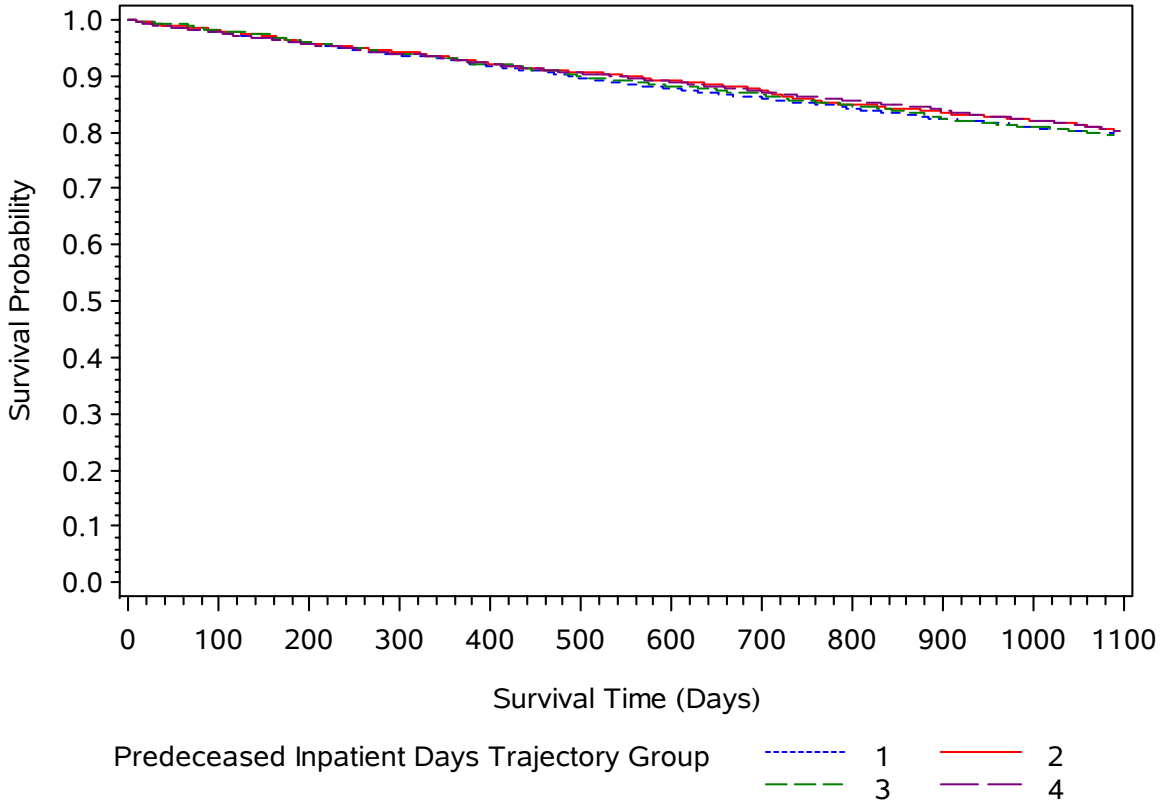
Group 5: Chronic high

Group 6: Steadily worsening

Log-Rank Test Result:

Chi-Square=4.1102, 5 df, p=0.5337

Figure 9
Kaplan-Meier Survival Curves for Widowed Spouses
By Predeceased Inpatient Days Trajectory Group



Predeceased Inpatient Days Trajectory Group Descriptions:

Group 1: Low with gradual increase

Group 2: Sharp acceleration in last 4 months

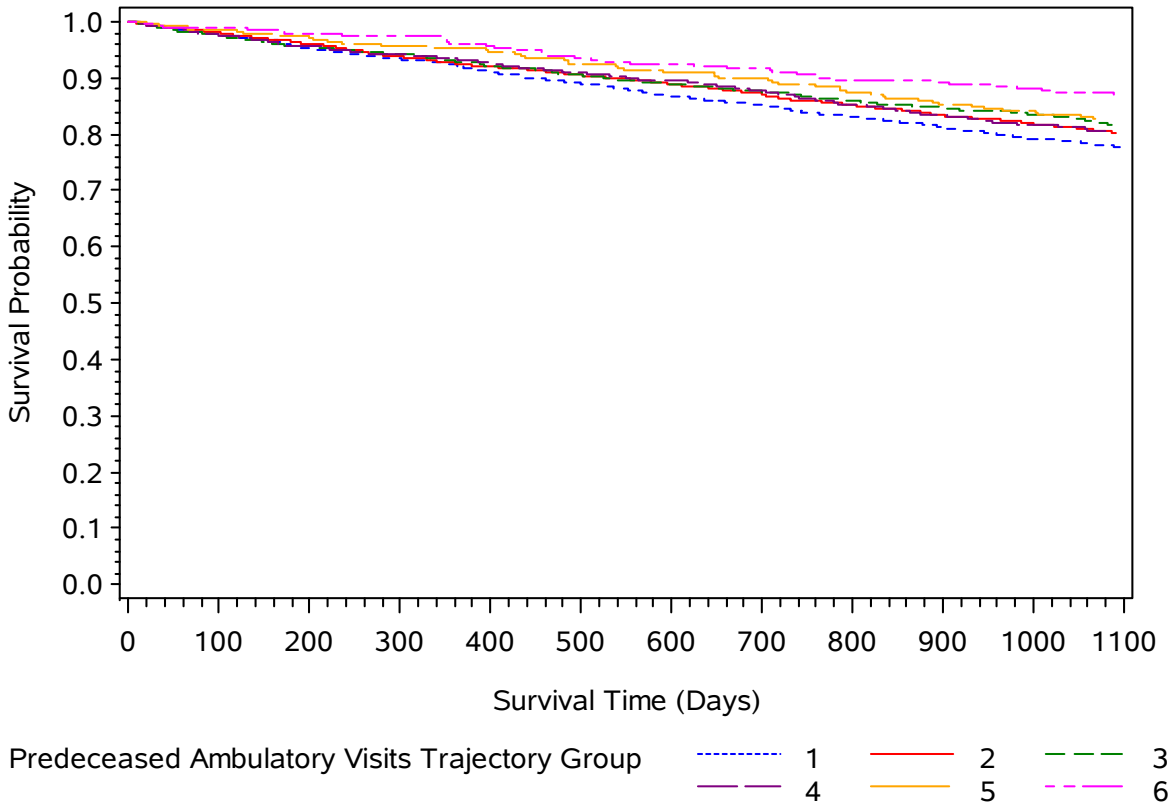
Group 3: Acceleration in last 6 months

Group 4: Zero or near zero, with very late increase in last month

Log-Rank Test Result:

Chi-Square=0.8512, 3 df, p=0.8372

Figure 10
Kaplan-Meier Survival Curves for Widowed Spouses
By Predeceased Ambulatory Visits Trajectory Group



Predeceased Ambulatory Visits Trajectory Group Descriptions:

Group 1: Stable zero or near-zero

Group 2: Stable low

Group 3: Stable medium

Group 4: Late increase

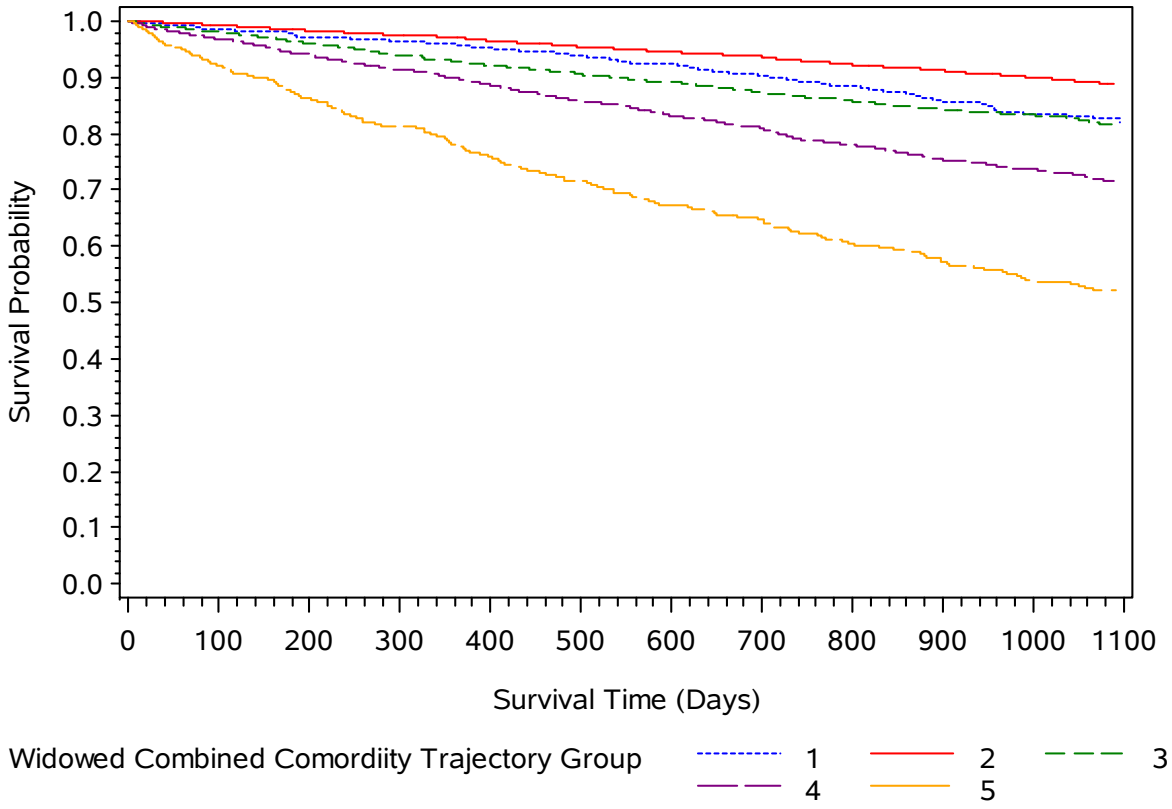
Group 5: Steady increase

Group 6: Chronic high

Log-Rank Test Result:

Chi-Square= 23.0766, 3 df, p=0.0003

Figure 11
Kaplan-Meier Survival Curves for Widowed Spouses
By Widowed Combined Comorbidity Trajectory Group



Widowed Combined Comorbidity Trajectory Group Descriptions:

Group 1: Low and decreasing

Group 2: Zero

Group 3: Very low but moderately increasing

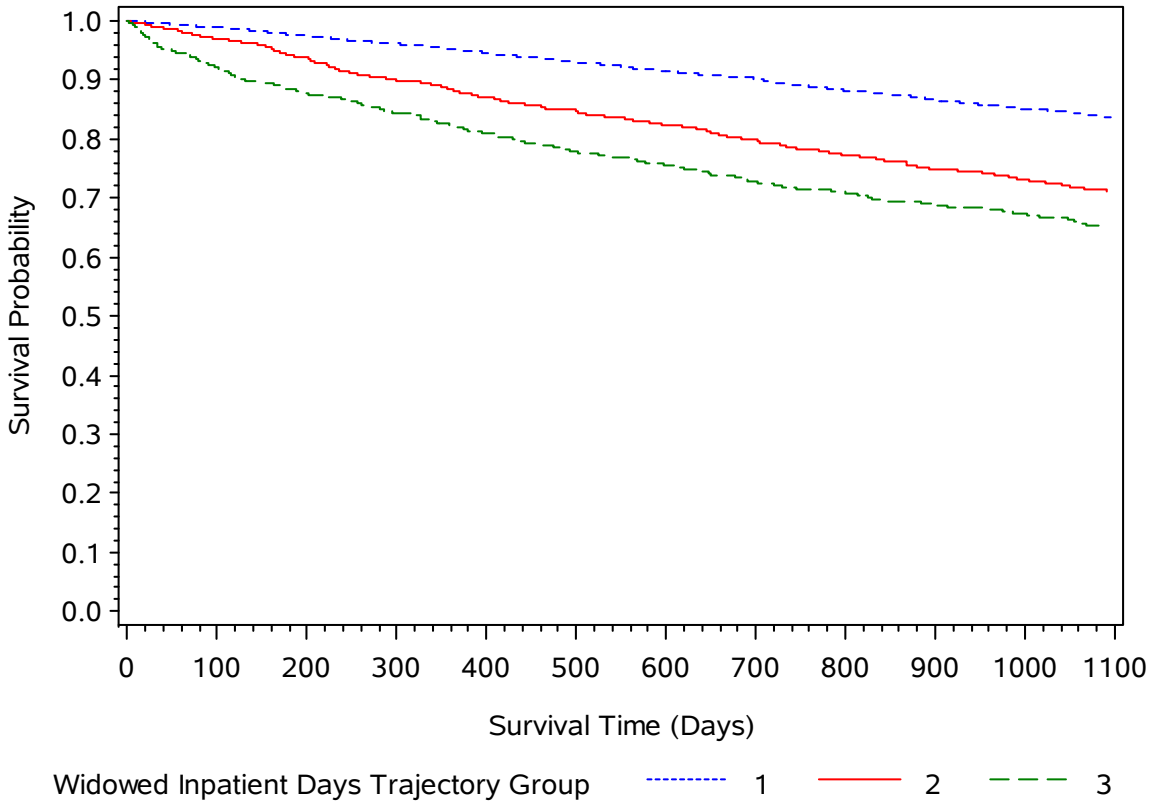
Group 4: Stable low-medium

Group 5: Chronic medium to high

Log-Rank Test Result:

Chi-square = 745.8445, 4 df, p <.0001

Figure 12
Kaplan-Meier Survival Curves for Widowed Spouses
By Widowed Inpatient Days Trajectory Group



Widowed Inpatient Days Trajectory Group Descriptions:

Group 1: Zero or near-zero

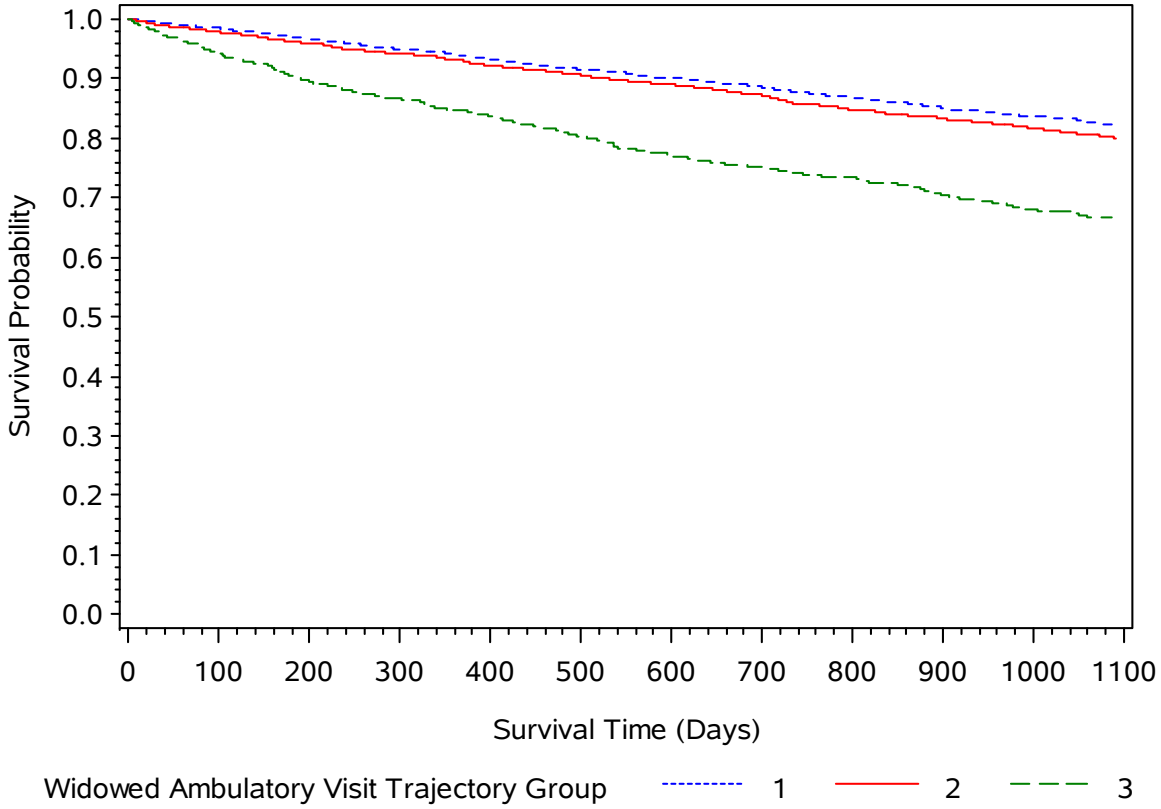
Group 2: Low and decreasing

Group 3: Low but increasing

Log-Rank Test Result:

