Reproductive History and Later Life Comorbidity Trajectories: Are the fertile Frail?

Heidi Hanson, University of Utah
Ken R. Smith, University of Utah
Zachary Zimmer, University of California, San Francisco

Abstract

The reproductive lives of men and women may provide significant insight into later life health and mortality. Sociological, biological, and evolutionary theories predict a relationship between reproductive history and later life health and mortality, however current research is lacking consensus on the direction of the relationship. In this study, the relationship between reproductive history and later life health is examined using data based on linkages between the Utah Population Database, a rich source of longitudinal data, and 18 years of Medicare Claims data. Later life health is measured using the Charlson Comorbidity Index, a construct that summarizes nearly all serious illnesses afflicting older individuals. Single year comorbidity scores are constructed by year from 1992 to 2009. We used group based trajectory modeling that accounts for non-random attrition due to death to identify the number and types of morbidity trajectories by sex and age group for 52,924 individuals aged 65-84 in 1992. For both males and females, trajectory groups ranged from a robust group with little to no comorbid conditions during the period of observation to a frail group with a consistently high comorbidity. Parity, age at first birth, age at last birth, marital status at time of birth, birth weight of offspring, and having a preterm birth predict trajectory group memberships for women but had little association with trajectory group membership for men.

Introduction

Understanding how individuals experience disease after age 65 is important to understanding the mechanisms of aging and longevity. Equally important is what predicts the observed patterns. The etiological model of chronic disease has shifted focus from adult risk factors to considering factors throughout the life course (Kuh and Ben-Shlomo 2004). Central to the life course approach is the idea that there are certain periods of plasticity, where individuals may experience physiological or social change that alter their future health trajectories. The reproductive period is a sensitive period for both men and women, in which the timing of births, number of births, and birth outcomes might have adverse or protective effects on later life health. It also presents a critical period for women as physiological changes related to pregnancy may have lifelong effects on the structure or function systems in the body (Kuh and Hardy 2002; Kuh and Ben-Shlomo 2004). Therefore, the reproductive lives of men and women may provide significant insight into later life health and mortality, however current research is lacking consensus on the direction of the relationship.

This study will examine the role of parity, young age at first birth, age at last birth, interbirth intervals, infant death, multiple births (twins), birth weight of offspring, and preterm births for both men and women on disease progression after age 65. This study utilizes Centers for Medicare (CMS) data spanning from 1992 – 2009 linked to the Utah Population Database, which is a rich source of longitudinal data. The goals of this analysis are threefold: 1- identify distinct trajectories of comorbidity from 1992 - 2009 for individuals age 66 – 84 in 1992 by sex and birth cohort; 2- estimate the association between measures of fertility and later life comorbidity trajectories while controlling for early life circumstances using information from a longitudinal, familial health database; 3- determine if the observed effects are part of a trajectory set in motion earlier in during infancy and childhood (i.e., does fertility mediate known relationships between early life circumstances and later life comorbidity trajectories (Smith, Hanson et al. 2012)).

Background

There is a substantial amount of variation in the morbidity profile of older adults, suggesting that morbidity is not an inevitable consequence of aging (Rowe and Kahn 1987;

Rowe and Kahn 1997). Understanding the sources of variation in patterns of aging is important for creating accurate population predictions, identifying at risk populations that may benefit from public health interventions, and characterizing the process of aging in a diverse population. Sources of heterogeneity in patterns of aging cannot be understood by restricting analyses to a single life stage nor can we understand its intricacies without simultaneously considering biological and social mechanisms. The pathology of chronic disease is multifaceted, determined by genetic profiles, biological and physiological development, and the social environment, with the strength and relative importance of each of these factors varying throughout the life course.

The literature lacks a clear consensus about a single definition of healthy or successful aging (Rowe and Kahn 1987; Rowe and Kahn 1997; Fried, Ferrucci et al. 2004; Ryff and Singer 2009), however chronic disease and comorbidity is often listed as one of the key components. Fried formally defines comorbidity as the "concurrent presence of two or more medically diagnosed diseases in the same individual, with the diagnosis of each contributing disease based on established, widely recognized criteria" (Fried, Ferrucci et al. 2004). While comorbidity can be defined in relation to an index disease (Valderas, Starfield et al. 2009), we will use the term comorbidity to refer to the presence of multiple diseases for the purpose of this paper.

The majority of studies assessing the relationship between reproductive history and health have focused on mortality and the results are mixed, however it is possible that this lack of consensus is due to different modeling strategies, data availability, and choice of measures (Hurt, Ronsmans et al. 2006). Numerous studies have also demonstrated the relationship between reproductive history and later life health as measured by activities of daily living (ADL), depressive symptoms, type 2 diabetes, cardiovascular disease, self-rated health, self-reported limiting chronic illness, cancer, and mental health (Kravdal 1995; Lawlor, Emberson et al. 2003; Davey Smith, Sterne et al. 2004; Yi and Vaupel 2004; Grundy and Tomassini 2005; Henretta 2008; Spence 2008; Myklestad, Vatten et al. 2012), yet none have looked at the relationship between reproductive history and comorbidity. These studies also often fail to account for early life conditions that may influence reproductive history and later life health.

Comorbidity is one of the major components of health aging and its presence increases with age (Guralnik 1996; Fried, Ferrucci et al. 2004) and there is variation in the rate at which a transition into a comorbid state occurs and the trajectory of disease once it has occurred. For

example, individuals exhibiting a robust phenotype may delay or evade chronic disease completely, while individuals exhibiting the frail phenotype experience multiple morbid conditions. (Evert, Lawler et al. 2003; Andersen, Sebastiani et al. 2012; Smith, Hanson et al. 2012). Identifying sources of this phenotypic variation is necessary to more fully understand the process of aging. Evolutionary, biological, and social theories predict that parity, age at first birth, age at last birth, interbirth intervals, twinning, birth weight of offspring, and giving birth prematurely may all be associated with later life morbidity and mortality. Focusing on morbidity profiles and may elucidate some of the mechanisms linking fertility and longevity.

Evolutionary and Genetic Theories Linking Reproductive Health to Aging

Evolutionary theories predict a close relationship between fertility and mortality. Optimization hypotheses suppose that the forces of evolution select for traits that maximize the reproductive success of an organism. Two such hypotheses, disposable soma and antagonistic pleiotrophy, predict a positive association between parity and comorbidity at advanced ages (Kirkwood and Rose 1991). The disposable soma theory argues that the two physiological costly functions of reproduction and somatic maintenance are in direct competition for a limited amount of resources. This "trade-off" yields optimal reproductive success at the cost of longevity for females (Kirkwood and Rose 1991). Similarly, antagonistic pleiotrophy suggests that genetic mutations that increase post-reproductive mortality may escape the force of natural selection if they increase fitness early on (Williams 1957; Kirkwood and Rose 1991). A recent study of fertility in breast cancer genes BRCA1 and BRCA2 carriers suggests that although these mutations significantly increase the risk of mortality, they may increase reproductive fitness and therefore have not been selected out of the population (Smith, Hanson et al. 2012). These theories predict that for females, young age at first birth and high parity are associated with increased comorbidity later in life.

High parity, late age at last birth, multiple births, and short birth intervals may also be associated with decreased comorbidity later in life. For example, it has been suggested that genetic variants influence both late female fertility and slowed rates of somatic aging (Smith, Gagnon et al. 2009). Fertility success may also be an indication of health status and robustness. Women with higher fertility, shorter birth intervals, twins, and later ages at last birth may have increased longevity because their fertility success is a marker of a robust phenotype (Hawkes

2010; Robson and Smith 2011; Robson and Smith 2012). While evolutionary theories are an important factor in the relationship between fertility and later life morbidity and mortality, it is necessary to consider the direct biological and indirect social effects of fertility history.

Direct Biological Effects of Reproductive Health

In the life course literature, physiological scarring has been used to define an event that permanently alters the physiological functioning of an organism. For women, pregnancy may trigger physiological changes that may favorably or adversely affect later life health. Increased parity and early age at first birth have been shown to lower the risk of post-menopausal reproductive cancer and it has been posited that biological factors are responsible for this link. Pregnancy is one of several factors that determines life time exposure to endogenous hormones and several hypotheses relate the level of endogenous hormones throughout the life course, such as androgen, insulin, progesterone, and estrogen, to cancer risk later in life (Kelsey, Gammon et al. 1993; Lukanova and Kaaks 2005; Kobayashi, Sugiura et al. 2012). There is an inverse association between parity and cancer incidence in tissues sensitive to hormone levels, such as breast, endometrial and ovarian (Kelsey, Gammon et al. 1993; Kvale, Heuch et al. 1994; Permuth-Wey and Sellers 2009; Kobayashi, Sugiura et al. 2012). Age at first birth has also a known risk factor for breast cancer, with younger age at first birth being a protective factor (MacMahon, Cole et al. 1973).

Reproductive history may also lead to physiological changes that adversely affect a woman's health. Pregnancy related biological responses may lead to increased risk for coronary heart disease and obesity later in life (Lawlor, Emberson et al. 2003; Bastian, West et al. 2005). A study of men and women aged 60 to 79 in Britain found a positive association between number of children and adverse lipid profiles and diabetes for women and not men, suggesting possible biological mechanisms (Lawlor, Emberson et al. 2003), however life style factors were also found to play a role in the association. Birth spacing and having multiple births (twins) may also leave a physiological imprint on the mother. The maternal depletion hypothesis argues that the physiological demands of pregnancy diminish physical resources and short birth intervals do not give the mother ample time to recover from the stresses of the previous pregnancy (Jelliffe and Jelliffe 1978; Kirkwood and Rose 1991). These theories predict a positive relationship between parity, short birth intervals, and multiple births and later life comorbidity.

Characteristics of offspring at birth may be a sentinel for later life health. Birth weight of the child and delivery of a preterm birth may be markers of the health and vitality of the mother (Davey-Smith 1997). Giving birth to a child that is considered large for gestational age is related to gestational diabetes (Casey, Lucas et al. 1997), a known risk factor for diabetes later in life (Bellamy, Casas et al. 2009). Studies have shown that there is a positive association between birth weight of a child and longevity (Smith, Hart et al. 1997; Smith, Whitley et al. 2000), however the studies do not test whether there is a threshold to this effect. Low offspring birth weight and premature delivery of a child have been associated with increased risk of cardiovascular disease and mortality later in life (Smith, Hart et al. 1997; Smith, Whitley et al. 2000). These studies suggest that high birth weight, low birth weight, and preterm babies are positively associated with later life comorbidity.