Chi-square = 315.6771, 2 df, p <.0001

Figure 13
Kaplan-Meier Survival Curves for Widowed Spouses
By Widowed Ambulatory Visits Trajectory Group



Widowed Ambulatory Visits Trajectory Group Descriptions:

Group 1: Stable zero or near-zero

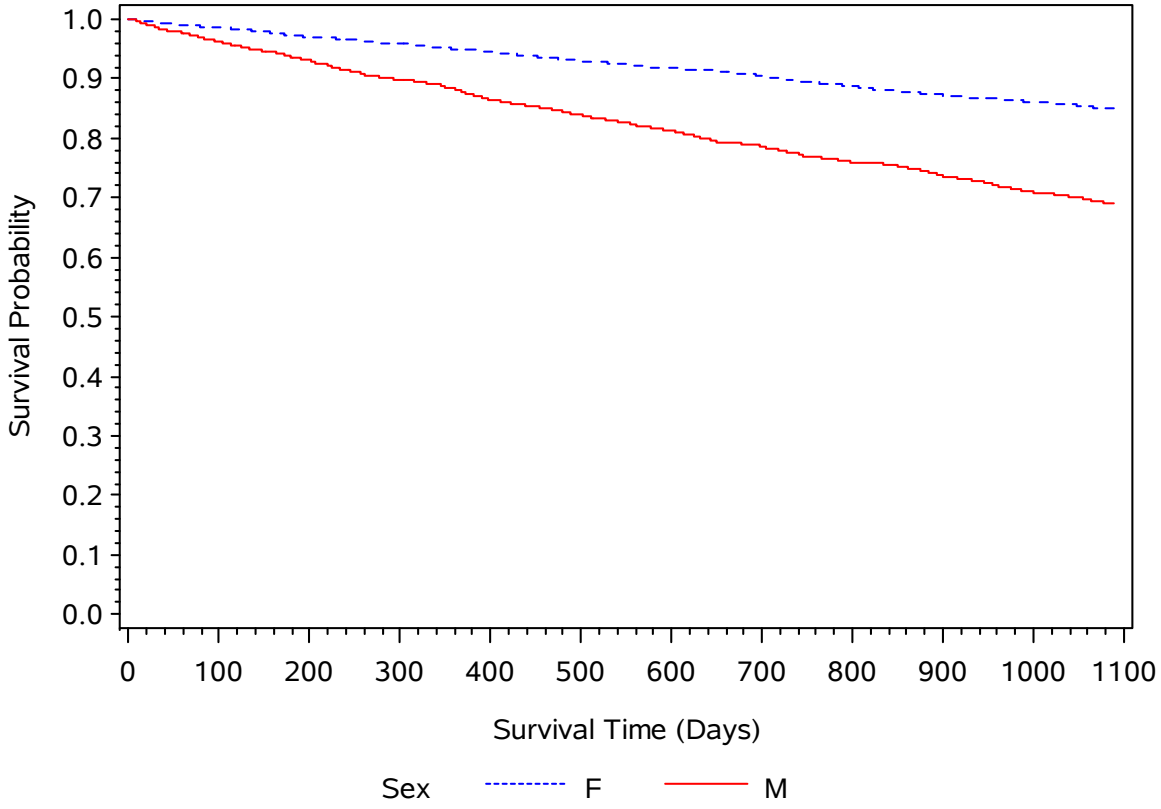
Group 2: Stable low

Group 3: Stable medium

Log-Rank Test Result:

Chi-square = 122.2487, 2 df, p <.0001

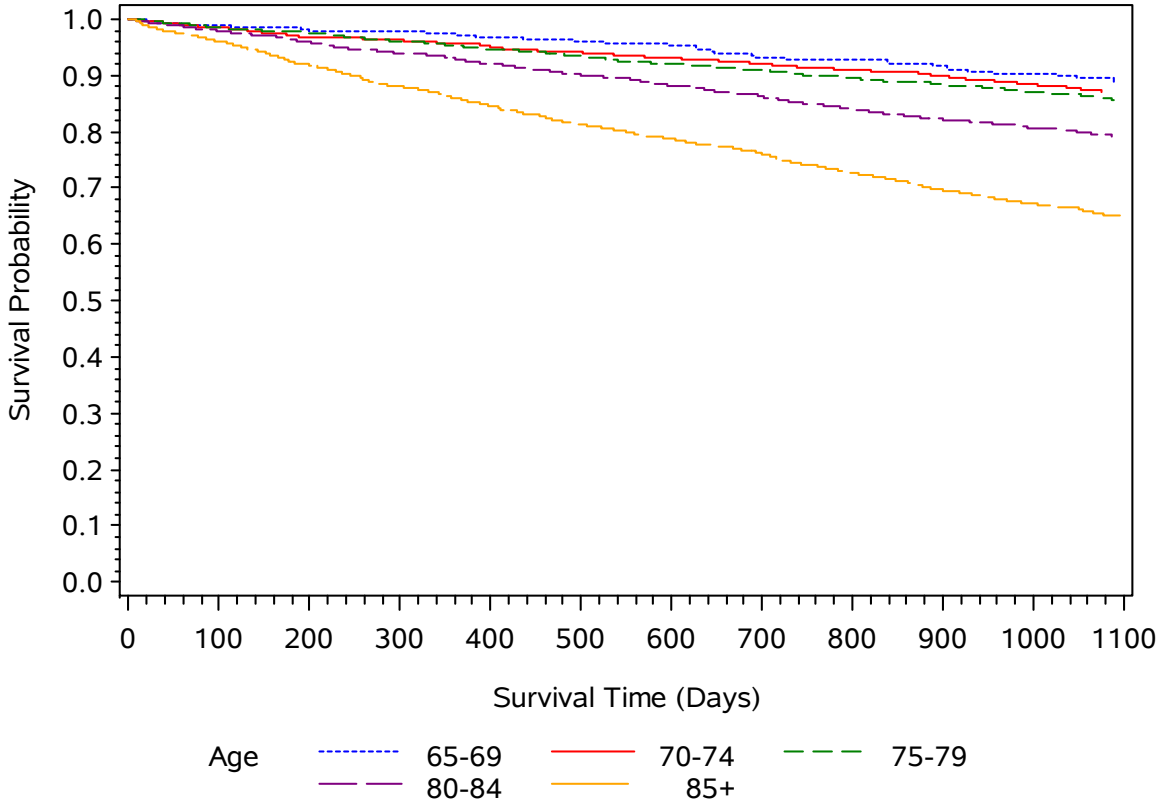
Figure 14
Kaplan-Meier Survival Curves for Widowed Spouses
By Gender



Log-Rank Test Result:

Chi-square = 301.7807, 1 df, p <.0001

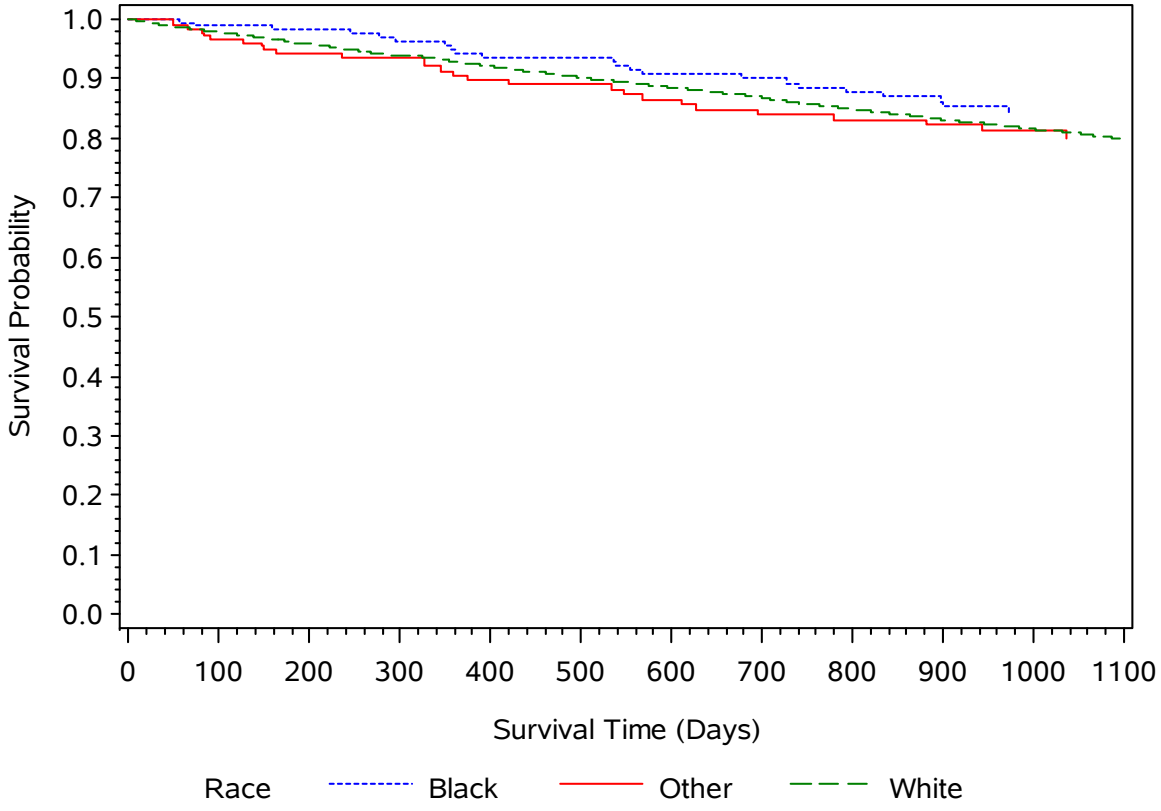
Figure 15
Kaplan-Meier Survival Curves for Widowed Spouses
By Age Group



Log-Rank Test Result:

Chi-square = 400.7447, 4 df, p <.0001

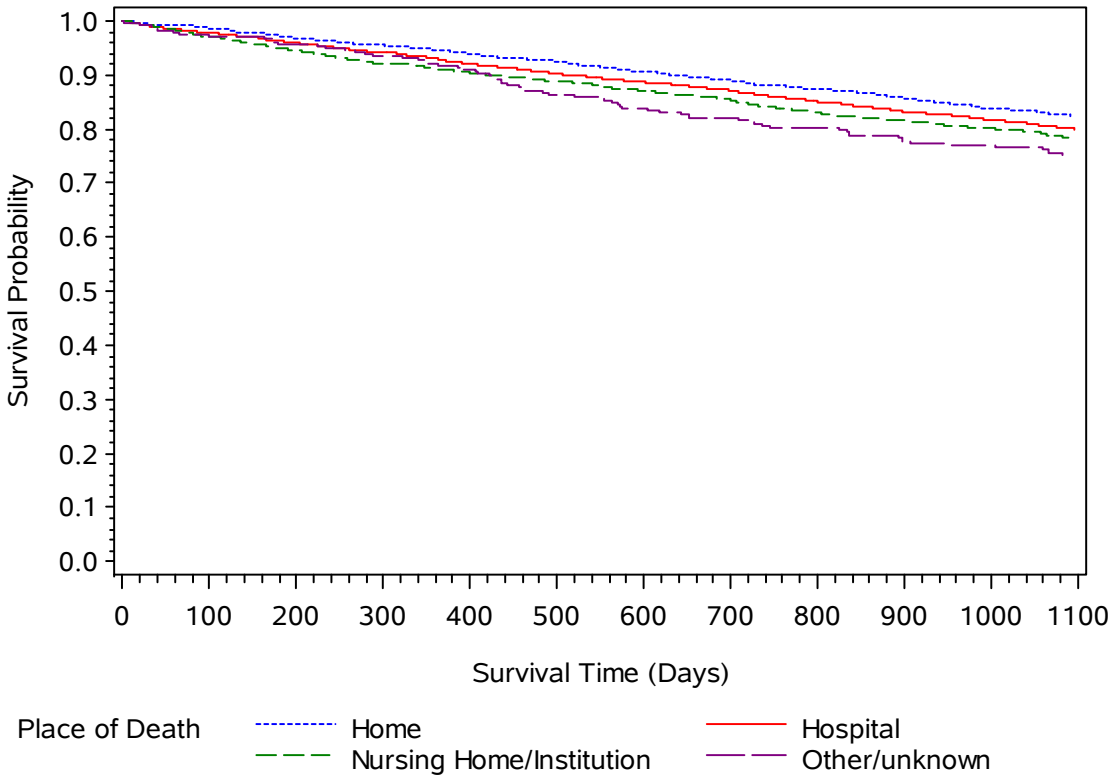
Figure 16
Kaplan-Meier Survival Curves for Widowed Spouses
By Race



Log-Rank Test Result:

Chi-square = 2.0912, 2 df, p = 0.3515

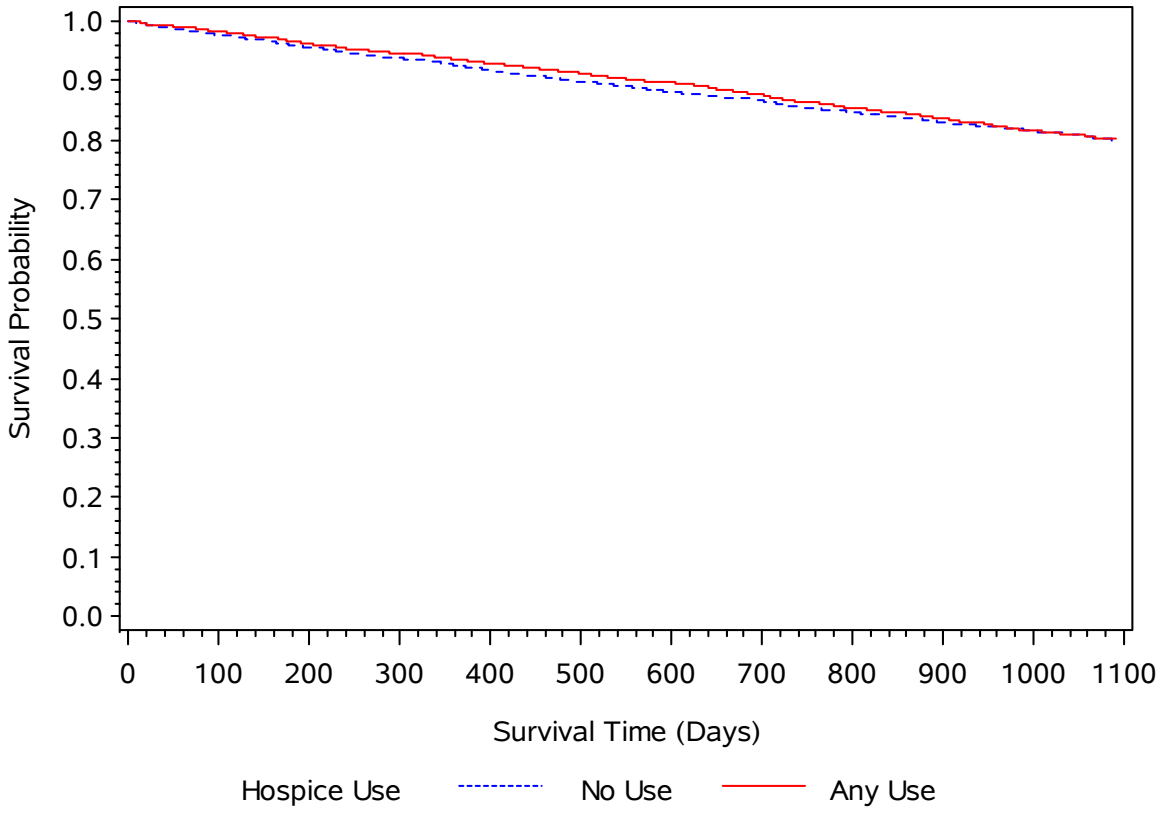
Figure 17
Kaplan-Meier Survival Curves for Widowed Spouses
By Predeceased Place of Death



Log-Rank Test Result:

Chi-square = 20.2208, 3 df, p = 0.0002

Figure 18
Kaplan-Meier Survival Curves for Widowed Spouses
By Predeceased Use of Hospice



Log-Rank Test Result:

Chi-square = 0.3840, 1 df, p=0.5355

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Appendix A:

Emory University Institutional Review Board Letter

EMORY UNIVERSITY | Institutional Review Board

DATE: December 18, 2013

RE: **Determination:** No IRB Review Required
Project Topic/Title: *Mortality Following Widowhood: the Role of Prior Spousal Health*
PI: Debra Heller, PhD

Dear Dr. Heller:

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the information you provided, we have determined that it does not require IRB review because it does not meet the definition of involving "human subjects" as set forth in Emory Policies and Procedures or federal regulations. In particular, this project aims to explore how the trajectory of health of the predeceased spouse during the period of up to two years before their death affects the subsequent mortality risk of the surviving widowed spouse. In order to investigate these aims, you will be solely using a de-identified data set provided by the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) program, which is a state program administered by the Pennsylvania Department of Aging. You will have no interaction or intervention with individuals, and no identifiable information can be obtained from the dataset.

Please note that this determination does not affect the ability to publish the results. If you have questions about this issue, please contact the IRB.

This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Thank you for consulting the IRB.

Sincerely,

(Signature Redacted)

Shara Karlebach, WHNP-BC, CIP
Research Services Consultant
Education and Quality Assurance
Emory University Institutional Review Board
1599 Clifton Rd, Atlanta, GA 30322

Appendix B:
SAS Code

```
*******************************************************************************;
* Program 1:  Morbidity Measure Computations                                   *;
*******************************************************************************;
libname thesis 'd:\SAS Share Files\Research\Debra\Thesis Research' ;
libname thenrol 'd:\SAS Share Files\Research\Debra\Thesis Research\En8906 Validation' ;
libname xtraj 'd:\SAS Share Files\Research\debra\thesis research\traj results' ;
options obs=max;

data dmedclm;
  merge thenrol.dmedclm(in=ina) thenrol.dperson(in=inb keep=personid spersonid enti0
  senti0 hmoi0 shmoi0 medpremon24 smedpremon24 indexyr hmopremon24 shmopremon24
  role group sex famid);
  by personid;
  if ina and inb;
  if (-730<=dvisitbeg<=-1) ;
  length annper01-annper13 ndm01-ndm12 nda01-nda13 3 ;

  if enti0 in ('1','2','3','A','B','C') and senti0 in ('1','2','3','A','B','C') ;
  if hmoi0 not in ('2','B','C') and shmoi0 not in ('2','B','C') ;
  if medpremon24=24 and smedpremon24=24 ;
  if hmopremon24=0 and shmopremon24=0;

  array meend {12} _temporary_ (-335 -305 -274 -244 -213 -183 -153 -122 -92 -62 -31 -1) ;
  array mestar {12} _temporary_ (-365 -334 -304 -273 -243 -212 -182 -152 -121 -91 -61 -30);
  array monstar {12} monstar01-monstar12 ;
  array monend {12} monend01-monend12 ;
  array ndm {12} ndm01-ndm12 ;
  do i=1 to 12;
    monend{i}=meend{i};
   monstar{i}=mestar{i} ;
   ndm{i}=(monend{i}-monstar{i})+1 ;
  if (mestar{i}<=dvisitbeg<=meend{i}) then moper=i;
  end;

  array ovend {13} _temporary_ (-365 -335 -305 -274 -244 -213 -183 -153 -122 -92 -62 -31 -1);
  array overstar {13} ovstar01-ovstar13 ;
  array overend {13} ovend01-ovend13 ;
  array nda {13} nda01-nda13 ;
  array annper {13} annper01-annper13 ;
  do i=1 to 13;
   overend{i}=ovend{i} ;
  overstar{i}=overend{i}-364;
  nda{i}=(overend{i}-overstar{i})+1 ;
  if (overstar{i}<=dvisitbeg<=overend{i}) then annper{i}=1;
  end;
  do i=1 to 13;
   if annper{i} ne 1 then annper{i}=0;
  if sum(of annper{*}) ge 1 then covperiod=1;
  end;
  if covperiod=1;
run;
proc freq; tables moper annper01-annper13;
run;
proc means n min max mean data=dmedclm;
  var ndm01-ndm12 nda01-nda13 ;
run;
```

```
proc means n min max mean data=dmedclm;
  var monstar01 monend01 monstar02 monend02 monstar03 monend03 monstar04 monend04
      monstar05 monend05 monstar06 monend06 monstar07 monend07 monstar08 monend08
      monstar09 monend09 monstar10 monend10 monstar11 monend11 monstar12 monend12 ;
run;
proc means n min max mean data=dmedclm;
  var ovstar01 ovend01 ovstar02 ovend02 ovstar03 ovend03 ovstar04 ovend04
      ovstar05 ovend05 ovstar06 ovend06 ovstar07 ovend07 ovstar08 ovend08
      ovstar09 ovend09 ovstar10 ovend10 ovstar11 ovend11 ovstar12 ovend12
      ovstar13 ovend13;
run;
proc freq data=dmedclm;
  tables filesrc;
run;

*************************************************************;
* Evaluate any hospice use (yes/no) by monthly period       *;
*************************************************************;
data hospice(keep=personid filesrc group dvisitbeg dvisitend moper hospuse);
  set dmedclm(where=(filesrc='HOS' and moper ne .));
  length hospuse 3 ;
  if moper ne . then hospuse=1; else hospuse=0;
run;
proc freq; tables filesrc hospuse;
run;
proc print data=hospice;
  where ranuni(4) le .0001;
run;
proc sort data=hospice;
  by personid moper;
run;
proc summary data=hospice max;
  var hospuse;
  output out=hospiceuse1(drop=_type_ _freq_) max=anyhospice ;
  by personid moper;
  id group ;
run;
proc freq; tables moper anyhospice;
run;
data hospiceuse(keep=personid anyhospice01-anyhospice12);
  set hospiceuse1(where=(moper ne .));
  by personid;
  length anyhospice01-anyhospice12 3 ;
  array hosp {12} anyhospice01-anyhospice12 ;
  retain anyhospice01-anyhospice12 ;
  if first.personid then do i=1 to 12;
    hosp{i}=. ;
  end;
  hosp{moper}=anyhospice;
  if last.personid then do ;
    do i=1 to 12;
   if hosp{i} ne 1 then hosp{i}=0;
    end;
    output;
  end;
run;

*************************************************************;
* Inpatient Data                                            *;
*************************************************************;
data inpat;
```

```
  set dmedclm(where=(filesrc='INP'));
run;
proc means data=inpat;
run;
proc sort data=inpat nodupkey;
  by personid dvisitbeg dvisitend;
run;
data inpat2;
  set inpat;
  by personid dvisitbeg;
  if last.dvisitbeg then output;
run;
proc sort data=inpat2;
  by personid dvisitend dvisitbeg;
data inpat3; /*use to count hosp admissions also*/
  set inpat2;
  by personid dvisitend;
  if first.dvisitend then output;
run;
data admits(keep=personid filesrc group dvisitbeg dvisitend moper);
  set inpat3;
  if filesrc='INP' and moper ne . ;
run;

*********************************************************************;
* Compute number of inpatient days per monthly period               *;
*********************************************************************;
data days(keep=personid dvisitbeg dvisitend d001-d365);
  set admits;
  length d001-d365 3 ;
  array dcov {365} d001-d365 ;
  do i=1 to 365;
    if dvisitbeg le (i*-1) and dvisitend ge (i*-1) then dcov{i}=1;
   else dcov{i}=0;
  end;
run;
proc print data=days;
  where ranuni(5) le .0001;
  var personid dvisitbeg dvisitend d001-d090 ;
run;
proc summary data=days max;
  var d001-d365;
  output out=days2 max= ;
  by personid;
run;
data inpatdays(keep=personid inpatdays01-inpatdays12);
  set days2;
  length inpatdays01-inpatdays12 3;
  inpatdays12=sum(of d001-d030) ;
  inpatdays11=sum(of d031-d061) ;
  inpatdays10=sum(of d062-d091) ;
  inpatdays09=sum(of d092-d121) ;
  inpatdays08=sum(of d122-d152) ;
  inpatdays07=sum(of d153-d182) ;
  inpatdays06=sum(of d183-d212) ;
  inpatdays05=sum(of d213-d243) ;
  inpatdays04=sum(of d244-d273) ;
  inpatdays03=sum(of d274-d304) ;
  inpatdays02=sum(of d305-d334) ;
  inpatdays01=sum(of d335-d365) ;
run;
```

```
proc means n min max mean data=inpatdays;
  var inpatdays01-inpatdays12;
run;
data review;
  merge inpat3(in=ina) inpatdays(in=inb);
  by personid;
  if ina;
run;
proc print data=review(obs=25) ;
  var dvisitbeg dvisitend inpatdays01-inpatdays12;
  by personid;
run;

*****************************************************;
* Count # of admissions by monthly period           *;
*****************************************************;
proc sort data=admits;
  by personid moper;
run;
proc summary data=admits n;
  var dvisitbeg ;
  output out=inpadmits1 n=_inpadmits ;
  by personid moper;
  id group ;
run;
proc means data=inpadmits1 n min max mean;
  var _inpadmits;
  class moper;
run;
data inpadmits(keep=personid inpadmits01-inpadmits12);
  set inpadmits1(where=(moper ne .));
  by personid;
  length inpadmits01-inpadmits12 3 ;
  array inpat {12} inpadmits01-inpadmits12 ;
  retain inpadmits01-inpadmits12 ;
  if first.personid then do i=1 to 12;
    inpat{i}=. ;
  end;
  inpat{moper}=_inpadmits;
  if last.personid then do ;
    do i=1 to 12;
   if inpat{i} =. then inpat{i}=0;
    end;
    output;
  end;
run;
data inpat4;
  set inpat3;
  by personid;
  retain _numinp;
  if first.personid then do;
    _numinp=0;
  end;
    _numinp=_numinp+1;
run;
proc freq; tables _numinp;
run;
data inpat5(keep=personid hosbeg01-hosbeg27 hosend01-hosend27);
  set inpat4;
  by personid;
  length hosbeg01-hosbeg27 hosend01-hosend27 4 ;
```

```
  array hosbeg {27} hosbeg01-hosbeg27 ;
  array hosend {27} hosend01-hosend27 ;
  retain  hosbeg01-hosbeg27 hosend01-hosend27 ;
  if first.personid then do i=1 to 27;
    hosbeg{i}=. ;
 hosend{i}=. ;
  end;
  hosbeg{_numinp}=dvisitbeg ;
  hosend{_numinp}=dvisitend ;
  if last.personid then output;
run;

*************************************************************;
* Evaluate ambulatory visits outside of hospitalization periods*;
*************************************************************;
/*Ambulatory visits are those whose place of service was a physician office=11,
 patient home=12, hospital outpatient setting=22, hospital emergency room=23,
 rural health clinic=72, public health clinic=71, urgent care=20 or amb surg center=24.
 Physician visits were defined as those that were for the purpose of
 evaluation and management only, not including pathology, and were based on BETOS codes
 for evaluation and management*/
data countamb1(keep=personid group filesrc dvisitbeg moper typesrvc fac_type);
  set dmedclm(where=(filesrc in ('OTP','CAR','HOS'))) ;
  array betos {13} $ betos01-betos13 ;
  array place {13} $ place01-place13;
  if filesrc in ('CAR') then do;
    do i=1 to 13;
     if substr(betos{i},1,1)='M' and betos{i} ne 'M5A' and
     place{i} in ('11','12','22','23','72','71','20','24','53') then havisit=1;
   /*home or ambulatory evaluation and management visit using modification of
    Nyweide and Dartmouth criteria*/
    end;
    if havisit ne 1 then havisit=0;
  end;
  if filesrc='CAR' and havisit ne 1 then delete;
run;
proc freq; tables filesrc typesrvc typesrvc*filesrc fac_type*filesrc ;
run;

proc sort data=countamb1 nodupkey;
  by personid dvisitbeg ;
run;
data countamb2;
  merge countamb1(in=ina) inpat5(in=inb);
  by personid;
  if ina;
  array hosbeg {29} hosbeg01-hosbeg29 ;
  array hosend {29} hosend01-hosend29 ;
  if inb=1 then do i=1 to 29;
    if (hosbeg{i}<=dvisitbeg<=hosend{i}) then during=1;
  end;
  if during ne 1 then during=0;
run;
proc freq; tables during;
run;
data countamb3(keep=personid filesrc group dvisitbeg moper);
  set countamb2;
  if during=0;
run;
proc sort data=countamb3; by personid moper;
proc summary data=countamb3 n;
```

```
  var dvisitbeg ;
  output out=ambvisits1 n=_ambvisits ;
  by personid moper;
  id group ;
run;
proc means n min max mean median data=ambvisits1 ;
  var _ambvisits;
  class moper group ;
run;
proc freq data=ambvisits1;
  tables moper;
run;
data ambvisits(keep=personid ambvisits01-ambvisits12);
  set ambvisits1(where=(moper ne .));
  by personid;
  length ambvisits01-ambvisits12 3 ;
  array amb {12} ambvisits01-ambvisits12 ;
  retain ambvisits01-ambvisits12 ;
  if first.personid then do i=1 to 12;
    amb{i}=. ;
  end;
  amb{moper}=_ambvisits;
  if last.personid then do ;
    do i=1 to 12;
   if amb{i}=. then amb{i}=0;
    end;
    output;
  end;
run;
proc means n min max mean data=ambvisits;
run;

data dates;
  length monstar01-monstar12 monend01-monend12 3 ovstar01-ovstar13 ovend01-ovend13 4 ;
  set dmedclm(keep=monstar01-monstar12 monend01-monend12 ovstar01-ovstar13
  ovend01-ovend13) ;
run;
proc sort data=dates nodupkey;
  by monstar01-monstar12 monend01-monend12 ovstar01-ovstar13 ovend01-ovend13 ;
run;
proc print data=dates;
run;

data monsumms1(drop=i);
  merge thenrol.dperson(in=ina keep=personid spersonid famid role group)
        inpadmits(keep=personid inpadmits01-inpadmits12)
        inpatdays(keep=personid inpatdays01-inpatdays12)
        hospiceuse(keep=personid anyhospice01-anyhospice12)
        ambvisits(keep=personid ambvisits01-ambvisits12) ;
  by personid;
  if ina;
  length anyhospice 3 ;
  array utizvars {48} inpadmits01-inpadmits12 inpatdays01-inpatdays12
                      anyhospice01-anyhospice12 ambvisits01-ambvisits12 ;
  do i=1 to 48;
    if utizvars{i}=. then utizvars{i}=0;
  end;
  anyhospice=max(of anyhospice01-anyhospice12) ;
run;
proc sql noprint;
/*attach the single row of dates to every person-level record (for PROC TRAJ)*/
```

```
  create table monsumms as
  select a.*, b.*
  from monsumms1 as a, dates as b;
quit;
run;
proc print data=monsumms(obs=10);
run;
proc contents;
run;
proc means n min max mean data=monsumms;
  class group;
run;

*************************************************************************************;
* Charlson, Elixhauser, and Combined Comorbidity Macro                              *;
*************************************************************************************;

%macro charelix(per) ;

data claim&per;
  set dmedclm;
  if annper&per=1;

  length pdx3dig dx3dig01-dx3dig10 line3dx01-line3dx13 $ 3 pdx4dig
         dx4dig01-dx4dig10 line4dx01-line4dx13 $ 4 ;


  array fulldx {24} $ pdgns_cd dgnscd01-dgnscd10 linedx01-linedx13;
  array just3 {24} $ pdx3dig dx3dig01-dx3dig10 line3dx01-line3dx13;
  array just4 {24} $ pdx4dig dx4dig01-dx4dig10 line4dx01-line4dx13;

  do i=1 to 24;
    just3{i}=substr(fulldx{i},1,3) ;
 /*create new variable that is just the first 3 digits of ICD-9-CM code*/
 just4{i}=substr(fulldx{i},1,4) ;
 /*create new variable that is just the first 4 digits of ICD-9-CM code*/
  end;

*************************************************************************************;
* Identify 17 Charlson comorbidities on claim  (scan all 24 diagnoses)              *;
*************************************************************************************;
do i=1 to 24;

if just3{i} in ('410','412') then cmi=1; /*Charlson myocardial infarction*/

if fulldx{i} in ('39891','40201','40211','40291','40401','40403',
 '40411','40413','40491','40493')
 or just4{i} in ('4254','4255','4256','4257','4258','4259') or just3{i}='428'
 then cchf=1; /*Charlson congestive heart failure*/

if just4{i} in ('0930','4373','4431','4432','4433','4434','4435','4436',
 '4437','4438','4439','4471','5571','5579','V434')
 or just3{i} in ('440','441') then cpvd=1; /*Charlson peripheral vascular disease*/

if fulldx{i}='36234' or just3{i} in ('430','431','432','433','434',
 '435','436','437','438')
 then ccereb=1; /*Charlson cerebrovascular disease*/

if just3{i}='290' or just4{i} in ('2941','3312') then cdement=1; /*Charlson dementia*/

if just4{i} in ('4168','4169','5064','5081','5088')
```

```
 or just3{i} in ('490','491','492','493','494','495','496','497',
'498','499','500','501','502','503','504','505')
 then cpulmon=1; /*Charlson chronic pulmonary disease*/

if just4{i} in ('4465','7100','7101','7102','7103','7104','7140','7141','7142','7148')
 or just3{i}='725'
  then crheum=1; /*Charlson rheumatic disease*/

if just3{i} in ('531','532','533','534') then cpeptic=1;
 /*Charlson peptic ulcer disease*/

if fulldx{i} in ('07022','07023','07032','07033','07044','07054')
  or just4{i} in ('0706','0709','5733','5734','5738','5739','V427')
 or just3{i} in ('570','571')
  then cmildliv=1; /*Charlson mild liver disease*/

if just4{i} in ('2500','2501','2502','2503','2508','2509')
 then cdiabwoc=1; /*Charlson diabetes without chronic complication*/

if just4{i} in ('2504','2505','2506','2507') then cdiabwic=1;
  /*Charlson diabetes with chromic complication*/

if just4{i} in ('3341','3440','3441','3442','3443','3444','3445','3446','3449')
  or just3{i} in ('342','343')
 then cplegia=1; /*Charlson hemiplegia or paraplegia*/

if fulldx{i} in ('40301','40311','40391','40402','40403','40412','40413','40492','40493')