Social Mechanisms Indirectly Linking Reproductive History to Later Life Health

Social theories predict both positive and negative relationships between parity and later life morbidity. Rowe and Kahn (1987) suggest that social engagement and interpersonal relations is one of three components of successful aging. The social benefits of adult children may negate any adverse physiological effects of having children by providing social support, social engagement, and receipt of instrumental help. Strong social support may foster feelings of meaning, reduce feelings of stress, and minimize risky behavior. Individuals with more social support and intimate ties have better health and lower levels of mortality (Berkman and Syme 1979; House, Landis et al. 1988). Children may provide a support network later in life and having more children may increase the chance of having regular contact with at least one child (Uhlenberg and Cooney 1990) and receipt of help from children (Grundy and Read 2012). Psychological, social, and economic impacts of children may also lead to a negative relationship between parity and later life morbidity. Increasing parity is associated with obesity and coronary heart disease for both men and women, suggesting that lifestyle factors associated with high parity may lead to increased risk of morbidity later in life (Lawlor, Emberson et al. 2003). Increased parity may not translate to increased social support. Smith (2002) suggests that high parity children may have less resources to devote to their parents and due to the intergenerational transmission of fertility, high parity may lead to decreased social support from children later in

life. These results suggest that the effect of fertility may be positive or negative for males and females.

Early parenthood may lead to decreased opportunities for education and employment (Ross and Huber 1985; Waldron, Weiss et al. 1998), which has been shown to lead to adverse health consequences later in life (Mirowsky 2005; Phelan, Link et al. 2010). Mirowsky (2005) suggests that the optimal period for childbirth in relation to health is in the mid-thirties, however this finding may be unique to the historical and social environment. The current literature presents conflicting findings related to the benefits of age at last birth after age 39, with some studies suggesting that later ages at last birth are protective (Smith, Mineau et al. 2002; Smith, Mineau et al. 2009) and others find adverse effects (Mirowsky 2005).

Considering events throughout the life course that affect fertility and morbidity

Failure to look at the relationship between fertility and morbidity using a life course perspective and controlling for early life circumstances can lead to an overstatement of their association. Early life factors may affect the reproductive health and behaviors of men and women (Rich-Edwards 2002; Doblhammer and Oeppen 2003), and therefore part of the observed association between fertility and later life morbidity is merely a reflection of genetic makeup or physiological changes during childhood. For example, adverse childhood and adolescent circumstances are also related to early motherhood (Geronimus and Korenman 1992) and later life health (Preston, Hill et al. 1998; Galobardes, Lynch et al. 2008; Smith, Mineau et al. 2009). For this reason, we will include measures of early life circumstances that may affect fertility and later-life health outcomes.

The research question addressed in this paper is whether measures of fertility and reproductive health are associated with morbidity profiles later in life. We will examine the role of parity, young age at first birth, age at last birth, interbirth intervals, infant death, multiple births (twins), marital status at time of birth, birth weight of offspring, and preterm births for both men and women. We are able to control for a range of early life circumstances including familial excess longevity, childhood socioeconomic status, and death of a parent during childhood. The specific hypothesis generated by suggested evolutionary, social, and biological mechanisms are as follows:

H1: *The optimization of life history traits leads to a "trade-off" between fertility and somatic maintenance.* According to this hypothesis, increased parity and shorter birth intervals should be positively associated with comorbidity after age 65 for females and age at last birth should be negatively associated with comorbidity after age 65.

H2: *Childbirth leads to physiological changes that adversely affect later life health*. According to this hypothesis increased parity, shorter birth intervals, later age at last birth, and unhealthy (high/low) birth weight of offspring should be adversely associated with later life comorbidity after age 65 for females and not males.

H3: *Reproductive history is a marker of a robust phenotype.* According to this hypothesis, increased parity, shorter birth intervals, later age at last birth, and twinning should be negatively associated with comorbidity after age 65 for both sexes and possibly stronger for females.

H4: *Social mechanisms are responsible for the observed association between reproductive history and comorbidity after 65.* According to this theory the observed effects of fertility history should be similar for males and females but there are competing hypotheses about the direction of the effect.

> H4a: Increased parity is negatively associated with comorbidity after age 65 because children provide material, instrumental, and social support for both men and women.
>
> H4b: Increased parity is positively associated with comorbidity after age 65 because the psychological, social, and economic effects of having children outweigh the social benefit. Children may also be unable to provide support because they are caring for their own large families.
>
> H4c: Early age at first birth is positively associated with comorbidity after age 65 because it leads to constrained economic and educational opportunities. Late age at first birth is negatively associated with comorbidity after age 65 because it leads to increased educational and economic opportunities.

Data

The majority of life-span epidemiological studies examine health influences of early and adult life conditions with relatively modest sample sizes. This study utilizes data drawn from the Utah Population Database (UPDB). The UPDB is one of the world's richest sources of linked population-based information for demographic, genetic, and epidemiological studies. UPDB has supported biodemographic studies as well numerous important epidemiological and genetic studies in large part because of its size, pedigree complexity, and linkages to numerous data sources. The full UPDB now contains data on nearly 7 million individuals due to longstanding and on-going efforts to add new sources of data and update records as they become available (e.g., including all statewide death certificate records (1904-present) and all Medicare claims (1992-2009). We have identified thousands of members of birth cohorts from the first half of the 20th century, individuals for whom early and midlife conditions are measured and who are linked to their adult medical records generated decades later. It is these complex data links that provide unparalleled data quality and depth that focus on families (nuclear, multigenerational, full pedigrees) and health outcomes that span entire life spans of individuals and their relatives.

Given the large sample sizes and the quickly changing morbidity risks by age and sex, we will conduct all analysis by sex and ten year age categories (66-74 and 75-84); the first age category begins at age 66 to eliminate the problems of prorating the partial year coverage of individuals who become age eligible part way into a year when they turn age 65. Ages are considered in 1992, the first year in which we have Medicare data. Separating samples by age effectively holds cohort constant and allows us to analyze the trends by birth cohort for an 18 year period. Individuals age 66 – 74 and 75 – 84 in 1992 are considered members of the young-old cohort (born between 1918 and 1926) and old-old cohort (born 1908 – 1917), respectively.

We selected once married parous individuals. Once married individuals were selected to limit complications related to fertility spanning more than one marriage partner. The CMS data requires an individual to survive to the age of 66, therefore all women would have completed their childbearing. Selecting parous individuals helps in the identification of the multivariate effects of both the intensity and timing of fertility on comorbidity trajectories. This analysis is not intended to account for the impact of childlessness (Smith, Mineau et al. 2002; Gagnon, Smith et al. 2009). Individuals were also required to have sufficient information about parents in the database, which allowed for the inclusion of early life circumstances in the model.

Centers for Medicare Services (CMS) provides files that allow us to assess whether an individual is sufficiently represented in the Medicare claims data so that they can contribute to the construction of the morbidity trajectories. Our goal is to avoid characterizing someone as being disease-free when in fact their health events are simply not well represented in the Medicare data. CMS provides a monthly HMO indicator variable that describes when a beneficiary was enrolled in a managed care plan. As expected, few claims exist in the file for individuals during the time they are enrolled in a managed care plan. For the purposes of this analysis, we exclude persons who have at least one month of enrollment in a managed care plan.

Subjects who met our data requirements (e.g., once married parous individuals for whom we have family data (parental death dates and full fertility history) are shown in Table 1. Individuals were then followed for a maximum of 18 years (to 2009), our last year of Medicare data, or until death. The total sample size is N=52,924; age specific sample sizes are shown in Table 1.

Table 1 here

A secondary analysis of individuals aged 66 to 74 in 1992 was done using the information from birth certificates. Birth certificate information in the UPDB is available from 1915 to 1921 and 1943 to the present, however birth weight was not recorded until 1947. Because we are interested in birth weight and prematurity, all individuals used in this analysis were required to have their first birth in 1947 or later and all births in Utah (giving us complete fertility information). Approximately 32% of women and 53% of men in the young-old cohort have birth certificate records for all births. Individuals age 66 and 74 in 1992 would have had to have their first birth at age 21 if they were the youngest members of the cohort 29 if they were the oldest. For females, the average age at first birth in the birth certificate sample is 4.5 years greater than those excluded (26.7 vs. 22.2, p=0.001) and for males it is 3 years greater than those excluded (27.6 vs. 24.6, p=0.001). These requirements make this a select cohort, however the benefits of linking birth outcomes to later life health trajectories makes this a valuable analysis.

Key Measures

Comorbidity

We are able to observe morbidity episodes from Medicare claims collected over time for each individual. Health experience over time is measured by the Charlson comorbidity index

(CCI) (Charlson, Pompei et al. 1987). The CCI was adapted for use with ICD-9 codes by Deyo et al (Deyo, Cherkin et al. 1992) and Romano et al (Romano, Roos et al. 1993). Deyo et al adapted the index for use with ICD-9 diagnosis and procedure codes. Romano et al included some diagnoses that were not in the original Charlson index. Both modifications were intended for use with the Medicare Part A records (Klabunde, Potosky et al. 2000). Klabunde and colleagues (Klabunde, Warren et al. 2002) created two indices, one for Medicare Part A records and one for Medicare Part B records. Introducing information from physician claims data significantly enhanced the index's predictive value for the risk of mortality. In the present study, we have adopted this variant of the CCI based on the SEER-Medicare Comorbidity macros (http://healthservices.cancer.gov/seermedicare/program/comorbidity.html). We classify individuals into similar trajectory groups with respect to their morbidity patterns identified by their shared health experiences over time.

The SEER-Medicare macro calculates the CCI with respect to cancer based on the Deyo adaptation of the index. Given that cancer originally was the index disease, it was not included as a co-morbid condition in this SEER-Medicare program. Accordingly, we have added cancer and as a co-morbid disease. We identified specific episodes of the following 17 major morbidities conditions occurring during the interval 1992-2009 on a per annum basis that form the basis of the CCI. Items are coded as 1 if they occur at any time during the year or 0 if they do not and then weighted based upon their ability to predict mortality:

1. Myocardial Infarction
2. Congestive Heart Failure
3. Peripheral Vascular Disease
4. Cerebrovascular disease
5. Dementia
6. Chronic pulmonary disease
7. Rheumatologic disease
8. Peptic Ulcer Disease
9. Mild Liver Disease
10. Diabetes (mild to moderate)
11. Diabetes with chronic complications
12. Hemiplegia or paraplegia
13. Renal (kidney) disease
14. Any malignancy
15. Moderate or severe liver disease
16. Metastatic Solid Tumor
17. AIDS

The independent variables used in the analysis can be partitioned into three domains; demographic, early life conditions (ELCs), and fertility.

Demographic Characteristics

All models controlled for age in 1992 centered on the mean for each sex and age group. Widowhood is a frequent occurrence among individuals in this age range and may be linked to changes in health status (Williams and Umberson 2004). Time-varying covariates are used to allow for altered shape of the trajectories do to loss of a spouse. An indicator variable for each year was created to for each year of observation and defined equal to 0 during all periods where the spouse is still alive and 1 during all periods where the spouse was deceased.

Measures of Early Life Conditions

Measures of age at parental death, childhood socioeconomic status, familial excess longevity (FEL), and religious participation are generated from the data held within the UPDB. Death of a parent during childhood may have adverse effects on health later in life (Umberson and Chen 1994; Andersson, Hogberg et al. 1996; Norton, Smith et al. 2011) and disruption of the family may affect the transition into adulthood, including timing of childbirth. Birth, marriage and death dates are recorded comprehensively in the UPDB and were used to construct eight categories of parental death. The gender of the deceased parent may have difference social and economic implications, therefore two categories were created (one mother and one father) for each of the following circumstances related to parental death; mother/father died when child was under age 18, both parent deceased when child was under 18 (orphan), and parent deceased after child was age 18 (reference category).

Childhood socioeconomic status may directly and indirectly influence marriage and reproductive success, timing of childbirth, and later life comorbidity (Geronimus and Korenman 1992; Doblhammer and Oeppen 2003; Kuh and Ben-Shlomo 2004). Childhood socioeconomic status is measured using usual occupation and industry information reported on their father's death certificate for fathers who died in Utah and for whom we have a death certificate (deaths occurring from 1904 forward). Occupational strings were converted to Nam-Powers socioeconomic (NP SES) scores, a measure of income and education based on occupational categories and range from 1 to 99, with higher scores being associated with higher socioeconomic status (Nam and Powers 1983). NP SES scores were unavailable for approximately 20% of the sample and values for these individual were imputed by substituting the mean plus a random number multiplied by the distribution of non-missing values and an additional variable indicating missing values. A large percentage of fathers from this era, a little

over 30%, have the occupation ‘farmer’, resulting in a large heaping at the NP SES score of 40. Farming may also confer a survival advantage related to life style factors (Gavrilov and Gavrilova 2012) and separate category was created for the occupation of farmer.

To control for unobservable genetic and shared environmental effects we used a measure of family history of longevity, Familial Excess Longevity (FEL). FEL is a statistic developed using deep genealogical data of multigenerational pedigrees drawn from the UPDB. We have published the development of this statistic (Kerber, O'Brien et al. 2001) and have applied it to other life-span studies using UPDB (Garibotti, Smith et al. 2006; Smith, Mineau et al. 2009; Kerber, O'Brien et al. 2012). At its foundation, the FEL is based on the assumption that family history of longevity follows Mendelian patterns of inheritance. To construct familial excess longevity we first measure individual level excess longevity, defined as the difference between an individual’s attained age and the age to which that individual was expected to live according to a model that incorporates basic life-span predictors (sex, birth year). Expected longevity is estimated from an accelerated failure time (AFT) model and excess longevity is simply the difference between expected and attained age. Expected longevity is based on the lognormal distribution and the AFT model was used because it provides a simple point estimate for duration and that fits the observed data. Excess longevity is then extended to blood relatives who reached the age of 65 for each individual, a restriction to focus on years less affected by external causes of death. Averaging the excess longevities of all blood kin over 65 for each ego, with the appropriate weighting scheme, generates a point estimate of familial excess longevity. The kinship coefficient, the probability that an individual shares a particular allele with another individual, is used as a weight in calculating familial excess longevity. We have found that individuals with high FEL live longer and experience more healthful disease trajectories as they age (Smith, Mineau et al. 2009; Smith, Hanson et al. 2012).

Active affiliation with the LDS church is associated with increased life expectancy (Enstrom and Breslow 2008) and high fertility rates (Arland 1979). Individuals actively affiliated with the LDS church are more likely to abstain from alcohol and tobacco use, fast once a month, and participation in church related social activities (Mineau, Smith et al. 2002). The UPDB contains information on baptism and endowment dates from family history records and these were used to classify individuals as active followers, inactive, or non-members. Individuals with an endowment date have agreed to live their lives following the doctrine of the

Church and re considered active church followers if endowed before age 40. Individuals with a baptism but no endowment date are considered inactive, and individual with no baptism or endowment date are considered non-members (reference category).

Measures of Fertility

Fertility information in UPDB comes from a combination of information collected from Family Group Sheets obtained from the Utah Family History Library and linked vital records, including birth certificate data from 1915 – 1921 and 1943 to the present. All women in the sample have completed fertility by definition because they are required to survive to at least age 65 to be visible in the Medicare Claims data.

Parity was measured with a set of dummy to indicate whether a woman had 1-2, 3-5, 6-8, or 9+ children. On average, women in this sample had four children and the category for 3-5 children was used as the reference category. To measure the effects of early and late childbirth, we create dummy variables for the following categories; age at first birth before the age of 18, between ages 18 and 24, and after age 25, with 18-24 used as the reference category. For age at last birth we constructed three categories, under age 35 (reference group), 35 – 39, and 40 or older. A dummy variable is used to identify parents of multiples (twins). Short birth intervals are defined as interbirth intervals less than 18 months and long birth intervals are defined as interbirth intervals > 60 months (Conde-Agudelo, Rosas-Bermudez et al. 2007). Separate variables were created to identify individuals with one or more short or long interbirth interval.

Infant mortality may be a marker for maternal health and adverse environments (McCormick, Shapiro et al. 1984), environments that lead to adverse health outcomes for the infant may also be risky for the parents. Individuals losing one or more children during the first year of life will also be identified with a dummy variable.

Birth certificate information in the UPDB is available from 1915 to 1921 and 1943 to the present. Birth certificates contain information on mother's marital status, prematurity, and birth weight (starting in 1947). Using the information from the birth certificates individuals are categoriezed as ever having a high birth weight baby (> 4000 grams) or low birth weight baby (<2500 and carried 37+ weeks) which reflects the WIC Nutrition Risk Criteria (Medicine 1996).

Preterm birth was defined as the birth of an infant before 37 weeks of gestation. Table 2 presents the descriptive statistics of all the measures by sex and age group.

Table 2 here

Constructing Morbidity Trajectories

We seek to determine how reproductive history and health affect the likelihood of having a particular later life comorbidity trajectory. Assessment of comorbidity trajectories are accomplished through the application of a finite mixture modeling approach that is currently available as a SAS procedure, called PROC TRAJ through the work of Dr. Daniel Nagin and his colleagues (Nagin and Tremblay 2001; Jones and Nagin 2007; Haviland, Nagin et al. 2008). The group-based modeling approach allows for identification of distinct clusters of individual trajectories.

Given the quickly changing health landscape of an aging population, all models are estimated within age-sex categories. The excess mortality risks of men and the generally higher rates of morbidity of women necessitates that we use sex-specific models. As age profoundly affects the risks of morbidity as encompassed in the CCI, as noted above we divide the sample into two birth cohorts determined by their age at baseline. Because the response variable in this analysis is a weighted count of the number of comorbid conditions, a zero-inflated Poisson (ZIP) based model was used. The ZIP model is an expansion of the Poisson model that corrects for overdispersion by accounting for more zeros than would be expected under a Poisson process. Both the Poisson and censored normal distributions were also considered, however the ZIP model provided the best fit for our data.

Trajectories were modeled for two to six groups as a quadratic function of time. Model fit was assessed using the Bayesian information criterion (BIC), the log likelihood plus a penalty for the number of parameters in the model. There are situations where BIC score continues to increase as more groups are added, however the additional groups are not necessary to summarize the distinct features of the data in a parsimonious way (Nagin 2005). Therefore, average posterior probability of assignment, odds of correct classification, and estimated group probabilities versus the proportion of the sample assigned to the group (Nagin 2005) were also used to assess the selected model's correspondence with the data.

Non-random attrition leads to altered characteristics of the population over time and can lead to biased estimates. Because we excluded individuals who were enrolled in a managed care plan during any period of a given year, our only source of truncation is death. PROC TRAJ is used to simultaneously model the comorbidity trajectories and the probability of death, allowing the modeled probability of death to vary across trajectory groups. Individuals in the analysis were required to be alive at time 1, and therefore the probability of dropout during this period is zero for all trajectory groups. All models accounted for non-random attrition due to death using the extension created by Haviland (Haviland, Jones et al. 2011; Zimmer, Martin et al. 2012). This extension jointly models the trajectories with a model of the logit of the dropout probability, in this case death, by group that includes dependence on the prior period response until dropout.

Group membership probabilities can vary as a function of time stable characteristics, or characteristics established before the observation periods (Jones and Nagin 2007). This third component jointly estimates a multinomial logit model that captures the effects of time stable characteristics on the probability of group membership. This makes it possible to test the effect of early life conditions and fertility on the probability of membership in each group (Nagin and Odgers 2010). PROC TRAJ also allows for the inclusion of time-varying covariates measured during the observation time that may alter the shape of the observed trajectories, such as widowhood.

A series of mediation analysis were conducted to test the hypothesis that fertility history mediated the relationship between early life conditions and later life health. Mediation tests used the Clogg test of differences in coefficients produced when fertility variables were added to the model (MacKinnon, Lockwood et al. 2002)

For each group, the following analyses were conducted. First, we derived the basic trajectory groups in which comorbidity is a function of time only in order to select the best model. Second, we fit a model with covariates from the demographic and ELCs. Third, we fit a model with the covariates from the demographic, ELCS, and fertility domains. All models accounted for non-random attrition due to death. In addition, we examined how ELCs in the probability of group membership are mediated by timing of childbirth (age at first and last birth), preterm birth, and parity.

Results

Trajectories of comorbidity and morbidity

The best fitting models for both males and females ages 66 – 74 (the young-old) in 1992 revealed six distinct groups of trajectory groups, while those for ages 75 – 84 (the old-od) showed five distinct groups. Figures 1- 4 show the predicted comorbidity trajectories by sex and age group. The figures show the diversity of comorbidity experience over the 18 year period of follow-up (the youngest individuals are 84 years old at the end of the follow-up period). To aid in the interpretation of results, trajectory groups have been labeled as follows: "robust"- characterized the absence of comorbid conditions; "slow initiates"- individuals in this group begin the observation period with no comorbid conditions, however the number gradually increases over time; "accelerated initiates"- individuals in this group begin the observation period with no comorbid conditions but the number of conditions quickly increases over time and then decelerates during the last two years of the 18 year period; "chronic low"- characterized by the steady level of comorbidity over time; "ailing"- this group of individuals has moderate levels of comorbidity at baseline which steadily increase over time; "frail"- these individuals have the highest level of comorbidity at baseline and remains high over time.

In addition to using BIC as model selection criteria, several other measures were used to assess the correspondence of our models with the data (Nagin 2005; Zimmer, Martin et al. 2012). First, we calculated the average posterior probability (APP) of membership in group *j* for all individuals who are most likely to belong to that group. The recommended criterion is that the APP for each group should exceed 0.70. All selected models met this criterion, with APP ranging from 0.81 to 0.91 for male and female models for the young-old and 0.75 to 0.89 for male and female models for the old-old. Second, we compared estimated proportions of group membership generated by the maximum likelihood procedure to the actual proportion of the sample assigned to each group based on maximum posterior probability of group membership. For this criterion, our models were satisfactory, with no more than a 4 point difference in any of the selected models.

The shape of the trajectories is similar between males and females in their respective age groups, however the intercepts differ. In each trajectory group, males tend to have more comorbid conditions at baseline and this pattern holds across age groups. For females in the young-old age category, group membership is fairly evenly distributed among the robust

(21.6%), slow initiate (18.3%), chronic (20.1%), and ailing (20.6%). Compared to females, males also have lower percentages of individuals in the robust (17.6%) and slow initiate (15.6%) groups and higher percentages of individuals in the ailing (24%), accelerated initiate (13.8%), and frail groups (8.2%). The frail category constitutes the lowest proportion of group membership for both males and females, 8.2% and 7.3% respectively. These findings are somewhat unexpected given the health-survival paradox, females have worse health and males have higher mortality, however recently reported prevalence estimates support our findings. The 2011 summary statistics for US adults reports higher prevalence rates of heart disease, hypertension, and diabetes for men (Schiller, Lucas et al. 2012). A separate report using National Health Interview Survey (NHIS) from 2009 estimated that a higher percentage of men (49%) than women (42.5%) had two or more chronic conditions (conditions considered included hypertension, heart disease, diabetes, cancer, stroke, chronic bronchitis, emphysema, current asthma, and kidney disease) (Fried, Bernstein et al. 2012).