  or just4{i} in ('5830','5831','5832','5833','5834','5835','5836','5837',
  '5880','V420','V451') or just3{i} in ('582','585','586','V56')
  then crenal=1; /*Charlson renal disease*/

if just3{i} in ('140','141','142','143','144','145','146','147','148','149','150',
 '151','152','153','154','155','156','157','158','159','160','161',
 '162','163','164','165','166','167','168','169','170','171','172'
 '174','175','176','177','178','179','180','181','182','183','184',
 '185','186','187','188','189','190','191','192','193','194','195',
 '200','201','202','203','204','205','206','207','208') or just4{i}='2386'
  then cmalig=1;
 /*Charlson malignancy, excluding non-melanoma skin cancer (173)
   and secondary cancers (196-199)*/

if just4{i} in ('4560','4561','4562','5722','5723','5724','5728') then csevliv=1;
/*Charlson severe liver disease*/

if just3{i} in ('196','197','198','199') then cmetas=1;
/*Charlson metastatic solid tumor*/

if just3{i} in ('042','043','044') then caids=1; /*Charlson AIDS/HIV*/

end;

array charlind {17} cmi cchf cpvd ccereb cdement cpulmon crheum cpeptic cmildliv
                    cdiabwoc cdiabwic cplegia crenal cmalig csevliv cmetas caids ;
do i=1 to 17;
 if charlind{i}=. then charlind{i}=0;
end;

*********************************************************************************;
* Identify 32 Elixhauser comorbidities on claim  (scan all 24 diagnoses)         *;
*********************************************************************************;
do i=1 to 24;
```

```
if fulldx{i} in ('39891','40201','40211','40291','40401','40403','40411','40413',
  '40491','40493') or just4{i} in ('4254','4255','4256','4257','4258','4259')
   or just3{i}='428'
   then echf=1; /* Elixhauser congestive heart failure (same codes as Charlson)*/

if fulldx{i} in ('42613','42610','42612','99601','99604')
  or just4{i} in ('4260','4267','4269','4270','4271','4272','4273','4274',
                  '4276','4277','4278','4279','7850','V450','V533')
   then earry=1;  /* Elixhauser cardiac arrhythmias*/

if just4{i} in ('0932','7463','7464','7465','7466','V422','V433')
  or just3{i} in ('394','395','396','397','424')
  then evalve=1;  /* Elixhauser valvular disease*/

if just4{i} in ('4150','4151','4170','4178','4179') or just3{i}='416'
   then epulcir=1;  /* Elixhauser pulmonary circulation disorders*/

if just4{i} in ('0930','4373','4431','4432','4433','4434','4435','4436','4437',
               '4438','4439','4471','5571','5579','V434')
   or just3{i} in ('440','441') then epvd=1; /* Elixhauser peripheral vascular disorders*/

if just3{i}='401' then ehypuc=1;  /* Elixhauser hypertension, uncomplicated*/

if just3{i} in ('402','403','404','405') then ehypc=1;
      /* Elixhauser hypertension, complicated*/;

if just4{i} in ('3341','3440','3441','3442','3443','3444','3445','3446','3449')
  or just3{i} in ('342','343') then epara=1;
     /* Elixhauser paralysis*/

if fulldx{i}='33392' or just4{i} in ('3319','3320','3321','3334','3335',
  '3362','3481','3483','7803','7843')
   or just3{i} in ('334','335','340','341','345')
   then eoneuro=1;  /* Elixhauser other neurological disorders*/

if just4{i} in ('4168','4169','5064','5081','5088')
  or just3{i} in ('490','491','492','493','494','495','496','497',
  '498','499','500','501','502','503','504','505')
  then epulmon=1;
    /* Elixhauser chronic pulmonary disease (same ICD-9 codes as Charlson)*/

if just4{i} in ('2500','2501','2502','2503') then ediabuc=1;
  /* Elixhauser diabetes, uncomplicated*/

if just4{i} in ('2504','2505','2506','2507','2508','2509') then ediabc=1;
  /* Elixhauser diabetes, complicated*/

if just4{i} in ('2409','2461','2468') or just3{i} in ('243','244') then ethyro=1;
  /* Elixhauser hypothyroidism*/

if fulldx{i} in ('40301','40311','40391','40402','40403',
                 '40412','40413','40492','40493')
  or just4{i} in ('5880','V420','V451') or just3{i} in ('585','586','V56')
  then erenal=1;  /* Elixhauser renal failure*/

if fulldx{i} in ('07022','07023','07032','07033','07044','07054')
  or just4{i} in ('0706','0709','4560','4561','4562','5722','5723','5724','5725',
                  '5726','5727','5728','5733','5734','5738','5739','V427')
  or just3{i} in ('570','571') then eliver=1;  /* Elixhauser liver disease*/
```

```
if just4{i} in ('5317','5319','5327','5329','5337','5339','5347','5349')
  then epudnb=1;  /* Elixhauser peptic ulcer disease, excluding bleeding*/

if just3{i} in ('042','043','044') then eaids=1;
   /* Elixhauser AIDS/HIV (same as Charlson)*/

if just3{i} in ('200','201','202') or just4{i} in ('2030','2386')
  then elymph=1;  /* Elixhauser lymphoma*/

if just3{i} in ('196','197','198','199') then emetas=1;
   /* Elixhauser metastatic cancer (same as Charlson)*/

if just3{i} in ('140','141','142','143','144','145','146','147','148','149',
                '150','151','152','153','154','155','156','157','158','159',
                '160','161','162','163','164','165','166','167','168','169',
                '170','171','172','174','175','176','177','178','179',
                '180','181','182','183','184','185','186','187','188','189',
                '190','191','192','193','194','195')
  then etumor=1;
   /* Elixhauser solid tumor without metastasis (excludes non-melanoma skin
      cancer, ICD9=173)*/

if just3{i} in ('446','714','720','725') or just4{i} in
  ('7010','7100','7101','7102','7103','7104','7108','7109',
   '7112','7193','7285') or fulldx{i} in ('72889','72930') then erheum=1;
   /* Elixhauser rheumatoid arthritis/collagen vascular diseases*/

if just3{i}='286' or just4{i} in ('2871','2873','2874','2875')
  then ecoag=1;  /* Elixhauser coagulopathy*/

if just4{i}='2780' then eobese=1;  /* Elixhauser obesity*/

if just3{i} in ('260','261','262','263') or just4{i} in ('7832','7994')
   then eweight=1;  /* Elixhauser weight loss*/

if just4{i}='2536' or just3{i}='276' then efluid=1;
   /* Elixhauser fluid and electrolyte disorders*/

if just4{i}='2800' then ebla=1;  /* Elixhauser blood loss anemia*/

if just4{i} in ('2801','2802','2803','2804','2805','2806','2807','2808','2809')
   or just3{i}='281' then edfa=1; /* Elixhauser deficiency anemia*/

if just4{i} in ('2652','2911','2912','2913','2915','2916','2917','2918','2919','3030',
                '3039','3050','3575','4255','5353','5710','5711','5712','5713''V113')
  or just3{i}='980' then ealc=1;  /* Elixhauser alcohol abuse*/

if just3{i} in ('292','304')
  or just4{i} in ('3052','3053','3054','3055','3056','3057','3058','3059')
  or fulldx{i}='V6542' then edrug=1;  /* Elixhauser drug abuse*/

if just4{i}='2938' or just3{i} in ('295','297','298')
  or fulldx{i} in ('29604','29614','29644','29654')
  then epsych=1;  /* Elixhauser psychoses*/

if just4{i} in ('2962','2963','2965','3004') or just3{i} in ('309','311')
  then edep=1;  /* Elixhauser depression*/

end;

ehyp=max(ehypuc,ehypc) ;
```

```
  /*Elixhauser hypertension (uncomplicated & complicated combined)*/

array elixind {32} echf earry evalve epulcir epvd ehyp ehypuc ehypc epara eoneuro epulmon
                   ediabuc ediabc ethyro erenal eliver epudnb eaids elymph emetas etumor
                   erheum ecoag eobese eweight efluid ebla edfa ealc edrug epsych edep ;
do i=1 to 32;
  if elixind{i}=. then elixind{i}=0;
end;

*********************************************************************************;
* Identify 20 Gagne Combined Romano-Elixhauser comorbidities on record (scan all dx)   *;
*********************************************************************************;
do i=1 to 24;

if just3{i} in ('196','197','198','199') then metastatic_romano = 1 ;

if fulldx{i} in ('40201', '40211', '40291') or just4{i} = '4293'
    or just3{i} in ('425','428') then chf_romano=1 ;

if just4{i} in ('3310', '3311', '3312') or just3{i} = '290' then dementia_romano=1;

if fulldx{i} in ('40311', '40391', '40412', '40492') or just3{i} in ('585', '586')
     or just4{i} in ('V420', 'V451', 'V560', 'V568') then renal_elixhauser=1 ;

if ('260' <= just3{i} <= '263') then wtloss_elixhauser=1;

if just3{i} in ('342', '344') then hemiplegia_romano=1;

if just4{i} in ('2911', '2912', '2915', '2918', '2919') or
 ('30390' <= fulldx{i} <= '30393') or ('30500' <= fulldx{i} <= '30503') or
  just4{i} = 'V113' then alcohol_elixhauser=1;

if ('140' <= just3{i} <= '171') or ('174' <= just3{i} <= '195') or
  just4{i} in ('2730','2733') or substr(fulldx{i},1,5) = 'V1046' or
 ('200' <= just3{i} <= '208') then tumor_romano = 1 ;

if fulldx{i} in ('42610', '42611', '42613') or ('4262' <= just4{i} <= '4264') or
  ('42650' <= fulldx{i} <= '42653') or ('4266' <= just4{i} <= '4268') or
 just4{i} in ('4270','4272') or fulldx{i} in ('42731','42760') or
  just4{i} in ('4279','7850','V450','V533')
  then arrhythmia_elixhauser=1;

if just4{i} in ('4150', '4168', '4169') or
  just3{i} in ('491','492','493','494','496') then pulmonarydz_romano=1;

if '2860' <= just4{i} <= '2869' or just4{i} = '2871' or ('2873' <= just4{i} <= '2875')
    then coagulopathy_elixhauser=1;

if ('25040' <= fulldx{i} <= '25073') or ('25090' <= fulldx{i} <= '25093')
    then compdiabetes_elixhauser=1 ;

if ('2801' <= just4{i} <= '2819') or just4{i} = '2859' then anemia_elixhauser=1;

if ('2760' <= just4{i} <= '2769') then electrolytes_elixhauser=1;

if fulldx{i} in ('07032','07033','07054') or just4{i} in ('4560','4561') or
   fulldx{i} in ('45620','45621') or just4{i} in ('5710','5712','5713') or
  ('57140' <= fulldx{i} <= '57149') or
   just4{i} in ('5715', '5716', '5718', '5719', '5723', '5728', 'V427')
   then liver_elixhauser=1;
```

```
if ('4400' <= just4{i} <= '4409') or just4{i} in ('4412', '4414', '4417', '4419') or
    ('4431' <= just4{i} <= '4439') or just4{i} in ('4471', '5571', '5579', 'V434')
    then pvd_elixhauser=1;

if ('29500' <= fulldx{i} <= '29899') or fulldx{i} in ('29910', '29911')
    then psychosis_elixhauser=1;

if just3{i} = '416' or just4{i} = '4179' then pulmcirc_elixhauser=1;

if just3{i} in ('042', '043', '044') then hivaids_romano=1;

if just4{i} in ('4011', '4019') or fulldx{i} in ('40210', '40290', '40410',
    '40490', '40511', '40519', '40591', '40599')
    then hypertension_elixhauser=1;

end;

array combcond {20}  metastatic_romano chf_romano dementia_romano renal_elixhauser
                     wtloss_elixhauser hemiplegia_romano alcohol_elixhauser tumor_romano
                     arrhythmia_elixhauser pulmonarydz_romano coagulopathy_elixhauser
                     compdiabetes_elixhauser anemia_elixhauser electrolytes_elixhauser
                     liver_elixhauser pvd_elixhauser psychosis_elixhauser
                     pulmcirc_elixhauser hivaids_romano hypertension_elixhauser ;
array combwts {20} _temporary_ (5  2  2  2  2  1  1  1  1  1  1  1  1  1  1  1  1  1 -1 -
1);

do i=1 to 20;
  if combcond{i}=. then combcond{i}=0;
end;

keep personid annper&per cmi cchf cpvd ccereb cdement cpulmon crheum cpeptic cmildliv
     cdiabwoc cdiabwic cplegia crenal cmalig csevliv cmetas caids
     echf earry evalve epulcir epvd ehypuc ehypc ehyp epara eoneuro epulmon ediabuc
     ediabc ethyro erenal eliver epudnb eaids elymph emetas etumor erheum ecoag eobese
     eweight efluid ebla edfa ealc edrug epsych edep  metastatic_romano chf_romano
     dementia_romano renal_elixhauser wtloss_elixhauser hemiplegia_romano
alcohol_elixhauser
     tumor_romano arrhythmia_elixhauser pulmonarydz_romano coagulopathy_elixhauser
     compdiabetes_elixhauser anemia_elixhauser electrolytes_elixhauser liver_elixhauser
     pvd_elixhauser psychosis_elixhauser pulmcirc_elixhauser hivaids_romano
     hypertension_elixhauser ;
run;
proc freq; tables annper&per;
run;
proc sort data=CLAIM&PER noequals; by personid;

proc summary data=CLAIM&PER max;
  var cmi cchf cpvd ccereb cdement cpulmon crheum cpeptic cmildliv
      cdiabwoc cdiabwic cplegia crenal cmalig csevliv cmetas caids
      echf earry evalve epulcir epvd ehyp ehypuc ehypc epara eoneuro epulmon
      ediabuc ediabc ethyro erenal eliver epudnb eaids elymph emetas etumor
      erheum ecoag eobese eweight efluid ebla edfa ealc edrug epsych edep
      metastatic_romano chf_romano dementia_romano renal_elixhauser wtloss_elixhauser
      hemiplegia_romano alcohol_elixhauser tumor_romano arrhythmia_elixhauser
      pulmonarydz_romano coagulopathy_elixhauser compdiabetes_elixhauser
      anemia_elixhauser electrolytes_elixhauser liver_elixhauser
      pvd_elixhauser psychosis_elixhauser pulmcirc_elixhauser hivaids_romano
      hypertension_elixhauser  ;
  output out=MAX&PER(drop=_type_ _freq_) max=;
  by personid;
  id annper&per;
```

```
run;

data score&per;
  set max&per;
  length charlson&per elix&per 3 ;
  elix&per=(echf+earry+evalve+epulcir+epvd+ehyp+epara+eoneuro+epulmon+
      ediabuc+ediabc+ethyro+erenal+eliver+epudnb+eaids+elymph+emetas+etumor+
      erheum+ecoag+eobese+eweight+efluid+ebla+edfa+ealc+edrug+epsych+edep) ;
  charlson&per=(1*cmi)+(1*cchf)+(1*cpvd)+(1*ccereb)+(1*cdement)+
      (1*cpulmon)+(1*crheum)+(1*cpeptic)+(1*cmildliv)+(1*cdiabwoc)+
      (2*cdiabwic)+(2*cplegia)+(2*crenal)+(2*cmalig)+
      (3*csevliv)+(6*cmetas)+(6*caids) ;
  combce&per=(5*metastatic_romano)+(2*chf_romano)+(2*dementia_romano)+
      (2*renal_elixhauser)+(2*wtloss_elixhauser)+(1*hemiplegia_romano)+
      (1*alcohol_elixhauser)+(1*tumor_romano)+(1*arrhythmia_elixhauser)+
      (1*pulmonarydz_romano)+(1*coagulopathy_elixhauser)+(1*compdiabetes_elixhauser)+
      (1*anemia_elixhauser)+(1*electrolytes_elixhauser)+(1*liver_elixhauser)+
      (1*pvd_elixhauser)+(1*psychosis_elixhauser)+(1*pulmcirc_elixhauser)+
      (-1*hivaids_romano)+(-1*hypertension_elixhauser) ;
  annper=&per;
run;

%mend;
%charelix(01) ;
%charelix(02) ;
%charelix(03) ;
%charelix(04) ;
%charelix(05) ;
%charelix(06) ;
%charelix(07) ;
%charelix(08) ;
%charelix(09) ;
%charelix(10) ;
%charelix(11) ;
%charelix(12) ;
%charelix(13) ;

run;

proc sort data=cheksample2; by personid;

data thenrol.comorbidity2(drop=i);
  length elix01-elix13 charlson01-charlson13 combce01-combce13 3 ;
  merge thenrol.dperson(in=ina keep=personid enti0 senti0 hmoi0 shmoi0 medpremon24
        smedpremon24 hmopremon24 shmopremon24 enrolix senrolix spersonid famid
        group role sample1-sample4)
        monsumms(in=inb)
        score01(keep=personid elix01 charlson01 combce01)
        score02(keep=personid elix02 charlson02 combce02)
        score03(keep=personid elix03 charlson03 combce03)
        score04(keep=personid elix04 charlson04 combce04)
        score05(keep=personid elix05 charlson05 combce05)
        score06(keep=personid elix06 charlson06 combce06)
        score07(keep=personid elix07 charlson07 combce07)
        score08(keep=personid elix08 charlson08 combce08)
        score09(keep=personid elix09 charlson09 combce09)
        score10(keep=personid elix10 charlson10 combce10)
        score11(keep=personid elix11 charlson11 combce11)
        score12(keep=personid elix12 charlson12 combce12)
        score13(keep=personid elix13 charlson13 combce13) ;
  by personid;
```

```
   if ina;
   array comorb {39} charlson01-charlson13 elix01-elix13 combce01-combce13 ;
   do i=1 to 39;
     if comorb{i} lt 0 then comorb{i}=0;
   end;
run;
proc means n min max mean data=thenrol.comorbidity2;