Individuals in the old-old cohort surviving the full 18 year period range in age from 92 to 102 in 2009. For both sexes in this cohort, five distinct trajectory groups were identified. The ailing category, with a CCI of approximately 1 at baseline that gradually increases over time, has the highest group membership for both sexes, with 32% of females and 34.2% of males falling into this category. Compared to the young-old, a smaller proportion of the old-old fall into the robust category (17.6% vs. 14.5% for males and 21.6% vs. 17.3% for females). As expected, the robust in this cohort do not maintain a disease free trajectory over the period of 18 years, with a predicted CCI of 1.0 for females and 1.6 for males. While the pattern of this trajectory is similar to the pattern of the slow initiates in the young-old cohort, individuals in the old-old robust category have a slower rate of increase over time and end the period with a lower predicted CCI (the difference in CCI_{2009} is 1.3 for females and 0.6 for males). Compared to the young-old, there is a near doubling in the proportion of frail females and a 50% increase for the males. Another notable difference between the young-old and old-old frail trajectories is the maximum predicted CCI, which is higher in the young-old category for both sexes.

We found six distinct trajectory groups for the male and female birth certificate samples. The parameter estimates and estimated group memberships were similar across samples (results not shown) with as slightly higher percentage in the robust group for both males and females.

This is not unexpected given the younger age distribution of these sub-samples. The following trajectories were identified; robust (male=18.5%, female=23.1%); slow initiate (male=15.8%, female=17.5%); accelerated initiate (male=15.1%, female=11.7%); chronic low (male=19.0%, female=19.9%); ailing (male=23.5%, female=20.2%); and frail (male=8.1%, female=7.7%).

Figures 5 – 8 display the probability of death for each sex and age-group. The probability of dropout due to death is modeled as a function of the comorbidity measurement in the previous year and allowed to vary by comorbidity group. Mortality trajectories follow the same hierarchy as the comorbidity trajectories, with the robust group generally having the lowest levels of mortality and the frail group having the highest. Females have lower probabilities of death than males in their respective cohorts and comorbidity groups. The young-old have lower probabilities of death than the old-old. Both of these patterns are consistent with expected patterns of mortality in these age groups.

Once the best fitting trajectory models were selected, we jointly modeled multinomial logit models by sex and cohort relating individual-level covariates to posterior probabilities to estimate the effects of ELCs and fertility on probability of group membership. The first set of nested models included only ELCs and the results are not displayed in this paper, however they are available upon request. Tables 3 – 6 display the odds ratios and 95% confident intervals for the full models that include demographic, ELCs, and fertility measures. Comorbidity, as defined above, is the existence of multiple diseases. Our results show that there are two groups in all models that escape transition into a comorbid state (two or more simultaneous conditions), the robust and chronic low. However, for ease of interpretation, the chronic low group will be referred to as a group with comorbid conditions. The contrast group in all tables is the robust category, meaning that we are comparing the probability of membership in groups with more comorbid conditions with the probability of membership in the group with the least number of comorbid conditions. All results discussed below are controlling for early life events and demographic measures.

For females in the young cohort, we find that compare to females have the average number of children, females having nine or more children are more likely to be in the ailing (OR=1.56, 95% CI=1.07, 2.27) and the chronic low (OR=1.51, 95% CI= 1.04, 2.2) vs. the robust category. Table 5 shows that compared to women having their first birth between the ages of 19

and 24, young age at first birth (<18) is significantly increases in the odds of being in a group with more morbidity with the exception of the initiate vs. robust comparison. Having and early childbirth doubles the odds of being in the frail vs. robust group (OR=2.04, 95% CI 1.36, 3.06). Age at last birth confers a protective effect, with women having an age at last birth at age 35 or later having a decrease in the odds of being in one of the groups with comorbid conditions vs. the robust group. Females that have their age at last birth between the ages of 35 and 39 and after age 40 have a 26% and 29% respective decrease in the odds of being in the frail vs. robust group compared to females ending childbearing earlier. There is no evidence of an association between twinning, long birth intervals, and infant deaths and later life comorbidity trajectories for this group. Having one or more short birth intervals decreases the odds of being in the chronic low vs. robust group decreases by 15% (95%CI = 0.74, 0.98), however this results is not replicated across other groups.

Table 6 shows the results for females in the old-old cohort. We find little association between parity and group membership for females in the old-old cohort with the exception of the frail group, where females having nine or more children are more likely to be in the frail vs. robust group (OR=2.51, 95% CI=1.48, 4.26). The relationship between age at first and comorbidity group membership are similar to the patterns observed in the young-old cohort. Females having their first birth during the teenage years are more likely to be in the chronic low , ailing, and frail vs. robust groups. There is no significant difference in group membership between females having their last birth before age 35 and females with an age at last birth between ages 35 – 39. The results for females having their last birth at age 40 and above are suggestive of a protective effect for the frail and chronic low groups, however these differences do not reach statistical significance at the 0.05 level. As with the female young-old cohort, we find no association between group membership and twinning and infant death. Our results provide some evidence that having a interbirth intervals affect later life comorbidity group membership for this cohort. Having one or more short birth interval reduces the odds of being in the ailing vs. robust group by 20% (95% CI= 0.64, 0.99), however this protective effect was not consistently found across groups. Having one or more long birth interval reduces the odds of being in any of the groups with more comorbid conditions vs. the robust, with an 18%, 13%, 33%, and 17% respective decrease in the risk of being in the initiate, chronic low, ailing, and

frail vs. robust group (the difference in the effect across groups does not reach statistical significance).

We find no association between parity and group membership for males in the young-old and old-old cohorts. For males in the young-old cohort, there is a pattern of reduction of the risk of being in one of the groups with more comorbidity vs. the robust (with the exception of the frail group) associated with increased parity, however the differences are not statistically significant. Having a later age at first birth (over the age of 25 vs. less than 25) is protective for men in both cohorts. Table 7 shows that for males in the young-old cohort, having their first birth at the age of 25 or older reduces the odds of being in the chronic low group by 19% (95% CI=0.70, 0.94) and the ailing group by 21% (95% CI=0.69, 0.91) compared to the robust group. Table 8 shows that for males in the old-old cohort, having and older age at first birth is associated with a 21% reduction in the risk of being in the frail vs. robust group (95% CI = 0.64, 0.99). Males in the young-old cohort having one or more short birth intervals are at increased risk of being in the frail (OR=1.25, 95% CI=1.02, 1.52) and chronic low (OR=1.27, 95%CI=10.8, 1.49) vs. robust groups. We do not find an association between twinning, age at last birth, long birth intervals, and infant deaths and group membership for males in these cohorts.

The results from of the birth certificate analysis are presented in figures 9 and 10. Individual included in these models were required to have birth certificate records for all births and therefore the results are based on a subsample of individuals in the young-old cohorts, with a higher percentage of the males from the full sample represented in the subsample than females (N_{Female}=5,119 and N_{Male}= 7,352). This is because on average, men have an older age at first birth and are therefore more likely to meet the selection criteria. All models controlled for early life conditions, parity, age at first birth, age at last birth, and ever having an infant death. As with the previous analyses, the multinomial logit model relates individual-level covariates to posterior probabilities of group membership. Models were run simultaneously with the trajectories and the reference group is the robust, or group with the lowest number of comorbidities. We find that for females in the young-old cohort, having one or more high birth weight (defined as >4,000 g) children increases the odds of being in the accelerated initiates (OR=1.41, 95% CI=1.04,1.91), chronic low (OR=1.29, 95% CI=0.99, 1.68), ailing (OR=1.49,

95% CI= 1.16, 1.93), and frail (OR=1.46, 95% CI=1.04, 2.07) vs. the robust. Females having one or more preterm births (defined as <37 weeks gestation) are more likely to be in the accelerated initiates (OR=1.43, 95% CI=1.02, 2.01), chronic low (OR=1.44, 95% CI=1.08, 1.92) and frail groups (OR=1.62, 95% CI=1.12, 2.35) vs. the robust group. We do not find an association between ever having a low birth weight (carried to term) baby and later life comorbidity trajectories for females. For males in the birth certificate analysis, we find no association between birth weight of child and group membership. However we do find that males having one or more children born prematurely have an increased likelihood of being in the slow initiate (OR=1.45, 95% CI=1.07, 1.97), accelerated initiate (OR=1.43, 95% CI=1.06, 1.92), and frail (OR=1.44, 95% CI=1.02, 2.04) vs. the robust group.

Mediation analyses were performed to test the mediating effects of fertility on early life conditions. Fertility variables were considered as possible intervening variables if they were significantly related to comorbidity group membership. While there were a few significant differences in coefficients, the percent change in the effects of the ELCs was small (ranging from 0.5% to 8%) and inconsistent. Therefore, we concluded that fertility history did not significantly mediate the relationship between early life conditions and later life health (results now shown here).

Discussion

The purpose of this study was threefold. First, we sought to identify distinct trajectories of comorbidity by sex for individuals in two age categories, the young-old and old-old. Second, we tested specific hypotheses relating fertility to trajectory group membership. Third, we tested the mediating role of fertility on the relationship between early life conditions and comorbidity. We found that there are distinct heterogeneous patterns of comorbidity that range from a robust group, escaping major morbid conditions for the majority of the observation period, to a frail group characterized by high comorbidity throughout the entire period of observation. Fertility history is associated with comorbidity trajectories after the age of 65 for both females and males when controlling for early life circumstances. High parity, age at first birth younger than 18, age at last birth greater than 35, giving birth to at least one high birth weight child, having one or more preterm birth, and long birth intervals were associated with comorbidity trajectory group membership for females. Age at first birth after age 25 and having one or more preterm birth

were associated with comorbidity trajectory group membership for males. These results provide evidence that evolutionary "trade-off" (H1), biological (H2), and social mechanisms (H4b, H4c) may all be associated with the observed relationship between fertility and later life health. While we found independent effects of early life conditions on later life comorbidity trajectories, we did not find robust evidence that fertility history is on the causal pathway between early life conditions and later life comorbidity.

The observed relationships between parity, age at last birth and comorbidity group membership present evidence of a "trade-off" between fertility and aging for females in the young-old cohort. Our finding of adverse effects at 9+ births is higher than the 5+ births reported in other studies of contemporary populations (Doblhammer 2000; Grundy and Tomassini 2005). However, both studies top coded fertility at 5+ births. Our findings support other studies suggesting that high levels of fertility are needed for a trade-off mechanism to operate (Kitagawa and Hauser 1973; Gagnon, Smith et al. 2009). We also find a consistent protective relationship between age at last birth and comorbidity group membership in the young-old cohort, with females having their last birth after age 35 more likely to be in the robust group. This is consistent with the prediction that older ages of reproduction are a marker for slowed rates of aging (Perls, Alpert et al. 1997). However, we do not see the same strong protective effect for females in the old-old cohort.

Related to the evolutionary theories discussed above are the biological mechanisms through which fertility is linked to later life comorbidity for women. We did find some support that there are biological consequences to childbirth for women (H2), however we did not find evidence supporting the maternal depletion hypothesis or the link between low birth weight and comorbidity (Smith, Hart et al. 1997; Davey Smith, Sterne et al. 2004). High parity (9+ births) and having at least one high birth weight baby had an adverse effect on later life health for females but not males, suggesting the costs of increased parity are biological. Having a least one long birth interval had a protective effect on comorbidity later in life for females in the old-old cohort. Long birth intervals have been linked to complications during reproductive years (Conde-Agudelo, Rosas-Bermudez et al. 2007), however this suggests that there are not long term consequences to widely spaced births.

We do not find strong evidence in favor of the robust phenotype hypothesis (H3), which argues that fertility success is a marker for female health and vitality. We find that short birth intervals are protective in some instances, but there is not a consistent with later life comorbidity. While the negative relationship between late age at last birth and comorbidity may be a marker for robustness, the hypothesized negative relationship between increased parity, shorter birth intervals, and twinning were not consistently significant across trajectory groups and cohorts. Therefore we are rejecting this hypothesis.

We do find evidence that social mechanisms explain some of the relationship between fertility and later life health. We do not find strong evidence of decreased comorbidity for individuals with more children, and therefore reject the social support hypothesis (H4a). The results do suggest that more children may be beneficial for men in the young-old cohort, but the differences are not statistically significant. While we do find a negative relationship between increased parity and comorbidity after age 65, it is likely that this result is not related to the social and economic constraints of having a large number of children because the effects would not vary by gender. We find strong evidence supporting the association between age at first birth and comorbidity after age 65. Young motherhood is related to adverse health outcomes in for both cohorts in this study and postponing fatherhood is protective for males when controlling for early life circumstances including childhood socioeconomic status. This suggests that policy aimed at reducing teenage pregnancy may have significant effects on later life health outcomes. The adverse effect of preterm birth for males and females suggests that adverse birth outcomes may produce a stress response that alters later life health (McEwen Bs 1993; Davis, Edwards et al. 2003) or be a marker of risky environments (Kramer, Séguin et al. 2000). We did not control for social environment at time of birth or current socioeconomic circumstance. Future research should not only consider the early life social environment, but the social environment throughout the life course.

Fertility decisions and outcomes are heavily influenced by social and historical circumstances, making it important to consider the historical context of these individuals' lives. The oldest members of the old-old cohort would have been born in 1908 and entered childbearing age (assuming it is 15) in 1923, with the childbearing years extending to 1965 for the youngest members of the cohort (assuming age at last birth is 50). The members of the

young-old cohort would have initiated childbearing in 1933 and ended in 1974. Infertility drugs would have been available for some individuals in these cohorts. This means that parity and late age at last birth may not be completely biologically determined. Individuals in both cohorts may have served during WWII, which may affect the timing of fertility. Individuals in both cohorts would have been parous during the baby boom, when fertility rates peaked at 3.8 (Westoff 1986). Members of the old-old cohort would also have been children during the 1918 influenza pandemic, an exposure that may have left them physiologically scarred affecting both fertility and mortality. A study by Smith et al. suggests that individuals exposed to influenza or pneumonia as children during the pandemic have lower ages at last birth and increased mortality (Smith, Reed et al. 2012).

This study has several limitations that should be addressed in future studies of the relationship between fertility and later life health. First, these results are based on once married parous individuals. Future studies should consider the relationship between nulliparity and later life comorbidity for both men and women. Second, we were unable to consider the role of all early life and reproductive outcomes (including the number of sibling, number of sons and daughters, the proportion of offspring born prematurely, and the proportion of offspring born high/low birth weight) and later life health. Third, while we controlled for childhood socioeconomic status, we were unable to control for SES at the time of birth and baseline. We are currently in the process of creating files to begin these analyses. Fourth, sibling and spouse designs may improve understanding of the mechanisms linking reproductive history and health.

Conclusion

The paths to aging are heterogeneous and more research needs to be done to both characterize these different phenotypes and the factors that influence them. While early life conditions explain a portion of the heterogeneity in aging, mid-life circumstances may also alter the trajectories of disease. Parity, timing of childbearing, and birth outcomes of offspring are significantly related to later life health outcomes. The differences in risk factors between men and women suggest that evolutionary, biological, and social mechanisms must all be considered when studying these heterogeneous aging processes.

References

Andersen, S. L., P. Sebastiani, et al. (2012). "Health Span Approximates Life Span Among Many Supercentenarians: Compression of Morbidity at the Approximate Limit of Life Span." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **67A**(4): 395-405.

Andersson, T., U. Hogberg, et al. (1996). "Survival of orphans in 19th century Sweden—the importance of remarriages." Acta Pædiatrica **85**(8): 981-985.

Arland, T. (1979). "Religion and Fertility: The Case of Mormonism." Journal of Marriage and Family **41**(1): 131-142.

Bastian, L. A., N. A. West, et al. (2005). "Number of children and the risk of obesity in older women." Preventive Medicine **40**(1): 99-104.

Bellamy, L., J.-P. Casas, et al. (2009). "Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis." The Lancet **373**(9677): 1773-1779.

Berkman, L. F. and S. L. Syme (1979). "Social Networks, Host Resistance, and Mortality: A nine-year follow-up study of Alameda County residents." American Journal of Epidemiology **109**(2): 186-204.

Casey, B. M., M. J. Lucas, et al. (1997). "Pregnancy Outcomes in Women With Gestational Diabetes Compared With the General Obstetric Population." Obstetrics & Gynecology **90**(6): 869-873.

Charlson, M. E., P. Pompei, et al. (1987). "A new method of classifying prognostic comorbidity in longitudinal studies: development and validation." J Chronic Dis **40**(5): 373-383.

Conde-Agudelo, A., A. Rosas-Bermudez, et al. (2007). "Effects of birth spacing on maternal health: a systematic review." Am J Obstet Gynecol **196**(4): 297-308.

Davey Smith, G., J. A. C. Sterne, et al. (2004). "Birth characteristics of offspring and parental diabetes: evidence for the fetal insulin hypothesis." Journal of Epidemiology and Community Health **58**(2): 126-128.

Davis, L., H. Edwards, et al. (2003). "The impact of very premature birth on the psychological health of mothers." Early Human Development **73**(1–2): 61-70.

Deyo, R. A., D. C. Cherkin, et al. (1992). "Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases." J Clin Epidemiol **45**(6): 613-619.

Doblhammer, G. (2000). "Reproductive history and mortality later in life: A comparative study of England and Wales and Austria." Population Studies **54**(2): 169-176.

Doblhammer, G. and J. Oeppen (2003). "Reproduction and longevity among the British peerage: the effect of frailty and health selection." Proceedings of the Royal Society of London. Series B: Biological Sciences **270**(1524): 1541-1547.

Enstrom, J. E. and L. Breslow (2008). "Lifestyle and reduced mortality among active California Mormons, 1980–2004." Preventive Medicine **46**(2): 133-136.
Evert, J., E. Lawler, et al. (2003). "Morbidity Profiles of Centenarians: Survivors, Delayers, and Escapers." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **58**(3): M232-M237.
Fried, L. P., L. Ferrucci, et al. (2004). "Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **59**(3): M255-M263.
Fried, V., A. Bernstein, et al. (2012). "Multiple chronic conditions among adults aged 45 and over: Trends over the past 10 years." NCHS data brief **100**.
Gagnon, A., K. R. Smith, et al. (2009). "Is there a trade-off between fertility and longevity? A comparative study of women from three large historical databases accounting for mortality selection." American Journal of Human Biology **21**(4): 533-540.
Gagnon, A., K. R. Smith, et al. (2009). "Is there a trade-off between fertility and longevity? A comparative study of women from three large historical databases accounting for mortality selection." American Journal of Human Biology **21**(4): 533-540.
Galobardes, B., J. W. Lynch, et al. (2008). "Is the association between childhood socioeconomic circumstances and cause-specific mortality established? Update of a systematic review." Journal of Epidemiology and Community Health **62**(5): 387-390.
Garibotti, G., K. R. Smith, et al. (2006). "Longevity and Correlated Frailty in Multigenerational Families." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **61**(12): 1253-1261.
Gavrilov, L. A. and N. S. Gavrilova (2012). "Biodemography of exceptional longevity: early-life and mid-life predictors of human longevity." Biodemography and Social Biology **58**(1): 14-39.
Geronimus, A. T. and S. Korenman (1992). "The Socioeconomic Consequences of Teen Childbearing Reconsidered." The Quarterly Journal of Economics **107**(4): 1187-1214.
Grundy, E. and S. Read (2012). "Social Contacts and Receipt of Help Among Older People in England: Are There Benefits of Having More Children?" The Journals of Gerontology Series B: Psychological Sciences and Social Sciences **67**(6): 742-754.
Grundy, E. and C. Tomassini (2005). "Fertility history and health in later life: a record linkage study in England and Wales." Social Science & Medicine **61**(1): 217-228.
Guralnik, J. M. (1996). "Assessing the impact of comorbidity in the older population." Annals of Epidemiology **6**(5): 376-380.
Haviland, A., D. S. Nagin, et al. (2008). "Combining group-based trajectory modeling and propensity score matching for causal inferences in nonexperimental longitudinal data." Dev Psychol **44**(2): 422-436.
Haviland, A. M., B. L. Jones, et al. (2011). "Group-based Trajectory Modeling Extended to Account for Nonrandom Participant Attrition." Sociological Methods & Research **40**(2): 367-390.
Hawkes, K. (2010). "How grandmother effects plus individual variation in frailty shape fertility and mortality: Guidance from human–chimpanzee comparisons." Proceedings of the National Academy of Sciences **107**(Supplement 2): 8977.
Henretta, J. C. G. E. M. D. O. L. C. W. M. E. J. (2008). "Early motherhood and mental health in midlife: A study of British and American cohorts." Aging & Mental Health **12**(5): 605-614.
House, J., K. Landis, et al. (1988). "Social relationships and health." Science **241**(4865): 540-545.
Hurt, L. S., C. Ronsmans, et al. (2006). "The effect of number of births on women's mortality: Systematic review of the evidence for women who have completed their childbearing." Population Studies **60**(1): 55-71.