  var charlson01-charlson13 elix01-elix13 combce01-combce13 ;
  class group;
run;
proc corr; var charlson01 charlson06 charlson12 charlson13
               elix01 elix06 elix12 elix13
               combce01 combce06 combce12 combce13 ;
run;

*************************************************************************************;
* Program 2: Trajectory Models                                                      *;
*************************************************************************************;
libname thenrol 'd:\SAS Share Files\Research\Debra\Thesis Research\En8906 Validation' ;
libname x4traj 'd:\SAS Share Files\Research\Debra\Thesis Research\Traj Results Jun2014' ;

*************************************************************************************;
*Trajectory Analysis, Comb. Charlson-Elixhauser (Gagne=G) Comorbidity, Decedents Only  *;
*************************************************************************************;
options pageno=1;
run;
data work1;
  set thenrol.comorbidity2(keep=personid combce01-combce13 ovend01-ovend13 group sample4);
  if group='DIED' ;
  if sample4=1;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 1 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop1 outstat=x4traj.zdgos1 out=x4traj.zdgof1
  outest=x4traj.zdgoe1 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 1;
  order 2  ;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 2 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop2 outstat=x4traj.zdgos2 out=x4traj.zdgof2
  outest=x4traj.zdgoe2 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 2;
  order 2 2   ;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 3 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop3 outstat=x4traj.zdgos3 out=x4traj.zdgof3
  outest=x4traj.zdgoe3 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 3;
  order 2 2 2  ;
run;
```

```
title 'Decedents Only, Combination Charl-Elix (Gagne) 4 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop4 outstat=x4traj.zdgos4 out=x4traj.zdgof4
  outest=x4traj.zdgoe4 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 4;
  order 2 2 2 2  ;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 5 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop5 outstat=x4traj.zdgos5 out=x4traj.zdgof5
  outest=x4traj.zdgoe5 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 5;
  order 2 2 2 2 2 ;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 6 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop6 outstat=x4traj.zdgos6 out=x4traj.zdgof6
  outest=x4traj.zdgoe6 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 6;
  order 2 2 2 2 2 2;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 7 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop7 outstat=x4traj.zdgos7 out=x4traj.zdgof7
  outest=x4traj.zdgoe7 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 7;
  order 2 2 2 2 2 2 2;
run;
title 'Decedents Only, Combination Charl-Elix (Gagne) 8 Group Model (ZIP)';
proc traj data=work1 outplot=x4traj.zdgop8 outstat=x4traj.zdgos8 out=x4traj.zdgof8
  outest=x4traj.zdgoe8 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 8;
  order 2 2 2 2 2 2 2 2;
run;

*************************************************************************************;
* Trajectory Analysis, Combination Charl-Elix (Gagne) Comorbidity, Widowed Only, ZIP   *;
*************************************************************************************;
options pageno=1;
run;

data work2;
  set thenrol.comorbidity2(keep=personid combce01-combce13 ovend01-ovend13 group sample4);
  if sample4=1;
  if group='SURV' ;
```

```
run;

title 'Widowed Only, Combination Charl-Elix (Gagne) 1 Group Model (ZIP)'; run;
proc traj data=work2 outplot=x4traj.zwgop1 outstat=x4traj.zwgos1 out=x4traj.zwgof1
  outest=x4traj.zwgoe1 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip ;
  ngroups 1;
  order 2 ;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 2 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop2 outstat=x4traj.zwgos2 out=x4traj.zwgof2
  outest=x4traj.zwgoe2 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 2;
  order 2 2   ;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 3 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop3 outstat=x4traj.zwgos3 out=x4traj.zwgof3
  outest=x4traj.zwgoe3 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 3;
  order 2 2 2  ;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 4 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop4 outstat=x4traj.zwgos4 out=x4traj.zwgof4
  outest=x4traj.zwgoe4 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 4;
  order 2 2 2 2  ;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 5 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop5 outstat=x4traj.zwgos5 out=x4traj.zwgof5
  outest=x4traj.zwgoe5 itdetail  ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 5;
  order 2 2 2 2 2 ;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 6 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop6 outstat=x4traj.zwgos6 out=x4traj.zwgof6
  outest=x4traj.zwgoe6 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 6;
  order 2 2 2 2 2 2;
```

```
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 7 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop7 outstat=x4traj.zwgos7 out=x4traj.zwgof7
  outest=x4traj.zwgoe7 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 7;
  order 2 2 2 2 2 2 2;
run;
title 'Widowed Only, Combination Charl-Elix (Gagne) 8 Group Model (ZIP)';
proc traj data=work2 outplot=x4traj.zwgop8 outstat=x4traj.zwgos8 out=x4traj.zwgof8
  outest=x4traj.zwgoe8 itdetail ;
  id personid ;
  var combce01-combce13 ;
  indep ovend01-ovend13 ;
  model zip;
  ngroups 8;
  order 2 2 2 2 2 2 2 2;
run;

*************************************************************************************;
* Trajectory Analysis, Ambulatory Visits, Predeceased Only, ZIP                     *;
*************************************************************************************;
options pageno=1;
run;
data work1;
  set thenrol.comorbidity2(keep=personid ambvisits01-ambvisits12 monend01-monend12
  group sample4);
  if group='DIED' ;
  if sample4=1;
run;
title 'Decedents Only, Ambulatory Visits 1 Group Model';
proc traj data=work1 outplot=x4traj.davop1 outstat=x4traj.davos1 out=x4traj.davof1
  outest=x4traj.davoe1 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 1 ;
  order 2    ;
run;
title 'Decedents Only, Ambulatory Visits 2 Group Model';
proc traj data=work1 outplot=x4traj.davop2 outstat=x4traj.davos2 out=x4traj.davof2
  outest=x4traj.davoe2itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 2 ;
  order 2 2   ;
run;
title 'Decedents Only, Ambulatory Visits 3 Group Model';
proc traj data=work1 outplot=x4traj.davop3 outstat=x4traj.davos3 out=x4traj.davof3
  outest=x4traj.davoe3 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 3;
```

```
  order 2 2 2  ;
run;
title 'Decedents Only, Ambulatory Visits 4 Group Model';
proc traj data=work1 outplot=x4traj.davop4 outstat=x4traj.davos4 out=x4traj.davof4
  outest=x4traj.davoe4 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 4;
  order 2 2 2 2  ;
run;
title 'Decedents Only, Ambulatory Visits 5 Group Model';
proc traj data=work1 outplot=x4traj.davop5 outstat=x4traj.davos5 out=x4traj.davof5
  outest=x4traj.davoe5 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 5;
  order 2 2 2 2 2 ;
run;
title 'Decedents Only, Ambulatory Visits 6 Group Model';
proc traj data=work1 outplot=x4traj.davop6 outstat=x4traj.davos6 out=x4traj.davof6
  outest=x4traj.davoe6 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 6;
  order 2 2 2 2 2 2;
run;
title 'Decedents Only, Ambulatory Visits 7 Group Model';
proc traj data=work1 outplot=x4traj.davop7 outstat=x4traj.davos7 out=x4traj.davof7
  outest=x4traj.davoe7 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 7;
  order 2 2 2 2 2 2 2;
run;
title 'Decedents Only, Ambulatory Visits 8 Group Model';
proc traj data=work1 outplot=x4traj.davop8 outstat=x4traj.davos8 out=x4traj.davof8
  outest=x4traj.davoe8 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 8;
  order 2 2 2 2 2 2 2 2;
run;

*************************************************************************************;
* Trajectory Analysis, Ambulatory Visits, Widowed Only                              *;
*************************************************************************************;
options pageno=1;
run;

data work2;
  set thenrol.comorbidity2(keep=personid ambvisits01-ambvisits12 monend01-monend12
```

```
  group sample4);
  if sample4=1;
  if group='SURV' ;
run;

title 'Widowed Only, Ambulatory Visits 1 Group Model';
proc traj data=work2 outplot=x4traj.wavop1 outstat=x4traj.wavos1 out=x4traj.wavof1
  outest=x4traj.wavoe1 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 1;
  order 2   ;
run;
title 'Widowed Only, Ambulatory Visits 2 Group Model';
proc traj data=work2 outplot=x4traj.wavop2 outstat=x4traj.wavos2 out=x4traj.wavof2
  outest=x4traj.wavoe2 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 2;
  order 2 2   ;
run;
title 'Widowed Only, Ambulatory Visits 3 Group Model';
proc traj data=work2 outplot=x4traj.wavop3 outstat=x4traj.wavos3 out=x4traj.wavof3
  outest=x4traj.wavoe3 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 3;
  order 2 2 2  ;
run;
title 'Widowed Only, Ambulatory Visits 4 Group Model';
proc traj data=work2 outplot=x4traj.wavop4 outstat=x4traj.wavos4 out=x4traj.wavof4
  outest=x4traj.wavoe4 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 4;
  order 2 2 2 2  ;
run;
title 'Widowed Only, Ambulatory Visits 5 Group Model';
proc traj data=work2 outplot=x4traj.wavop5 outstat=x4traj.wavos5 out=x4traj.wavof5
  outest=x4traj.wavoe5 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 5;
  order 2 2 2 2 2 ;
run;
title 'Widowed Only, Ambulatory Visits 6 Group Model';
proc traj data=work2 outplot=x4traj.wavop6 outstat=x4traj.wavos6 out=x4traj.wavof6
  outest=x4traj.wavoe6 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
```

```
  model zip ;
  ngroups 6;
  order 2 2 2 2 2 2;
run;
title 'Widowed Only, Ambulatory Visits 7 Group Model';
proc traj data=work2 outplot=x4traj.wavop7 outstat=x4traj.wavos7 out=x4traj.wavof7
  outest=x4traj.wavoe7 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 7;
  order 2 2 2 2 2 2 2;
run;
title 'Widowed Only, Ambulatory Visits 8 Group Model';
proc traj data=work2 outplot=x4traj.wavop8 outstat=x4traj.wavos8 out=x4traj.wavof8
  outest=x4traj.wavoe8 itdetail;
  id personid ;
  var ambvisits01-ambvisits12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 8;
  order 2 2 2 2 2 2 2 2;
run;

*************************************************************************************;
* Trajectory Analysis, Inpatient Days Comorbidity, Decedents Only                   *;
*************************************************************************************;
options pageno=1;
run;
proc contents data=thenrol.comorbidity2;
run;
data work1;
  set thenrol.comorbidity2(keep=personid inpatdays01-inpatdays12 monend01-monend12
  group sample4);
  if group='DIED' ;
  if sample4=1;
  array inpatdays {12} inpatdays01-inpatdays12;
  sumdays=sum(of inpatdays{*}) ;
  if sumdays ge 1 then anydays=1; else anydays=0;
run;

title 'Decedents Only, Inpatient Days 1 Group Model';
proc traj data=work1 outplot=x4traj.didop1 outstat=x4traj.didos1 out=x4traj.didof1
  outest=x4traj.didoe1 itdetail altstart;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 1 ;
  order 2    ;
run;
proc print data=x4traj.didoe1;
run;
title 'Decedents Only, Inpatient Days 2 Group Model';
proc traj data=work1 outplot=x4traj.didop2 outstat=x4traj.didos2 out=x4traj.didof2
  outest=x4traj.didoe2 itdetail ;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
```

```
  ngroups 2 ;
  order 2 2   ;
run;
title 'Decedents Only, Inpatient Days 3 Group Model';
proc traj data=work1 outplot=x4traj.didop3 outstat=x4traj.didos3 out=x4traj.didof3
  outest=x4traj.didoe3 itdetail altstart;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 3;
  order 2 2 2  ;
  iorder 2 ;
run;
title 'Decedents Only, Inpatient Days 4 Group Model';
proc traj data=work1 outplot=x4traj.didop4 outstat=x4traj.didos4 out=x4traj.didof4
  outest=x4traj.didoe4 itdetail altstart;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 4;
  order 2 2 2 2  ;
  iorder 2 ;
run;
title 'Decedents Only, Inpatient Days 5 Group Model';
proc traj data=work1 outplot=x4traj.didop5 outstat=x4traj.didos5 out=x4traj.didof5
  outest=x4traj.didoe5 itdetail altstart;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 5;
  order 1 2 2 2 2 ;
  iorder 2 ;
run;
title 'Decedents Only, Inpatient Days 6 Group Model';
proc traj data=work1 outplot=x4traj.didop6 outstat=x4traj.didos6 out=x4traj.didof6
  outest=x4traj.didoe6 itdetail /*altstart*/;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 6;
  order 0 1 2 2 2 2;
  iorder 2 ;
run;
title 'Decedents Only, Inpatient Days 7 Group Model';
proc traj data=work1 outplot=x4traj.didop7 outstat=x4traj.didos7 out=x4traj.didof7
  outest=x4traj.didoe7 itdetail /*altstart*/;
  id personid ; /*does not converge*/
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 7;
  order 0 1 2 2 2 2 2 ;
  iorder 2 ;
run;
title 'Decedents Only, Inpatient Days 8 Group Model';
proc traj data=work1 outplot=x4traj.didop8 outstat=x4traj.didos8 out=x4traj.didof8
  outest=x4traj.didoe8 itdetail /*altstart*/;
```

```
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 8;
  order 0 1 1 2 2 2 2 2;
  iorder 2 ;
 run;

*******************************************************************************************;
* Trajectory Analysis, Inpatient Days Comorbidity, Widowed Only                           *;
*******************************************************************************************;
options pageno=1;
run;

data work2;
  set thenrol.comorbidity2(keep=personid inpatdays01-inpatdays12 monend01-monend12
  group sample4);
  if sample4=1;
  if group='SURV' ;
  array inpatdays {12} inpatdays01-inpatdays12;
  sumdays=sum(of inpatdays{*}) ;
  if sumdays ge 1 then anydays=1; else anydays=0;
run;
proc freq; tables anydays;
run;

title 'Widowed Only, Inpatient Days 1 Group Model'; run;
proc traj data=work2 outplot=x4traj.widop1 outstat=x4traj.widos1 out=x4traj.widof1
  outest=x4traj.widoe1 itdetail altstart;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 1;
  order 2    ;
 run;
title 'Widowed Only, Inpatient Days 2 Group Model';
proc traj data=work2 outplot=x4traj.widop2 outstat=x4traj.widos2 out=x4traj.widof2
  outest=x4traj.widoe2 itdetail ; /*altstart failed to converge*/
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 2;
  order 2 2   ;
run;
title 'Widowed Only, Inpatient Days 3 Group Model';
proc traj data=work2 outplot=x4traj.widop3 outstat=x4traj.widos3 out=x4traj.widof3
  outest=x4traj.widoe3 itdetail /*altstart failed*/;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 3;
  order 2 2 2  ;
run;
title 'Widowed Only, Inpatient Days 4 Group Model';
proc traj data=work2 outplot=x4traj.widop4 outstat=x4traj.widos4 out=x4traj.widof4
  outest=x4traj.widoe4 itdetail   ;
  id personid ;
```

```
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 4;
  order 1 1 2 2  ;
run;
title 'Widowed Only, Inpatient Days 5 Group Model';
proc traj data=work2 outplot=x4traj.widop5 outstat=x4traj.widos5 out=x4traj.widof5
  outest=x4traj.widoe5 itdetail /*altstart not used*/;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 5;
  order 1 2 2 2 2 ;
 run;
title 'Widowed Only, Inpatient Days 6 Group Model';
proc traj data=work2 outplot=x4traj.widop6 outstat=x4traj.widos6 out=x4traj.widof6
  outest=x4traj.widoe6 itdetail itdetail /*altstart gave FC*/;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 6;
  order 1 1 1 2 2 2;
 run;
title 'Widowed Only, Inpatient Days 7 Group Model';
proc traj data=work2 outplot=x4traj.widop7 outstat=x4traj.widos7 out=x4traj.widof7
  outest=x4traj.widoe7 itdetail;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 7;
  order 0 1 2 2 2 2 2;
 run;
title 'Widowed Only, Inpatient Days 8 Group Model';
proc traj data=work2 outplot=x4traj.widop8 outstat=x4traj.widos8 out=x4traj.widof8
  outest=x4traj.widoe8 itdetail;
  id personid ;
  var inpatdays01-inpatdays12 ;
  indep monend01-monend12 ;
  model zip ;
  ngroups 8;
  order 0 1 1 2 2 2 2 2;
 run;

*************************************************************************************;
* Program 3:  Create Final Data Set Combining All Info for Bereaved Sample          *;
*************************************************************************************;
libname thenrol 'd:\SAS Share Files\Research\Debra\Thesis Research\En8906 Validation' ;
libname x4traj 'd:\SAS Share Files\Research\Debra\Thesis Research\Traj Results Jun2014' ;

options obs=max;
proc contents data=thenrol.dperson;
run;
proc contents data=thenrol.comorbidity2;
run;

proc sort data=thenrol.dperson out=dperson;
  by personid;
```

```
proc sort data=thenrol.comorbidity2(where=(sample4=1))
  out=comorbidity2(keep=personid combce01-combce13 ambvisits01-ambvisits12
                        inpatdays01-inpatdays12 anyhospice);
  by personid;
run;
data work1;
  merge dperson(in=ina) comorbidity2(in=inb);
  by personid;
  if ina and inb;
  if sample4=1;
  array inpatdays {12} inpatdays01-inpatdays12 ;
  if sum(of inpatdays{*}) ge 1 then anyhospital=1;
  else anyhospital=0;
run;
proc freq; tables group role anyhospital group*anyhospital;
run;

proc format;
  value place 1='1:Hosp. Inpatient'
              2='2:Hosp. Outpatient'
              3='3:Hosp. DOA'
              4='4:Hosp UK'
              5='5:Nursing Home'
              6='6:Home'
              7='7:Other'
              9='8:Unknown'
              .='99: No Cert' ;
  value agefmt  65-74='65-74'
                75-84='75-84'
                85-HIGH='85+' ;
  value $racefmt '1'='White'
                 '2'='Black'
                 '0','3','4','5','6'='Other' ;
  value $resfmt '1'='Own'
                '2'='Rent'
                '3','4','9'='Nurs/PersCare'
                '5'='Relative'
                '6','0'='Other/Missing' ;
  value zero 0='Zero'
        other='Nonzero' ;
run;

options pageno=1 dtreset;
title 'Descriptive Information for Table 1' ;
proc freq data=work1; tables indexyr dage sex race resid place sanyhospice;
  where group='SURV' ;
  format dage agefmt. race $racefmt. resid $resfmt. sresid $resfmt.;
run;
proc freq data=work1;
  tables sanyhospice*(sanyhospice07 sanyhospice08 sanyhospice09 sanyhospice10
sanyhospice11 sanyhospice12);
  where group='SURV' ;
run;
proc means data=work1 n median; var indexyr dage;
  class group;
run;
title 'Morbidity Information for Predeceased Spouses, Table 2.A' ;
run;
proc means data=work1 n min max mean std p25 p50 p75 ;
  where group='DIED' ;
  var combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
```

```
      inpatdays12 ambvisits01 ambvisits06 ambvisits12 ;
run;
proc freq data=work1;
  where group='DIED' ;
  tables combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
    inpatdays12 ambvisits01 ambvisits06 ambvisits12 ;
  format combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
    inpatdays12 ambvisits01 ambvisits06 ambvisits12 zero. ;
run;
title 'Morbidity Information for Bereaved Spouses, Table 2.B' ;
run;
proc means n min max mean std p25 p50 p75 ;
  where group='SURV' ;
  var combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
      inpatdays12 ambvisits01 ambvisits06 ambvisits12 ;
run;
proc freq data=work1;
  where group='SURV' ;
  tables combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
      inpatdays12 ambvisits01 ambvisits06 ambvisits12 ;
  format combce01 combce06 combce12 combce13 inpatdays01 inpatdays06
      inpatdays12 ambvisits01 ambvisits06 ambvisits12 zero. ;
run;

title 'Create Bereaved File Which Will be Used for Survival Analysis';
run;
data bereaved1;
  set work1;
  if group='SURV' and sample4=1;
  length v1-v36 iter censor 3 dur 4 ;
  array pbeg {14} dpacebeg1-dpacebeg14 ;
  array pend {14} dpaceend1-dpaceend14 ;
  array postpace {36} pdayspo1-pdayspo36 ;
  array zeroval {36} v1-v36 ;
  do i=1 to 36;
    if postpace{i} le 0 then zeroval{i}=i;
 else zeroval{i}=99;
  end;
  minmonth=min(of zeroval{*}) ;
  if minmonth lt 99 then minday=round(minmonth*30.25) ;
  else if minmonth=99 then minday=1095;
  do i=1 to 14;
    if pbeg{i} le 0 and pend{i} ge 1095 then fullen1=1;
   /*single line of coverage covers all 3 years*/
    if dsecdod ge 0 and pbeg{i} le 0 and pend{i} ge dsecdod then fullen2=1;
   /*single lines of coverage covers up to death date*/
  end;
  if (dsecdod=. or dsecdod gt 1095) and fullen1=1 then do;
    iter=1;
   /*iter=1: single line of coverage spans study period and dsecdod gt 1095...
    censor at end of study*/
    censor=0;
 dur=1095;
  end;
  else if (0<=dsecdod<=1095) and fullen1=1 then do;
    iter=2;
   /*iter=2: single coverage line spans whole study period, but died before end of
    study... event time=deathdt*/
 censor=1;
 dur=dsecdod;
end;
```

```
 else if (0<=dsecdod<=1095) and fullen2=1 then do;
   iter=3;
  /*iter=3: single line of coverage spans from beginning of study up until death date...
   event time=deathdt*/
 censor=1;
 dur=dsecdod;
 end;
 else if dsecdod=. and minmonth=99 then do;
    iter=4;
 /*iter=4: no death date, and first month with zero days PACE coverage is after end
    of study ...censor at study end*/
 censor=0;
 dur=1095;
 end;
 else if (0<=dsecdod<=minday) then do;
    iter=5;
 /*iter=5: death date between study beginning and first month with zero days PACE
    coverage ... event time=death date*/
 censor=1;
 dur=dsecdod;
 end;
 else if (0<=minday<dsecdod) and minmonth ne 99 then do;
    iter=6;
 /*iter=6: first day with zero days PACE coverage is before death date ...
  censor at beginning of 1st month with zero coverage*/
 censor=0;
 dur=minday;
 end;
 else if dsecdod gt 1095 and minmonth=99 then do;
    iter=7;
 /*iter=7: died after study end and first day with zero days PACE coverage is after
    study end ... censor at study end*/
 censor=0;
 dur=1095;
 end;
 else if dsecdod=. and minmonth ne 99 and (0<=minday<=1095) then do;
  iter=8;
 /*iter=8: no death date, and first month with zero days PACE coverage is before
   study  end ... censor at beginning of month with no covg*/
 censor=0;
 dur=minday;
 end;
run;
proc freq; tables iter event censor event*censor;
run;
proc print data=bereaved1;
  where iter=4 and ranuni(4) le .01;
  var dsecdod fullen1 fullen2 iter event dur minday minmonth dpacebeg1
      dpaceend1 dpacebeg2 dpaceend2 dpacebeg3 dpaceend3 ;
run;

data dcctraj6; /*deceased 6-grp membership for combined comorbidity*/
  set x4traj.zdgof6(keep=personid group rename=(group=dcc6grp personid=spersonid));
  label dcc6grp='Deceased CombComorb Group (from 6-grp dsoln)' ;
run;
data dcctraj5; /*deceased 5-grp membership for combined comorbidity*/
  set x4traj.zdgof5(keep=personid group rename=(group=dcc5grp personid=spersonid));
  label dcc5grp='Deceased CombComorb Group (from 5-grp dsoln)' ;
run;
data davtraj6; /*deceased 6-grp membership for amb visits*/
  set x4traj.davof6(keep=personid group rename=(group=dav6grp personid=spersonid));
```

```
  label dav6grp='Deceased AmbVisit Group (from 6-grp dsoln)' ;
run;
data davtraj5; /*deceased 5-grp membership for amb visits*/
  set x4traj.davof5(keep=personid group rename=(group=dav5grp personid=spersonid));
  label dav5grp='Deceased AmbVisit Group (from 5-grp dsoln)' ;
run;
data didtraj4; /*deceased 4-grp membership for inpat days*/
  set x4traj.didof4(keep=personid group rename=(group=did4grp personid=spersonid));
  label did4grp='Deceased Inpat Days Group (from 4-grp dsoln)' ;
run;

data wcctraj5; /*widowed 5-grp membership for combined comorbidity*/
  set x4traj.zwgof5(keep=personid group rename=(group=wcc5grp));
  label wcc5grp='Widowed CombComorb Group (from 5-grp wsoln)' ;
run;
data wavtraj3; /*widowed 3-grp membership for amb visits*/
  set x4traj.wavof3(keep=personid group rename=(group=wav3grp));
  label wav3grp='Widowed AmbVisit Group (from 3-grp wsoln)' ;
run;
data widtraj3; /*widowed 3-grp membership for inpat days*/
  set x4traj.widof3(keep=personid group rename=(group=wid3grp));
  label wid3grp='Widowed Inpat Days Group (from 3-grp wsoln)' ;
run;
proc freq data=dcctraj5;
  tables dcc5grp;
run;

proc sort data=bereaved1;
  by spersonid;
proc sort data=dcctraj6;
  by spersonid;
proc sort data=dcctraj5;
  by spersonid;
proc sort data=davtraj6;
  by spersonid;
proc sort data=didtraj4;
  by spersonid;
run;

data bereaved2;
  merge bereaved1(in=ina) dcctraj6(in=inb) dcctraj5(in=inc)
        davtraj6(in=ind) davtraj5(in=ine) didtraj4(in=inf);
  by spersonid;
  if ina and inb and inc and ind and ine and inf;
run;

proc sort data=bereaved2;
  by personid;
proc sort data=wcctraj5;
  by personid;
proc sort data=wavtraj3;
  by personid;
proc sort data=widtraj3;
  by personid;
run;
data thenrol.bereaved(label='Bereaved Sample Working File for Survival Modeling, N=9967');
  merge bereaved2(in=ina) wcctraj5(in=inb) wavtraj3(in=inc) widtraj3(in=ind);
  by personid;
  if ina and inb and inc and ind;
run;
```

```
*******************************************************************************;
* Program 4:  Trajectory Plotting Macro File                                  *;
* Modified from download from PROC TRAJ website from Jones                    *;
* Original macro was written by H. Seltman and J. Lam, 1/19/1998              *;
*******************************************************************************;

/* SAS macro to plot expected and actual trajectories from PROC TRAJ */
/* H. Seltman and J. Lam, 1/19/98                                    */
/* Parameters:
    Name of outplot= dataset (not in quotes)
    Name of outstat= dataset (not in quotes)
    Title (in quotes)
    Subtitle (in quotes)
    Label for Y axis (in quotes, default is 'Outcome')
    Label for X axis (in quotes, default is 'T')
*/
/* Sample calls:
    %include 'c:\sas\traj\trajplot.mac';
    proc traj outplot=op outstat=os;
      ...
    run;
    %trajplot(op,os,'Main Title','Subtitle','y-axis text','x-axis text')
    %trajplot(op,os,'Main Title',' ','y-axis text','x-axis text')
    %trajplot(op,os,'Main Title','Subtitle','y-axis text')
    %trajplot(op,os,'Main Title','Subtitle')
    %trajplot(op,os,'Main Title')
*/


%macro trajplotrev(PlotFile,StatFile,Title1,/*Title2,*/Ylab,Xlab);
  %local Cnt GpPcts;
  %local pi1 pi2 pi3 pi4 pi5 pi6 pi7 pi8 pi9;
  %local maxcolor col1 col2 col3 col4 col5;
  %local i j clr aline pline;

*goptions reset=all ftext="Helvetica-Bold" dev=pdfc gsfname=output gsfmode=replace;
*filename output 'multirun.pdf';

  goptions reset=global gunit=pct cback=white colors=(black red green blue
    orange magenta cyan purple lime) rotate=portrait vsize=4.2in hsize=6in
    htitle=3.5 htext=3.5 ftext="Albany AMT"
    /*ftext="Helvetica-Bold"*/
    /*ftext=zapf dev=pdfc gsfname=output gsfmode=append rotate=landscape*/ device=emf
    /*targetdevice=pdfc*/ ;
  %CntPred(&PlotFile)
  %let Cnt=&PredCnt;

  /* Table of colors -- cycles back through used colors after maxcolor */
  %let maxcolor=9;
  %let col1=%STR(red);
  %let col2=%STR(green);
  %let col3=%STR(blue);
  %let col4=%STR(black);
  %let col5=%STR(orange);
  %let col6=%STR(magenta);
  %let col7=%STR(cyan) ;
  %let col8=%STR(purple) ;
  %let col9=%STR(lime) ;
  %DO i=%EVAL(&maxcolor + 1) %TO &Cnt;
    %let j=%EVAL(&i - &maxcolor);
```

```
    %let clr=&&col&j;
    %let col&i=&clr;
  %END;

  %DO i=1 %TO &Cnt;
    %let clr=&&col&i;
    symbol&i  color=&clr interpol=join value=&i. height=3;
  %END;
  %DO i=1 %TO &Cnt;
    %let clr=&&col&i;
    symbol1&i color=&clr interpol=join line=2;
  %END;

  %if %length(&Ylab)=0 %then %let Ylab='Outcome';
  %if %length(&Xlab)=0 %then %let Xlab='T';

  /* Dynamically create avgn*t ... and predn*t ... lines */
  %LET aline=;
  %LET pline=;
  %DO i=1 %TO &Cnt;
    %LET aline=%STR(&aline avg&i*t);
    %LET pline=%STR(&pline pred&i*t);
  %END;

  /* Get group percentages */
  %GetPIs
  %let GpPcts=;
  %do i=1 %to &Cnt;
     %let GpPcts=%str(&GpPcts %'&&pi&i%');
  %end;
  %do i=1 %to &Cnt;
     %let GpPcts=%str(&GpPcts %' %');
  %end;

  /* Make plots */
  legend1 label=(h=3.5 'Group Percentages:') value=(%unquote(&GpPcts)) across=&Cnt;
  axis1 label=(h=3.5)
        order=(/*-365*/ -335 -305 -274 -244 -213 -183 -153 -122 -92 -62 -31 -1) ;
  axis2 label=("Predicted" justify=r "&unit" /*"Score"*/ h=3.5)
        order=(0 to 14 by 2) ;
    /*combined comorbidity - use 0 to 11 by 1, -365 to -1*/
    /*inpatient days - use 0 to 14 by 2, -335 to -1*/
    /*ambulatory visits - use 0 to 6 by 1, -335 to -1*/
  proc gplot data=&PlotFile;
    title1 &Title1 justify=left h=3.5;
 title2 ' ' h=0.5;
    plot  &pline / overlay legend=legend1 haxis=axis1 vaxis=axis2;
 format t 4.0 /*_numeric_ 4.0*/ pred1-pred&cnt 3.0 ;
    label t=&Xlab;
  run;

 %OUT:
 quit;
%mend trajplotrev;


/* Macro to find number of times in plot file */
%macro CntPred(PltData);
  %global PredCnt;
  %let PredCnt=0;
  proc contents data=&PltData noprint out=CPredTmp(keep=name);
```

```
  run;
  data _null_;
    retain icnt 0;
    set CPredTmp;
    if index(name,"PRED")>0 then icnt=icnt+1;
    call symput('PredCnt',left(put(icnt,12.)));
  run;
  proc datasets nolist;
    delete CPredTmp;
  run;
%mend CntPred;


/* Macro to get group percentages from stat file */
%macro GetPIs;
  data _null_;
    set &StatFile;
    call symput('pi'||left(put(_n_,1.)),left(put(pi,4.1)));
  run;
%mend GetPIs;

*************************************************************************************;
* Program 5:  Local PC Plotting with SAS Graph                                      *;
*************************************************************************************;
libname subtraj 'x:\research\debra\thesis research\Traj Results Jun2014' ;

*********************************************************;
* Run for each of these outcomes: zdg zwg did wid dav wav *;
*********************************************************;
%let prefix=zdg ;
%let dist=ZIP;
%let set=Exploratory Quadratic Trajectories ;
%let xtext=Time Before Index Date (Days) ;

data _null_;
 length sample $ 20 outcome $ 25 shortoutcome unit $ 6 ;
 if "&prefix"='zdg' then do;
 sample='Predeceased Spouses' ;
 outcome='Combined Comorbidity' ;
 shortoutcome='Combco' ;
 unit='Score' ;
 end;
 else if "&prefix"='zwg' then do;
 sample='Widowed Spouses' ;
 outcome='Combined Comorbidity' ;
 shortoutcome='Combco' ;