Jelliffe, D. and E. Jelliffe (1978). Human Milk in the Modern World: Psychological, Nutritional, and Economic Significance.
Jones, B. L. and D. S. Nagin (2007). "Advances in Group-Based Trajectory Modeling and an SAS Procedure for Estimating Them." Sociological Methods & Research **35**(4): 542-571.
Kelsey, J. L., M. D. Gammon, et al. (1993). "Reproductive Factors and Breast Cancer." Epidemiol Rev **15**(1): 36-47.
Kerber, R. A., E. O'Brien, et al. (2012). "A Genome-Wide Study Replicates Linkage of 3p22-24 to Extreme Longevity in Humans and Identifies Possible Additional Loci." PLoS ONE **7**(4): e34746.
Kerber, R. A., E. O'Brien, et al. (2001). "Familial Excess Longevity in Utah Genealogies." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **56**(3): B130-B139.
Kirkwood, T. B. L. and M. R. Rose (1991). "Evolution of Senescence: Late Survival Sacrificed for Reproduction." Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences **332**(1262): 15-24.
Kitagawa, E. and P. Hauser (1973). Differential Mortality in the United States: A Study in Socioeconomic Epidemiology.
Klabunde, C. N., A. L. Potosky, et al. (2000). "Development of a comorbidity index using physician claims data." J Clin Epidemiol **53**(12): 1258-1267.
Klabunde, C. N., J. L. Warren, et al. (2002). "Assessing comorbidity using claims data: an overview." Med Care **40**(8 Suppl): IV-26-35.
Kobayashi, S., H. Sugiura, et al. (2012). "Reproductive history and breast cancer risk." Breast Cancer **19**(4): 302-308.
Kramer, M. S., L. Séguin, et al. (2000). "Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly?" Paediatric and perinatal epidemiology **14**(3): 194-210.
Kravdal, Ø. (1995). "Relationship between Childbearing and Cancer Incidence due to Biology or Lifestyle? Examples of the Importance of Using Data on Men." International Journal of Epidemiology **24**(3): 477-484.
Kuh, D. and Y. Ben-Shlomo (2004). A life course approach to chronic disease epidemiology, Oxford University Press, USA.
Kuh, D. and R. Hardy (2002). A life course approach to women's health, Oxford University Press.
Kvale, G., I. Heuch, et al. (1994). "Parity in Relation to Mortality and Cancer Incidence: A Prospective Study of Norwegian Women." International Journal of Epidemiology **23**(4): 691-699.
Lawlor, D. A., J. R. Emberson, et al. (2003). "Is the Association Between Parity and Coronary Heart Disease Due to Biological Effects of Pregnancy or Adverse Lifestyle Risk Factors Associated With Child-Rearing?" Circulation **107**(9): 1260-1264.
Lukanova, A. and R. Kaaks (2005). "Endogenous Hormones and Ovarian Cancer: Epidemiology and Current Hypotheses." Cancer Epidemiology Biomarkers & Prevention **14**(1): 98-107.
MacKinnon, D. P., C. M. Lockwood, et al. (2002). "A comparison of methods to test mediation and other intervening variable effects." Psychol Methods **7**(1): 83.
MacMahon, B., P. Cole, et al. (1973). "Etiology of Human Breast Cancer: A Review." Journal of the National Cancer Institute **50**(1): 21-42.
McCormick, M. C., S. Shapiro, et al. (1984). "High-risk young mothers: infant mortality and morbidity in four areas in the United States, 1973-1978." American Journal of Public Health **74**(1): 18-23.
McEwen Bs, S. E. (1993). "Stress and the individual: Mechanisms leading to disease." Archives of Internal Medicine **153**(18): 2093-2101.
Medicine, I. o. (1996). WIC Nutrition Risk Criteria: A Scientific Assessment. National Academy Press Washington DC.
Mineau, G. P., K. R. Smith, et al. (2002). "Historical trends of survival among widows and widowers." Social Science & Medicine **54**(2): 245-254.

Mirowsky, J. (2005). "Age at First Birth, Health, and Mortality." Journal of Health and Social Behavior **46**(1): 32-50.
Myklestad, K., L. J. Vatten, et al. (2012). "Offspring Birth Weight and Cardiovascular Risk in Parents—A Population-based HUNT 2 Study." American Journal of Epidemiology **175**(6): 546-555.
Nagin, D. (2005). Group-based modeling of development, Harvard University Press.
Nagin, D. S. and C. L. Odgers (2010). "Group-Based Trajectory Modeling in Clinical Research." Annual Review of Clinical Psychology **6**(1): 109-138.
Nagin, D. S. and R. E. Tremblay (2001). "Analyzing developmental trajectories of distinct but related behaviors: a group-based method." Psychol Methods **6**(1): 18-34.
Nam, C. B. and M. G. Powers (1983). The socioeconomic approach to status measurement: With a guide to occupational and socioeconomic status scores, Cap and Gown Press Houston.
Norton, M. C., K. R. Smith, et al. (2011). "Early parental death and remarriage of widowed parents as risk factors for Alzheimer disease: the Cache County study." The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry **19**(9): 814-824.
Perls, T. T., L. Alpert, et al. (1997). "Middle-aged mothers live longer." Nature **389**(6647): 133-133.
Permuth-Wey, J. and T. Sellers (2009). Epidemiology of Ovarian Cancer. Cancer Epidemiology. M. Verma, Humana Press. **472:** 413-437.
Phelan, J. C., B. G. Link, et al. (2010). "Social Conditions as Fundamental Causes of Health Inequalities: Theory, Evidence, and Policy Implications." Journal of health and social behavior **51**(1 suppl): S28-S40.
Preston, S. H., M. E. Hill, et al. (1998). "Childhood conditions that predict survival to advanced ages among African-Americans." Social science & medicine (1982) **47**(9): 1231.
Rich-Edwards, J. (2002). "A life course approach to women's reproductive health." A Life Course Approach to Women's Health. Oxford University Press, Oxford: 23-43.
Robson, S. L. and K. R. Smith (2011). "Twinning in humans: maternal heterogeneity in reproduction and survival." Proceedings of the Royal Society B: Biological Sciences **278**(1725): 3755-3761.
Robson, S. L. and K. R. Smith (2012). "Parity progression ratios confirm higher lifetime fertility in women who bear twins." Proceedings of the Royal Society B: Biological Sciences **279**(1738): 2512-2514.
Romano, P. S., L. L. Roos, et al. (1993). "Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives." J Clin Epidemiol **46**(10): 1075-1079; discussion 1081-1090.
Ross, C. E. and J. Huber (1985). "Hardship and Depression." Journal of Health and Social Behavior **26**(4): 312-327.
Rowe, J. and R. Kahn (1987). "Human aging: usual and successful." Science **237**(4811): 143-149.
Rowe, J. W. and R. L. Kahn (1997). "Successful Aging." The Gerontologist **37**(4): 433-440.
Ryff, C. D. and B. Singer (2009). "Understanding healthy aging: Key components and their integration."
Schiller, J., J. Lucas, et al. (2012). "Summary health statistics for U.S. adults: National Health Interview Survey, 2011." National Center for Health Statistics **Vital Halth Stat 10**(256).
Smith, G. D., C. Hart, et al. (1997). "Birth Weight of Offspring and Mortality in the Renfrew and Paisley Study: Prospective Observational Study." BMJ: British Medical Journal **315**(7117): 1189-1193.
Smith, G. D., E. Whitley, et al. (2000). "Birth dimensions of offspring, premature birth, and the mortality of mothers." The Lancet **356**(9247): 2066-2067.
Smith, K., G. Mineau, et al. (2009). "Effects of childhood and middle-adulthood family conditions on later-life mortality: evidence from the Utah Population Database, 1850-2002." Social science & medicine (1982) **68**(9): 1649.
Smith, K. R., A. Gagnon, et al. (2009). "Familial Aggregation of Survival and Late Female Reproduction." The Journals of Gerontology Series A: Biological Sciences and Medical Sciences **64A**(7): 740-744.

Smith, K. R., H. A. Hanson, et al. (2012). "Effects of BRCA1 and BRCA2 mutations on female fertility." Proceedings of the Royal Society B: Biological Sciences **279**(1732): 1389-1395.
Smith, K. R., H. A. Hanson, et al. (2012). Early Life Conditions and Later Life (65+) Co-Morbidity Trajectories: The Utah Population Database Linked to Medicare Claims Data. Population Association of America 2012. San Fransico, CA.
Smith, K. R., G. P. Mineau, et al. (2002). "Fertility and post-reproductive longevity." Biodemography and Social Biology **49**(3): 185-205.
Smith, K. R., G. P. Mineau, et al. (2002). "Fertility and post-reproductive longevity." Biodemography and Social Biology **49**(3-4): 185-205.
Smith, K. R., G. P. Mineau, et al. (2009). "Effects of childhood and middle-adulthood family conditions on later-life mortality: Evidence from the Utah Population Database, 1850-2002." Social Science & Medicine **68**(9): 1649-1658.
Smith, K. R., G. P. Mineau, et al. (2009). "Effects of childhood and middle-adulthood family conditions on later-life mortality: Evidence from the Utah Population Database, 1850–2002." Social Science & Medicine **68**(9): 1649-1658.
Smith, K. R., D. L. Reed, et al. (2012). "All in the Family: Fertility and Mortality Consequences for Child Survivors of the 1918 Influenza Pandemic." Social Science History Association 2012 Annual Meeting.
Spence, N. J. (2008). "The Long-Term Consequences of Childbearing: Physical and Psychological Well-Being of Mothers in Later Life." Research on Aging **30**(6): 722-751.
Uhlenberg, P. and T. M. Cooney (1990). "Family Size and Mother-Child Relations in Later Life." The Gerontologist **30**(5): 618-625.
Umberson, D. and M. D. Chen (1994). "Effects of a Parent's Death on Adult Children: Relationship Salience and Reaction to Loss." American Sociological Review **59**(1): 152-168.
Valderas, J. M., B. Starfield, et al. (2009). "Defining Comorbidity: Implications for Understanding Health and Health Services." The Annals of Family Medicine **7**(4): 357-363.
Waldron, I., C. C. Weiss, et al. (1998). "Interacting Effects of Multiple Roles on Women's Health." Journal of Health and Social Behavior **39**(3): 216-236.
Westoff, C. F. (1986). "Fertility in the United States." Science **234**(4776): 554-559.
Williams, G. C. (1957). "Pleiotropy, natrual selection, and teh evolution of senescence." Evolution **11**: 298-411.
Williams, K. and D. Umberson (2004). "Marital Status, Marital Transitions, and Health: A Gendered Life Course Perspective." Journal of Health and Social Behavior **45**(1): 81-98.
Yi, Z. and J. W. Vaupel (2004). "Association of late childbearing with healthy longevity among the oldest-old in China." Population Studies **58**(1): 37-53.
Zimmer, Z., L. Martin, et al. (2012). "Modeling Disability Trajectories and Mortality of the Oldest-Old in China." Demography **49**(1): 291-314.