 unit='Score';
 end;
 else if "&prefix"='dav' then do;
 sample='Predeceased Spouses' ;
 outcome='Ambulatory Visits' ;
 shortoutcome='AmbVis' ;
 unit='Visits' ;
 end;
 else if "&prefix"='wav' then do;
 sample='Widowed Spouses' ;
 outcome='Ambulatory Visits' ;
 shortoutcome='AmbVis' ;
 unit='Visits' ;
 end;
 else if "&prefix"='did' then do;
```

```
 sample='Predeceased Spouses' ;
 outcome='Inpatient Days' ;
 shortoutcome='InpDay' ;
 unit='Days' ;
 end;
 else if "&prefix"='wid' then do;
 sample='Widowed Spouses' ;
 outcome='Inpatient Days' ;
 shortoutcome='InpDay' ;
 unit='Days' ;
 end;
 call symput ('sample',sample) ;
 call symput ('outcome',trim(outcome)) ;
 call symput ('shortoutcome',trim(shortoutcome)) ;
 call symput ('unit',trim(unit)) ;
run;

 /*format of statement = trajplotrev(PlotFile,StatFile,Title1,Ylab,Xlab)*/
*goptions device=emf colors=(black) rotate=landscape;
options orientation=portrait nodate nonumber;
ods rtf image_dpi=300 startpage=never bodytitle
  file="x:\research\debra\thesis research\Traj Results
Jun2014\Jun26_&shortoutcome._&sample..rtf";
data _null_;
    file print;
    put "FIGURE X, &PREFIX";
    file log;
run;
title "Figure &Prefix" ;
run;
%MACRO LOOPLOT(num);
  %include 'x:\research\debra\thesis research\programs\trajplotrev production
24Jun2014.sas';
  %TRAJPLOTREV(subtraj.&prefix.op&num,subtraj.&prefix.os&num,
     "&num Group Model", "&shortoutcome",
     "&xtext");
%MEND LOOPLOT;
run;
%LOOPLOT(1) ;
%LOOPLOT(2) ;
%LOOPLOT(3);
%LOOPLOT(4);
%LOOPLOT(5);
%LOOPLOT(6);
%LOOPLOT(7);
%LOOPLOT(8);
run;
quit;
run;
title ' ' ;
ods rtf close;
run;
quit;
run;

*******************************************************************************;
* Program 6:  Survival Analysis                                                *;
*******************************************************************************;
libname thesis 'd:\SAS Share Files\Research\Debra\Thesis Research' ;
libname thenrol 'd:\SAS Share Files\Research\Debra\Thesis Research\En8906 Validation' ;
libname x4traj 'd:\SAS Share Files\Research\Debra\Thesis Research\Traj Results Jun2014' ;
```

```
proc format;
  value age5fmt 65-69='65-69'
                70-74='70-74'
                75-79='75-79'
                80-84='80-84'
                85-HIGH='85+' ;
  value $racefmt '1'='White'
                 '2'='Black'
                 '0','3','4','5','6'='Other' ;
  value zero 0='Zero'
        other='Nonzero' ;
  value $pla2fmt 'HOME'='Home'
              'OTH','UK','ZZ'='Other/unknown'
             'NH'='Nursing Home/Institution'
             'INP','OUT','DOA'='Hospital'
              other='zother' ;
  value anyuse 0='No Use'
               1='Any Use' ;
run;
data work1;
  set thenrol.bereaved;

  ****************************************************;
  * create dummy variables to assess multicollinearity *;
  ****************************************************;

  length xfemale x6574 x7584 x85 xblack xothrace xhome xnh xhospital xothplace
         xdcc6grp1-xdcc6grp6 xwcc5grp1-xwcc5grp5 xdid4grp1-xdid4grp4
         xwid3grp1-xwid3grp3 xdav6grp1-xdav6grp6 xwav3grp1-xwav3grp3 3 ;

  if sex='F' then xfemale=1; else xfemale=0;

  if (65<=dage<=74) then x6574=1; else x6574=0;
  if (75<=dage<=79) then x7579=1; else x7579=0;
  if (80<=dage<=84) then x8084=1; else x8084=0;
  if dage ge 85 then x85=1; else x85=0;

  if race='2' then xblack=1; else xblack=0;
  if race in ('0','3','4','5','6') then xothrace=1; else xothrace=0;

  if place='HOME' then xhome=1; else xhome=0;
  if place='NH' then xnh=1; else xnh=0;
  if place in ('INP','OUT','DOA') then xhospital=1; else xhospital=0;
  if sum(xhome,xnh,xhospital) le 0 then xothplace=1; else xothplace=0;

  if dcc6grp=1 then xdcc6grp1=1; else xdcc6grp1=0;
  if dcc6grp=2 then xdcc6grp2=1; else xdcc6grp2=0;
  if dcc6grp=3 then xdcc6grp3=1; else xdcc6grp3=0;
  if dcc6grp=4 then xdcc6grp4=1; else xdcc6grp4=0;
  if dcc6grp=5 then xdcc6grp5=1; else xdcc6grp5=0;
  if dcc6grp=6 then xdcc6grp6=1; else xdcc6grp6=0;

  if wcc5grp=1 then xwcc5grp1=1; else xwcc5grp1=0;
  if wcc5grp=2 then xwcc5grp2=1; else xwcc5grp2=0;
  if wcc5grp=3 then xwcc5grp3=1; else xwcc5grp3=0;
  if wcc5grp=4 then xwcc5grp4=1; else xwcc5grp4=0;
  if wcc5grp=5 then xwcc5grp5=1; else xwcc5grp5=0;

  if did4grp=1 then xdid4grp1=1; else xdid4grp1=0;
  if did4grp=2 then xdid4grp2=1; else xdid4grp2=0;
```

```
  if did4grp=3 then xdid4grp3=1; else xdid4grp3=0;
  if did4grp=4 then xdid4grp4=1; else xdid4grp4=0;

  if wid3grp=1 then xwid3grp1=1; else xwid3grp1=0;
  if wid3grp=2 then xwid3grp2=1; else xwid3grp2=0;
  if wid3grp=3 then xwid3grp3=1; else xwid3grp3=0;

  if dav6grp=1 then xdav6grp1=1; else xdav6grp1=0;
  if dav6grp=2 then xdav6grp2=1; else xdav6grp2=0;
  if dav6grp=3 then xdav6grp3=1; else xdav6grp3=0;
  if dav6grp=4 then xdav6grp4=1; else xdav6grp4=0;
  if dav6grp=5 then xdav6grp5=1; else xdav6grp5=0;
  if dav6grp=6 then xdav6grp6=1; else xdav6grp6=0;

  if wav3grp=1 then xwav3grp1=1; else xwav3grp1=0;
  if wav3grp=2 then xwav3grp2=1; else xwav3grp2=0;
  if wav3grp=3 then xwav3grp3=1; else xwav3grp3=0;
run;
title 'Assess Multicollinearity for Combined Comorbidity Model Series' ;
proc reg data=work1;
/*exclude dummy reference groups of x6574 xmale xdcc6grp5 xwcc5grp2 xwhite xinp
nohospice*/
model dur=sanyhospice
  xhome xnh xothplace
  xdcc6grp1 xdcc6grp2 xdcc6grp3 xdcc6grp4 xdcc6grp6
  xwcc5grp1 xwcc5grp3 xwcc5grp4 xwcc5grp5
  x7579 x8084 x85 xblack xothrace
  / tol vif collin ;
run;
title 'Assess Multicollinearity for Inpatient Hospital Days Model Series' ;
proc reg data=work1; /*exclude dummy reference groups of x6574 xmale xdid4grp1 xwid3grp1
xwhite xinp nohospice*/
model dur=sanyhospice
  xhome xnh xothplace
  xdid4grp2 xdid4grp3 xdid4grp4
  xwid3grp2 xwid3grp3
  x7579 x8084 x85 xblack xothrace
/ tol vif collin ;
run;
title 'Assess Multicollinearity for Ambulatory Visit Model Series' ;
proc reg data=work1; /*exclude dummy reference groups of x6574 xmale xdcc6grp2 xwav3grp1
xwhite xinp nohospice*/
model dur=sanyhospice
  xhome xnh xothplace
  xdav6grp1 xdav6grp3 xdav6grp4 xdav6grp5 xdav6grp6
  xwav3grp2 xwav3grp3
  x7579 x8084 x85 xblack xothrace
  / tol vif collin ;
run;
title 'Assess Multicollinearity Among Morbidity Measures Only' ;
proc reg data=work1; /*exclude dummy reference groups */
model dur=xdcc6grp1 xdcc6grp2 xdcc6grp3 xdcc6grp4 xdcc6grp6
  xdid4grp2 xdid4grp3 xdid4grp4
  xdav6grp1 xdav6grp3 xdav6grp4 xdav6grp5 xdav6grp6
  xwcc5grp1 xwcc5grp3 xwcc5grp4 xwcc5grp5
  xwid3grp2 xwid3grp3
  xwav3grp2 xwav3grp3
  / tol vif collin ;
run;
title 'Assess Multicollinearity Among All E and V Measures' ;
proc reg data=work1; /*exclude dummy reference groups */
```

```
model dur=xdcc6grp1 xdcc6grp2 xdcc6grp3 xdcc6grp4 xdcc6grp6
  xdid4grp2 xdid4grp3 xdid4grp4
  xdav6grp1 xdav6grp3 xdav6grp4 xdav6grp5 xdav6grp6
  sanyhospice xhome xnh xothplace x7579 x8084 x85 xblack xothrace
  xwcc5grp1 xwcc5grp3 xwcc5grp4 xwcc5grp5
  xwid3grp2 xwid3grp3
  xwav3grp2 xwav3grp3
  / tol vif collin ;
run;
title 'Cross-Tabulations of Hospice Use and Morbidity' ;
proc freq data=work1;
  tables (dcc6grp did4grp dav6grp)*sanyhospice / nocol nopercent chisq;
run;
title 'Cross-Tabulations of Place of Death and Morbidity' ;
proc freq data=work1;
  tables place*sanyhospice / chisq;
  format place $pla2fmt. ;
run;

/*Save file and then use local PC SAS, not remote SAS, for graphics printing*/
data thesis.work1;
  set work1;
run;
libname xthesis 'x:\Research\Debra\Thesis Research' ;
data work1;
  set xthesis.work1;
  label dage='Age Group'
        dcc6grp='Predeceased Combined Comorbidity Trajectory Group'
        sex='Sex'
        race='Race'
        resid='Resid'
        dur='Survival Time (Days)'
        dav6grp='Predeceased Ambulatory Visits Trajectory Group'
        did4grp='Predeceased Inpatient Days Trajectory Group'
        wid3grp='Widowed Inpatient Days Trajectory Group'
        wav3grp='Widowed Ambulatory Visit Trajectory Group'
        wcc5grp='Widowed Combined Comorbidity Trajectory Group' ;
run;
title 'Overall Survival and Failure Functions' ;
proc lifetest data=work1 method=km timelist=(365 730 1095);
  time dur*censor(0) ;
run;
%macro lifeplot(groupvar) ;
proc lifetest data=work1 method=km outsurv=&groupvar.est timelist=(365 730 1095);
   time dur*censor(0);
   strata &groupvar / test=logrank;
   format dage age5fmt. race $racefmt. place $pla2fmt.  ;
   label dage="Age" place="Place of Death"  sanyhospice="Hospice Use" ;
run;
%mend;
%lifeplot(sex) ;
%lifeplot(dage) ;
%lifeplot(race) ;
%lifeplot(place) ;
%lifeplot(sanyhospice) ;
%lifeplot(dcc6grp) ;
%lifeplot(did4grp) ;
%lifeplot(dav6grp) ;
%lifeplot(wcc5grp) ;
%lifeplot(wid3grp) ;
%lifeplot(wav3grp) ;
```

```
run;
ods graphics on / border=off;
ods rtf image_dpi=300 startpage=never file="x:\research\debra\thesis research\Traj Results
Jun2014\KM1.rtf";
options nodate nonumber orientation=portrait;
title ' ' ;
goptions reset=global gunit=pct cback=white colors=(black red green blue orange
  magenta cyan purple lime) rotate=portrait vsize=4.2in hsize=6in
  htitle=3.5 htext=3.5 ftext="Albany AMT" device=emf ;
symbol1 line=2 color=blue i=stepj ;
symbol2 line=1 color=red i=stepj ;
symbol3 line=3 color=green i=stepj ;
symbol4 line=4 color=purple i=stepj ;
symbol5 line=5 color=orange i=stepj ;
symbol6 line=14 color=magenta i=stepj ;
axis1 label=(angle=90 'Survival Probability') order=(0.0 to 1 by 0.10);
axis2 label=('Survival Time (Days)') ;
proc gplot data=dcc6grpest;
  plot survival*dur=dcc6grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=did4grpest;
  plot survival*dur=did4grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=dav6grpest;
  plot survival*dur=dav6grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=wcc5grpest;
  plot survival*dur=wcc5grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=wid3grpest;
  plot survival*dur=wid3grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=wav3grpest;
  plot survival*dur=wav3grp / vaxis=axis1 haxis=axis2;
run;
proc gplot data=sexest;
  plot survival*dur=sex / vaxis=axis1 haxis=axis2;
run;
proc gplot data=dageest;
  plot survival*dur=dage / vaxis=axis1 haxis=axis2;
  format dage age5fmt. ;
run;
proc gplot data=raceest;
  plot survival*dur=race / vaxis=axis1 haxis=axis2;
  format race $racefmt.  ;
run;
proc gplot data=placeest;
  plot survival*dur=place / vaxis=axis1 haxis=axis2;
  format place $pla2fmt. ;
run;
proc gplot data=sanyhospiceest;
  plot survival*dur=sanyhospice / vaxis=axis1 haxis=axis2;
  format sanyhospice anyuse. ;
run;
quit;
ods rtf close;
run;

/*resume remote SAS session for Cox modeling*/
options nodate nonumber dtreset orientation=landscape;
*******************************************************************************;
```

```
* COMBINED COMORBIDITY                                                                *;
*************************************************************************************;
*FULL MODEL:  All E & V, plus all 2-way ExV interactions *;
 /*Predeceased 6-Group DCC Groups:
 Group 1:  Very low with late increase (11.9%)
 Group 2:  Stable low (23.4%)
 Group 3:  Worsen in last 6 mo (8.0%)
 Group 4:  Chronic medium (26.4%)
 Group 5:  Chronic high (19.5%) REF
 Group 6:  Steadily worsening (10.8%)
*/

proc phreg data=work1; /*initial full model, all variables*/
  class sex(ref='F') dage(ref=first) race(ref='White') dcc6grp(ref='5') wcc5grp(ref='2')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp wcc5grp dage sex race place sanyhospice
                        dcc6grp*wcc5grp dcc6grp*dage dcc6grp*sex dcc6grp*race
dcc6grp*place
                        dcc6grp*sanyhospice  ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;

proc phreg data=work1; /*chunk test dropping all interactions*/
  class sex(ref='F') dage(ref=first) race(ref='White') dcc6grp(ref='5') wcc5grp(ref='2')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp wcc5grp dage sex race place sanyhospice ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;

proc phreg data=work1; /*drop nonsignificant 2-way ix terms using backward elimination to
produce reduced full model (gold standard)*/
  class sex(ref='F') dage(ref=first) race(ref='White') dcc6grp(ref='5') wcc5grp(ref='2')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp wcc5grp dage sex race place sanyhospice
                        dcc6grp*wcc5grp dcc6grp*dage dcc6grp*sex dcc6grp*race
                        dcc6grp*place
                        dcc6grp*sanyhospice / selection=backward include=7;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;

proc phreg data=work1;
  /*reduced full model (gold standard) with contrasts and hazard ratios*/
  class sex(ref='F') dage(ref=first) race(ref='White') dcc6grp(ref='5') wcc5grp(ref='2')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp wcc5grp dage sex race place sanyhospice
                        dcc6grp*sanyhospice ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;

  hazardratio dcc6grp / diff=ref alpha=0.05 ;
  hazardratio sanyhospice / diff=ref alpha=0.05;

  /*alternatively to make all 6 x 2 table comparisons relative to the lowermost right
    cell (Group=5, No hospice) as in AEPI536D use following contrasts*/
  contrast 'DCC6GRP=1, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 1 0 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 1 0 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=2, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 1 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 1 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=3, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 1 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 1 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=4, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 1 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 1 0 / estimate=exp e ;
```

```
  contrast 'DCC6GRP=6, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 0 1
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 0 1 / estimate=exp e ;
run;

title 'Confounding Step 1: Drop Place';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') dcc6grp(ref='5') wcc5grp(ref='2')
  sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp dage sex race ;
  format dage age5fmt. race $racefmt.   ;
  hazardratio dcc6grp / diff=ref  ;
  hazardratio dcc6grp / at (sanyhospice=ALL); /****/
run;

title 'Confounding Step 2: Drop Race';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dcc6grp(ref='5') wcc5grp(ref='2')
  sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp dage sex ;
  format dage age5fmt.   ;
  hazardratio dcc6grp / diff=ref  ;
run;

title 'Confounding Step 3: Drop Sex';
proc phreg data=work1;
  class dage(ref=first) dcc6grp(ref='5') wcc5grp(ref='2') sanyhospice(ref='0') /
  param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp dage ;
  format dage age5fmt.  ;
  hazardratio dcc6grp / diff=ref  ;
run;

title 'Confounding Step 4: Add Sex Back to Model, Drop Age';
proc phreg data=work1; ;
  class sex(ref='F') dcc6grp(ref='5') wcc5grp(ref='2') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp sex ;
  hazardratio dcc6grp / diff=ref  ;
run;