Table 1. Sample Selection

Exclusion Criteria	**Female 66 -74**	**Female 75 -84**	**Male 66 -74**	**Male 75 - 84**	Total
N linked to the Utah Population Database	53,137	40,428	49,417	32,891	175,873
N Missing Information on Spouse	15,758	12,602	14,362	9,378	52,100
N with more than 1 spouse	5,389	3,924	5,756	3,936	19,005
No Children	7,593	6,110	7,917	5,885	27,505
Do not have complete fertility information	358	509	320	357	1,544
Enrolled in a managed care plan anytime between 1992 and 2009	3,693	2,551	3,543	2,050	11,837
Missing information on parents	4,124	1,408	3,743	1,683	10,958
Sample Used in Analysis	**16,222**	**13,324**	**13,776**	**9,602**	**52,924**

Table 2. Descriptive Statistics by Gender and Age Group

	Female 66-74 in 1992	Female Birth Certificate*	Female 75 - 84 in 1992	Male 66-74 in 1992	Male Birth Certificate*	Male 75 - 84 in 1992
	N=16222	N=5119	N=13324	N=13776	N= 7352	N=9602
Early Life Conditions			Mean (standard deviation) or %			
Father's Nam-Powers SES Score	49.6 (19.68)	51.39 (20.45)	47.50 (18.43)	49.58 (19.24)	50.03 (19.42)	47.29 (18.21)
Father Farmer	28.6%	26.3%	36.1%	29.7%	29.5%	36.3%
Father Missing SES	23.5%	22.78%	23.1%	22.9%	20.4%	23%
Active LDS	51.6%	47%	50.2%	51.9%	46.5%	51.2%
InActive LDS	24%	22.6%	28.3%	22.4%	23.1%	25.6%
Non-LDS	24.4%	30.4%	21.5%	25.7%	30.4%	23.2%
FEL Bottom 25%	22.7%	20.9%	23.7%	23%	22.4%	22.2%
FEL Middle 50%	43.9%	41.7%	43.8%	43.2%	42.1%	42.2%
FEL Top 25%	22.6%	22.8%	25.6%	23.3%	22.8%	28.3%
FEL Missing	10.8%	14.7%	6.9%	10.5%	12.7%	7.27%
Mother Died when Ego <18	9.8%	9.8%	10.6%	10.1%	9.9%	10.8%
Mother Died when Ego 18+	87.3%	87.9%	86.6%	86.6%	87.3%	85.9%
Father Died when Ego <18	11.1%	11.3%	11%	10.9%	11.2%	11.6%
Father Died when Ego 18+	85.9%	85.76%	86.3%	85.8%	85.9%	85%
Both Parents Died Before 18	2.97%	2.99%	2.7%	3.3%	2.9%	3.3%
Fertility History						
Children 1-2	28.2%	37.9%	36.1%	26.3%	31.7%	33.9%
Children 3-5	53.4%	50.75%	49.5%	55.4%	54.3%	51.1%
Children 6-9	15.9%	10.31%	12.2%	16%	12.5%	12.9%
Children 9+	2.9%	1%	2.24%	2.3%	1.5%	2.05%
Average Number of Children						
Infant Death (Y/N)	5.8%	3.95%	7.6%	5.4%	4.5%	6.7%
Short Birth Interval (Y/N)	26.7%	24.3%	20.3%	28.8%	26.8%	21%
Long Birth Interval (Y/N)	41.9%	29.07%	46.2%	39.6%	33.8%	45%
Mother/Father of Twin	4%	3.15%	3.8%	3.8%	3.4%	3.96%
Age at First Birth	23.64 (4.09)	26.75 (4.25)	25.09 (5.05)	25.92(4.32)	27.60 (4.43)	27.81 (5.03)
Age at First Birth Less than 18	3.14%	n/a	4.2%	0.19%	n/a	0.17%
Age at First Birth 18 - 24	67.6%	39.7%	51.4%	47.7%	29.7%	21.8%
Age at First Birth 25+	29.3%	60.34%	44.4%	52.2%	70.3%	68.6%
Age at Last Birth >= 35	39.5%	42.6%	48.1%	51.6%	46.7%	62.9%
Age at Last Birth 35 - 39	24.66%	27.4%	25.5%	26.3%	26.5%	24%
Age at Last Birth >=40	14.86%	15.2%	22.6%	25.3%	26.8%	38.9%
Information from Utah Birth Certificates						
At least 1 High Birth Weight Baby		16.7%			18.04%	
At least 1 Low Birth Weight Baby		8%			13.5%	
At Least One Preterm Birth		13.1%			14.1%	
Demographic Measures						
Age at Baseline	70.1 (2.6)	68.9 (2.6)	78.93 (2.82)	69.99 (2.57)	69.17 (2.46)	78.67 (2.76)
Spouse Alive at Baseline	75.2%	78.7%	33.61%	95.72%	96%	88.51%

*Age 66-74 in 1992 with birth certificate data on all births, making this a select sample. Females in the birth certificate sample are 1.2 years younger than the full sample of young-old age 66-74 (average age=68.9, range 66 - 74) and had to have their first birth after age 20 (1947 is the first year BC available). Males are slightly younger and had to have their first birth after age 20.

Table 3. Effects of Early Life Conditions and Fertility on Comorbidity Trajectory Group Membership: Women age 66 – 74 in 1992

	Slow Initiates (18.3%)	Accelerated Initiates (12.2%)	Chronic Low (20.2%)	Ailing (20.6%)	Frail (7.3%)
Early Life Conditions			Odd Ratio (95% CI)		
Active Member of LDS Church	0.7 (0.58,0.85)	0.54 (0.45,0.66)	0.62 (0.52,0.73)	0.38 (0.32,0.45)	0.39 (0.32,0.48)
Inactive Member of LDS Church	0.81 (0.66,0.99)	0.59 (0.48,0.73)	0.71 (0.58,0.85)	0.5 (0.42,0.6)	0.57 (0.45,0.71)
Non-Member (reference)	1.00	1.00	1.00	1.00	1.00
Father's NP SES (unit=10)	0.98 (0.95,1.01)	0.94 (0.91,0.97)	0.97 (0.94,1)	0.95 (0.92,0.98)	0.95 (0.91,0.98)
Father Farmer	0.97 (0.84,1.12)	0.81 (0.69,0.95)	0.99 (0.87,1.14)	0.78 (0.68,0.9)	0.71 (0.59,0.86)
Missing SES	0.84 (0.72,0.98)	0.85 (0.72,1.01)	0.96 (0.83,1.11)	0.84 (0.73,0.97)	0.87 (0.72,1.05)
FEL in Bottom Quartile	1.15 (0.98,1.35)	1.28 (1.08,1.52)	1.28 (1.1,1.48)	1.45 (1.26,1.67)	1.41 (1.16,1.7)
FEL in Mid 50% (reference)	1.00	1.00	1.00	1.00	1.00
FEL in Top Quartile	0.79 (0.69,0.91)	0.73 (0.62,0.85)	0.75 (0.65,0.85)	0.6 (0.52,0.69)	0.71 (0.59,0.86)
FEL Missing	1.09 (0.86,1.38)	0.98 (0.76,1.26)	0.82 (0.65,1.03)	0.73 (0.59,0.91)	0.7 (0.52,0.93)
Orphaned before Age 18	1.08 (0.72,1.62)	1.12 (0.74,1.68)	1.12 (0.78,1.62)	1.32 (0.94,1.86)	1.91 (1.28,2.85)
Mother Died before Child 18	1.07 (0.88,1.32)	1.2 (0.97,1.5)	1 (0.82,1.22)	1.2 (1,1.44)	1.3 (1.02,1.66)
Father Died before Child 18	1.25 (1.03,1.52)	1.27 (1.03,1.57)	1.13 (0.93,1.37)	1.35 (1.13,1.61)	1.38 (1.09,1.74)
Both Parents Alive at 18 (reference)	1.00	1.00	1.00	1.00	1.00
Fertility					
1-2 Children	0.96 (0.82,1.13)	1.11 (0.93,1.31)	0.93 (0.8,1.08)	1.07 (0.92,1.23)	1.13 (0.93,1.37)
3-5 Children (reference)	1.00	1.00	1.00	1.00	1.00
6-8 Children	1.02 (0.84,1.23)	1.07 (0.87,1.32)	1.11 (0.93,1.33)	1.16 (0.98,1.39)	1.08 (0.84,1.38)
9+ Children	1.05 (0.68,1.61)	1.14 (0.71,1.83)	1.51 (1.04,2.2)	1.56 (1.07,2.27)	1.15 (0.64,2.04)
Age at First Birth < 18	1.25 (0.86,1.82)	1.56 (1.06,2.28)	1.41 (1,1.99)	1.48 (1.06,2.06)	2.04 (1.36,3.06)
Age at First Birth 18 - 24 (ref)	1.00	1.00	1.00	1.00	1.00
Age at first Birth >= 25	0.99 (0.86,1.14)	0.95 (0.81,1.11)	0.95 (0.83,1.09)	0.89 (0.78,1.02)	1.12 (0.93,1.33)
Age at Last Birth 35 - 39	0.9 (0.77,1.05)	0.78 (0.66,0.93)	0.77 (0.67,0.9)	0.8 (0.69,0.93)	0.74 (0.61,0.91)
Age at Last Birth >= 40	0.73 (0.59,0.9)	0.75 (0.6,0.94)	0.74 (0.61,0.89)	0.7 (0.58,0.85)	0.71 (0.54,0.92)
Mother of Twins	1.05 (0.78,1.41)	0.95 (0.68,1.34)	0.89 (0.67,1.19)	1.11 (0.85,1.46)	0.9 (0.6,1.34)
One or More Short Birth Intervals	0.92 (0.79,1.06)	1.01 (0.86,1.18)	0.85 (0.74,0.98)	0.92 (0.81,1.06)	1.06 (0.88,1.28)
One or More Long Birth Intervals	1.01 (0.88,1.16)	1.14 (0.98,1.32)	0.99 (0.87,1.12)	1.08 (0.95,1.22)	0.98 (0.82,1.16)
One or More Infant Deaths	0.99 (0.77,1.27)	0.79 (0.59,1.05)	0.81 (0.63,1.03)	0.98 (0.78,1.24)	1.14 (0.84,1.54)
Age in 1992 (Centered)	1.08 (1.06,1.11)	1.11 (1.08,1.14)	1.12 (1.09,1.14)	1.12 (1.1,1.15)	1.13 (1.1,1.17)

Table 4. Effects of Early Life Conditions and Fertility on Comorbidity Trajectory Group Membership: Women age 75 – 84 in 1992