title 'Confounding Step 5: Add DAGE Back to Model, Drop WCC5GRP';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dcc6grp(ref='5') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice dage sex ;
  format dage age5fmt.   ;
  hazardratio dcc6grp / diff=ref  ;
run;

title 'DCC Parsimonious Model';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dcc6grp(ref='5') wcc5grp(ref='2')
  sanyhospice(ref='0') /  param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp dage sex ;
  format dage age5fmt.   ;
  hazardratio sex /diff=ref ;
  hazardratio dage / diff=ref;
  hazardratio wcc5grp / diff=ref;
  hazardratio dcc6grp / diff=ref  ;
  hazardratio sanyhospice / diff=ref ;
  /*alternatively to make all 6 x 2 table comparisons relative to the lowermost right cell
  (Group=5, No hospice) as in AEPI536D use following contrasts*/
```

```
  contrast 'DCC6GRP=1, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 1 0 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 1 0 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=2, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 1 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 1 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=3, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 1 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 1 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=4, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 1 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 1 0 / estimate=exp e ;
  contrast 'DCC6GRP=6, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 0 1
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 0 1 / estimate=exp e ;
run;
title "Rerun Parsimonious DCC Model to Test for Violation of PH Assumption (Kleinbaum &
Klein Method)";
run;
proc phreg data=work1(keep=sex dage dcc6grp wcc5grp sanyhospice dur censor);
/*Kleinbaum and Klein Goodness-of-Fit test for PH*/
  class sex(ref='F') dage(ref=first) dcc6grp(ref='5') wcc5grp(ref='2')
  sanyhospice(ref='0') /  param=ref;
  model dur*censor(0) = dcc6grp sanyhospice wcc5grp dage sex dcc6grp*sanyhospice;
  format dage age5fmt.   ;
  output out=resid ressch=r1-r25  ;
run;
proc contents data=resid; /*see how many residuals were actually created*/
run;
data events; /*should be 1686 events*/
  set resid;
  if censor=1;
run;
proc rank data=events out=ranked ties=mean;
  var dur;
  ranks timerank;
run;
proc corr data=ranked ;
  var r1-r20;
  with timerank  ;
run;

data verify; /*to help verify that contrasts were specified correctly*/
  set work1;
  if dcc6grp='1' and sanyhospice=0 then newcat='1N' ;
  else if dcc6grp='1' and sanyhospice=1 then newcat='1H';
  else if dcc6grp='2' and sanyhospice=0 then newcat='2N' ;
  else if dcc6grp='2' and sanyhospice=1 then newcat='2H';
  else if dcc6grp='3' and sanyhospice=0 then newcat='3N' ;
  else if dcc6grp='3' and sanyhospice=1 then newcat='3H';
  else if dcc6grp='4' and sanyhospice=0 then newcat='4N' ;
  else if dcc6grp='4' and sanyhospice=1 then newcat='4H';
  else if dcc6grp='5' and sanyhospice=0 then newcat='5N' ;
  else if dcc6grp='5' and sanyhospice=1 then newcat='5H';
  else if dcc6grp='6' and sanyhospice=0 then newcat='6N' ;
  else if dcc6grp='6' and sanyhospice=1 then newcat='6H';
run;

title 'FINAL REDUCED MODEL';
proc phreg data=verify;
  class sex(ref='F') dage(ref=first) newcat(ref='5N') wcc5grp(ref='2') / param=ref;
  model dur*censor(0) = newcat wcc5grp dage sex wcc5grp*gt;
  if dur le 547 then gt=0;
  else if dur gt 547 then gt=1;
  format dage age5fmt.   ;
  hazardratio sex /diff=ref ;
```

```
  hazardratio dage / diff=ref;
  hazardratio wcc5grp / diff=ref;
  hazardratio newcat / diff=ref  ;
run;
title 'Final Extended Cox Model for DCC';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dcc6grp(ref='5') wcc5grp(ref='2')
  sanyhospice(ref='0') /  param=ref;
  model dur*censor(0) = dcc6grp sanyhospice dcc6grp*sanyhospice wcc5grp dage sex
  wcc5grp*gt ;
  format dage age5fmt.   ;
  if dur le 547 then gt=0;
  else if dur gt 547 then gt=1;
  hazardratio sex /diff=ref ;
  hazardratio dage / diff=ref;
  hazardratio wcc5grp / at (gt=0) diff=ref;
  hazardratio wcc5grp / at (gt=1) diff=ref;
  hazardratio dcc6grp / diff=ref  ;
  hazardratio sanyhospice / diff=ref ;
  hazardratio dcc6grp / at (sanyhospice=ALL) diff=ref;
  /*alternatively to make all 6 x 2 table comparisons relative to the lowermost
   right cell (Group=5, No hospice) as in AEPI536D use following contrasts*/
  contrast 'DCC6GRP=1, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 1 0 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 1 0 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=2, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 1 0 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 1 0 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=3, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 1 0 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 1 0 0 / estimate=exp e ;
  contrast 'DCC6GRP=4, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 1 0
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 1 0 / estimate=exp e ;
  contrast 'DCC6GRP=6, SANYHOSPICE=0 vs DCC6GRP=5, SANYHOSPICE=0' DCC6GRP 0 0 0 0 1
SANYHOSPICE 1 DCC6GRP*SANYHOSPICE 0 0 0 0 1 / estimate=exp e ;
run;


*******************************************************************************;
* INPATIENT HOSPITAL DAYS                                                     *;
*******************************************************************************;
*FULL MODEL:  All E & V, plus all 2-way ExV interactions *;
 /*Predeceased 4-Group DID Groups:
Group 1:  Low with gradual increase (35.0%)
Group 2:  Sharp acceleration in last 4 months (24.9%)
Group 3:  Acceleration in last 6 months (7.6%)
Group 4:  Zero or near zero, with very late increase in last month (28.3%)
*/
proc phreg data=work1; /*initial full model, all variables*/
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race place sanyhospice
                        did4grp*wid3grp did4grp*dage did4grp*sex did4grp*race
                        did4grp*place did4grp*sanyhospice  ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;
proc phreg data=work1; /*drop nonsignificant 2-way ix terms using backward elimination to
produce reduced full model (gold standard)*/
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race place sanyhospice
                        did4grp*wid3grp did4grp*dage did4grp*sex did4grp*race
                        did4grp*place did4grp*sanyhospice / selection=backward include=7;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
```

```
run;
title 'Reduced Full Model (Gold Standard), Inpatient Days';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race place sanyhospice ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
  hazardratio did4grp / diff=ref;
run;

title 'Reduced Full Model (Gold Standard), Inpatient Days, Drop V variables (automated
backward selection)';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race place sanyhospice
  /selection=backward slstay=0 include=1 ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;
title 'Step 1: Drop SANYHOSPICE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  place (ref='Hospital') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race place  ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
  hazardratio did4grp / diff=ref;
run;
title 'Step 2: Drop PLACE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') did4grp(ref='1') wid3grp(ref='1')
  / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex race   ;
  format dage age5fmt. race $racefmt.  ;
  hazardratio did4grp / diff=ref;
run;
title 'Step 3: Drop RACE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) did4grp(ref='1') wid3grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex   ;
  format dage age5fmt.   ;
  hazardratio did4grp / diff=ref;
run;
title 'Step 4: Keep Race Out, Now Drop WID3GRP';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) did4grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp dage sex    ;
  format dage age5fmt.   ;
  hazardratio did4grp / diff=ref;
run;
title 'Step 5: Add WID3GRP Back, Drop DAGE';
proc phreg data=work1;
  class sex(ref='F') did4grp(ref='1') wid3grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp wid3grp sex    ;
  hazardratio did4grp / diff=ref;
run;
title 'Step 5: Add DAGE Back, Drop Sex';
proc phreg data=work1;
  class did4grp(ref='1') wid3grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage     ;
  format dage age5fmt.   ;
  hazardratio did4grp / diff=ref;
```

```
run;
title 'Step 6: Add Sex Back, Final Reduced Model for Inpatient Days (Same as Step 4)';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) did4grp(ref='1') wid3grp(ref='1')  / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex   ;
  format dage age5fmt.   ;
  hazardratio did4grp / diff=ref;
  hazardratio wid3grp / diff=ref;
  hazardratio dage / diff=ref;
  hazardratio sex / diff=ref;
run;
title "Rerun Final DID Model to Test for Violation of PH Assumption (Kleinbaum & Klein
Goodness-of-Fit Method)";
proc phreg data=work1(keep=sex dage did4grp wid3grp sanyhospice dur censor);
  /*Kleinbaum and Klein Goodness-of-Fit test for PH*/
  class sex(ref='F') dage(ref=first) did4grp(ref='1') wid3grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex   ;
  format dage age5fmt.   ;
  format dage age5fmt.   ;
  output out=resid ressch=r1-r25  ;
run;
proc contents data=resid; /*see how many residuals were actually created*/
run;
data events; /*should be 1686 events*/
  set resid;
  if censor=1;
run;
proc rank data=events out=ranked ties=mean;
  var dur;
  ranks timerank;
run;
proc corr data=ranked ;
  var r1-r10;
  with timerank  ;
run;
title "Final Extended Cox Model for DID";
proc phreg data=work1(keep=sex dage did4grp wid3grp sanyhospice dur censor);
  class sex(ref='F') dage(ref=first) did4grp(ref='1') wid3grp(ref='1') / param=ref;
  model dur*censor(0) = did4grp wid3grp dage sex wid3grp*gt ;
  format dage age5fmt.  ;
  if dur le 547 then gt=0;
  else if dur gt 547 then gt=1;
  hazardratio did4grp / diff=ref;
  hazardratio wid3grp / at (gt=0) diff=ref;
  hazardratio wid3grp / at (gt=1) diff=ref ;
  hazardratio dage / diff=ref;
  hazardratio sex / diff=ref ;
run;

*************************************************************************************;
* AMBULATORY VISITS                                                                 *;
*************************************************************************************;
*FULL MODEL:  All E & V, plus all 2-way ExV interactions *;
 /*Predeceased 6-Group DAV Groups:
Group 1:  Stable zero or near-zero (32.2%)
Group 2:  Stable low (29.7%)
Group 3:  Stable medium (17.0%)
Group 4:  Late increase (12.4%)
Group 5:  Steady increase (4.7%)
Group 6:  Chronic high (4.0%)
*/
```

```
proc freq; tables dav6grp*(sanyhospice place) / chisq;
  format place $pla2fmt. ;
run;

proc phreg data=work1; /*initial full model, all variables*/
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race place sanyhospice
                        dav6grp*wav3grp dav6grp*dage dav6grp*sex dav6grp*race
dav6grp*place dav6grp*sanyhospice  ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;
proc phreg data=work1; /*drop nonsignificant 2-way ix terms using backward elimination to
produce reduced full model (gold standard)*/
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race place sanyhospice
                        dav6grp*wav3grp dav6grp*dage dav6grp*sex dav6grp*race
                        dav6grp*place dav6grp*sanyhospice / selection=backward include=7;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;
title 'Reduced Full Model (Gold Standard)';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race place sanyhospice ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
  hazardratio dav6grp / diff=ref;
run;
title 'Reduced Full Model (Gold Standard), Inpatient Days, Drop V variables (automated
backward selection)';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  place (ref='Hospital') sanyhospice(ref='0') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race place sanyhospice
  /selection=backward slstay=0 include=1 ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
run;
title 'Confounding Step 1: Drop SANYHOSPICE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  place (ref='Hospital') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race place ;
  format dage age5fmt. race $racefmt. place $pla2fmt.  ;
  hazardratio dav6grp / diff=ref;
run;
title 'Confounding Step 2: Drop PLACE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) race(ref='White') dav6grp(ref='3') wav3grp(ref='1')
  / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex race ;
  format dage age5fmt. race $racefmt.  ;
  hazardratio dav6grp / diff=ref;
run;
title 'Confounding Step 3: Drop RACE';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dav6grp(ref='3') wav3grp(ref='1') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex  ;
  format dage age5fmt.  ;
  hazardratio dav6grp / diff=ref;
run;
```

```
title 'Confounding Step 4: Drop WAV3GRP';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dav6grp(ref='3') / param=ref;
  model dur*censor(0) = dav6grp dage sex  ;
  format dage age5fmt.  ;
  hazardratio dav6grp / diff=ref;
run;
title 'Confounding Step 5: Add WAV3GRP Back and Drop DAGE';
proc phreg data=work1;
  class sex(ref='F') dav6grp(ref='3') wav3grp(ref='1') / param=ref;
  model dur*censor(0) = dav6grp wav3grp sex  ;
  hazardratio dav6grp / diff=ref;
run;
title 'Parsimonious Model for Ambulatory Visits';
proc phreg data=work1;
  class sex(ref='F') dage(ref=first) dav6grp(ref='3') wav3grp(ref='1') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex  ;
  format dage age5fmt.  ;
  hazardratio dav6grp / diff=ref;
  hazardratio wav3grp / diff=ref;
  hazardratio dage / diff=ref;
  hazardratio sex / diff=ref ;
run;
title "Rerun Parsimonious DAV Model to Test for Violation of PH Assumption (Schoenfeld
Residual Goodness-of-Fit Method)";
proc phreg data=work1(keep=sex dage dav6grp wav3grp sanyhospice dur censor);
/*Kleinbaum and Klein Goodness-of-Fit test for PH*/
  class sex(ref='F') dage(ref=first) dav6grp(ref='3') wav3grp(ref='1') / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex  ;
  format dage age5fmt.  ;
  format dage age5fmt.   ;
  output out=resid ressch=r1-r25  ;
run;
proc contents data=resid; /*see how many residuals were actually created*/
data events; /*should be 1686 events*/
  set resid;
  if censor=1;
run;
proc rank data=events out=ranked ties=mean;
  var dur;
  ranks timerank;
run;
title 'PH Diagnostics for Parsimonious DAV Model' ;
proc corr data=ranked ;
  var r1-r12;
  with timerank  ;
run;
title "Final Extended Cox Model for DAV";
proc phreg data=work1(keep=sex dage dav6grp wav3grp sanyhospice dur censor);
  class sex(ref='F') dage(ref=first) dav6grp(ref='3') wav3grp(ref='1')  / param=ref;
  model dur*censor(0) = dav6grp wav3grp dage sex wav3grp*gt ;
  format dage age5fmt.  ;
  format dage age5fmt.   ;
  if dur le 547 then gt=0;
  else if dur gt 547 then gt=1;
  hazardratio dav6grp / diff=ref;
  hazardratio wav3grp / at (gt=0) diff=ref;
  hazardratio wav3grp / at (gt=1) diff=ref ;
  hazardratio dage / diff=ref;
  hazardratio sex / diff=ref ;
run;
```