	Initiate (21%)	Chronic Low (15.7%)	Ailing (32.3%)	Frail (13.7%)
ELCS		Odd Ratio (95% CI)		
Active Member of LDS Church	0.85 (0.69,1.04)	0.68 (0.57,0.8)	0.9 (0.72,1.14)	0.73 (0.59,0.9)
Inactive Member of LDS Church	0.97 (0.78,1.2)	0.79 (0.65,0.94)	0.87 (0.68,1.11)	0.9 (0.72,1.12)
Non-Member (reference)	1.00	1.00	1.00	1.00
Father's NP SES (unit=10)	1.01 (0.98,1.05)	1 (0.97,1.03)	1.01 (0.97,1.06)	0.98 (0.94,1.02)
Father Farmer	0.98 (0.83,1.16)	1.14 (0.98,1.32)	1.12 (0.93,1.35)	0.97 (0.81,1.15)
Missing SES	0.83 (0.69,1)	0.91 (0.78,1.07)	1.01 (0.83,1.24)	0.91 (0.75,1.09)
FEL in Bottom Quartile	1.28 (1.06,1.55)	1.49 (1.27,1.75)	1.28 (1.04,1.59)	1.54 (1.28,1.86)
FEL in Mid 50% (reference)	1.00			
FEL in Top Quartile	0.8 (0.68,0.94)	0.71 (0.62,0.82)	0.88 (0.73,1.05)	0.66 (0.55,0.79)
FEL Missing	0.89 (0.66,1.2)	0.72 (0.56,0.94)	0.9 (0.64,1.26)	0.72 (0.53,1)
Orphaned before Age 18	0.8 (0.5,1.25)	1.49 (1.05,2.11)	1.09 (0.68,1.75)	0.8 (0.48,1.33)
Mother Died before Child 18	1.15 (0.92,1.45)	1.11 (0.91,1.36)	1.24 (0.97,1.59)	1.19 (0.94,1.5)
Father Died before Child 18	1.16 (0.93,1.46)	1.27 (1.05,1.55)	1.12 (0.87,1.45)	1.13 (0.89,1.43)
Both Parents Alive at 18 (reference)	1.00	1.00	1.00	1.00
Fertility				
1-2 Children	1.1 (0.92,1.32)	0.99 (0.84,1.15)	0.98 (0.8,1.19)	0.99 (0.82,1.2)
3-5 Children (reference)	1.00	1.00	1.00	1.00
6-8 Children	1.12 (0.88,1.43)	1.19 (0.96,1.47)	0.97 (0.74,1.28)	1.19 (0.93,1.54)
9+ Children	1.41 (0.81,2.46)	1.53 (0.94,2.49)	1.01 (0.53,1.92)	2.51 (1.48,4.26)
Age at First Birth < 18	1.41 (0.87,2.3)	1.68 (1.1,2.55)	1.75 (1.04,2.94)	1.96 (1.24,3.1)
Age at First Birth 18 - 24 (ref)	1.00	1.00	1.00	1.00
Age at first Birth >= 25	0.83 (0.71,0.97)	0.82 (0.71,0.95)	0.74 (0.62,0.89)	0.78 (0.66,0.93)
Age at Last Birth < 35	1.00	1.00	1.00	1.00
Age at Last Birth 35 - 39	1.09 (0.9,1.3)	0.97 (0.83,1.14)	1.22 (1,1.5)	1.03 (0.85,1.25)
Age at Last Birth >= 40	1.03 (0.83,1.27)	0.85 (0.71,1.02)	1.16 (0.91,1.47)	0.81 (0.64,1.01)
Mother of Twins	0.9 (0.63,1.27)	0.85 (0.63,1.16)	0.87 (0.58,1.3)	0.91 (0.63,1.3)
One or More Short Birth Intervals	1.01 (0.84,1.22)	1.03 (0.88,1.21)	0.8 (0.64,0.99)	0.97 (0.79,1.18)
One or More Long Birth Intervals	0.82 (0.7,0.97)	0.87 (0.75,0.99)	0.67 (0.56,0.81)	0.83 (0.7,0.98)
One or More Infant Deaths	0.84 (0.63,1.11)	1.08 (0.86,1.36)	1.1 (0.82,1.48)	1.12 (0.85,1.46)
Age in 1992 (Centered)	1.08 (1.05,1.11)	1.14 (1.11,1.16)	1.14 (1.11,1.18)	1.12 (1.09,1.15)

Table 5. Effects of Early Life Conditions and Fertility on Comorbidity Trajectory Group Membership: Men age 66-74 in 1992

	Slow Initiates (15.6%)	Accelerated Initiates (13.8%)	Chronic Low (20.8%)	Ailing (24%)	Frail (8.2%)
ELCS		Odd Ratio (95% CI)			
Active Member of LDS Church	0.76 (0.61,0.95)	0.52 (0.42,0.65)	0.67 (0.55,0.82)	0.41 (0.34,0.49)	0.29 (0.23,0.37)
Inactive Member of LDS Church	0.79 (0.61,1.01)	0.72 (0.57,0.91)	0.77 (0.61,0.97)	0.62 (0.51,0.77)	0.49 (0.38,0.62)
Non-Member (ref)	1.00	1.00	1.00	1.00	1.00
Father's NP SES (unit=10)	0.98 (0.94,1.02)	0.97 (0.93,1.01)	0.98 (0.94,1.01)	1 (0.97,1.04)	1 (0.96,1.04)
Father Farmer	0.97 (0.82,1.16)	1.02 (0.86,1.22)	0.86 (0.74,1.01)	1.12 (0.97,1.31)	1 (0.82,1.23)
Missing SES	1.1 (0.91,1.32)	1.03 (0.86,1.25)	0.89 (0.75,1.06)	1 (0.85,1.18)	1.12 (0.91,1.38)
FEL in Bottom Quartile	1.29 (1.06,1.58)	1.27 (1.05,1.55)	1.42 (1.19,1.7)	1.57 (1.33,1.85)	1.4 (1.13,1.72)
FEL in Mid 50% (ref)	1.00	1.00	1.00	1.00	1.00
FEL in Top Quartile	0.81 (0.68,0.96)	0.74 (0.62,0.89)	0.77 (0.66,0.9)	0.71 (0.61,0.82)	0.65 (0.53,0.79)
FEL Missing	1.32 (0.98,1.77)	1.25 (0.94,1.65)	1.1 (0.84,1.44)	0.79 (0.61,1.03)	0.61 (0.44,0.84)
Orphaned before Age 18	0.5 (0.31,0.81)	0.7 (0.46,1.06)	0.91 (0.63,1.33)	0.83 (0.58,1.19)	0.99 (0.65,1.52)
Mother Died before Child 18	0.96 (0.75,1.23)	1.19 (0.94,1.51)	1.06 (0.85,1.33)	1.07 (0.87,1.32)	1.2 (0.92,1.56)
Father Died before Child 18	1.03 (0.8,1.31)	1.16 (0.91,1.47)	1.09 (0.87,1.37)	1.29 (1.05,1.59)	1.17 (0.9,1.53)
Both Parents Alive at 18 (ref)	1.00	1.00	1.00	1.00	1.00
Fertility					
1-2 Children	0.99 (0.81,1.2)	1.09 (0.9,1.31)	1.07 (0.9,1.28)	1.04 (0.88,1.23)	1.13 (0.91,1.4)
3-5 Children (ref)	1.00	1.00	1.00	1.00	1.00
6-8 Children	0.81 (0.64,1.01)	0.86 (0.68,1.08)	0.85 (0.7,1.05)	0.85 (0.7,1.04)	1.03 (0.79,1.34)
9+ Children	0.77 (0.47,1.26)	0.81 (0.5,1.31)	0.64 (0.4,1.02)	0.76 (0.5,1.16)	0.98 (0.55,1.75)
Age at First Birth 18 - 24 (ref)	1.00	1.00	1.00	1.00	1.00
Age at first Birth >= 25	0.96 (0.81,1.12)	0.87 (0.75,1.03)	0.81 (0.7,0.94)	0.79 (0.69,0.91)	0.88 (0.74,1.06)
Age at Last Birth < 35	1.00	1.00	1.00	1.00	1.00
Age at Last Birth 35 - 39	1.03 (0.85,1.24)	0.99 (0.82,1.21)	1.05 (0.88,1.25)	1 (0.85,1.18)	0.92 (0.74,1.14)
Age at Last Birth >= 40	0.96 (0.76,1.22)	1.05 (0.84,1.32)	0.91 (0.73,1.12)	1.04 (0.85,1.26)	0.81 (0.62,1.05)
Father of Twins	0.97 (0.67,1.41)	0.97 (0.66,1.41)	1.16 (0.84,1.61)	1.01 (0.73,1.4)	1.01 (0.66,1.56)
One or More Short Birth Intervals	1.18 (0.99,1.4)	1.12 (0.94,1.34)	1.27 (1.08,1.49)	1.14 (0.98,1.33)	1.25 (1.02,1.52)
One or More Long Birth Intervals	1.04 (0.88,1.23)	0.99 (0.84,1.17)	1.13 (0.97,1.31)	1.01 (0.88,1.16)	1.12 (0.93,1.35)
One or More Infant Deaths	0.85 (0.61,1.19)	1.03 (0.75,1.41)	1.03 (0.78,1.37)	0.92 (0.7,1.21)	0.96 (0.67,1.37)
Age in 1992 (Centered)	1.04 (1.02,1.08)	1.08 (1.05,1.12)	1.1 (1.07,1.13)	1.15 (1.12,1.18)	1.15 (1.11,1.19)

Table 6. Effects of Early Life Conditions and Fertility on Comorbidity Trajectory Group Membership: Men age 75-84 in 1992

	Initiates (16.1%) vs. Robust	Chronic Low (23%) vs. Robust	Ailing (34.2%) vs. Robust	Frail (12.3%) vs. Robust
ELCS	Odd Ratio (95% CI)			
Active Member of LDS Church	0.78 (0.6,1.02)	0.74 (0.59,0.95)	0.77 (0.62,0.96)	0.59 (0.46,0.77)
Inactive Member of LDS Church	0.97 (0.72,1.31)	0.94 (0.72,1.24)	1.04 (0.82,1.33)	0.9 (0.68,1.2)
Non-Member (reference)	1.00	1.00	1.00	1.00
Father's NP SES (unit=10)	0.99 (0.94,1.05)	0.99 (0.95,1.04)	0.98 (0.93,1.02)	1 (0.95,1.05)
Father Farmer	0.86 (0.68,1.08)	0.87 (0.71,1.07)	0.91 (0.76,1.09)	1.04 (0.83,1.3)
Missing SES	1.53 (0.18,13.09)	1.09 (0.16,7.55)	2.5 (0.44,14.1)	1.08 (0.13,8.86)
FEL in Bottom Quartile	1.51 (1.15,1.99)	1.4 (1.09,1.8)	1.77 (1.42,2.21)	2.02 (1.57,2.6)
FEL in Mid 50% (reference)	1.00	1.00	1.00	1.00
FEL in Top Quartile	0.89 (0.72,1.1)	0.79 (0.65,0.96)	0.77 (0.65,0.92)	0.77 (0.62,0.96)
FEL Missing	0.7 (0.46,1.06)	0.88 (0.61,1.26)	0.74 (0.53,1.03)	0.72 (0.49,1.08)
Orphaned before Age 18	1.25 (0.74,2.12)	1.17 (0.72,1.9)	1.02 (0.65,1.6)	1 (0.59,1.7)
Mother Died before Child 18	1.14 (0.84,1.54)	0.99 (0.74,1.32)	1.19 (0.93,1.53)	1 (0.73,1.35)
Father Died before Child 18	1.02 (0.76,1.37)	0.84 (0.64,1.11)	1.07 (0.84,1.35)	1.12 (0.85,1.49)
Both Parents Alive at 18 (reference)	1.00	1.00	1.00	1.00
Fertility				
1-2 Children	1.09 (0.84,1.4)	1.14 (0.91,1.44)	1.05 (0.86,1.29)	1.16 (0.91,1.49)
3-5 Children (reference)	1.00	1.00	1.00	1.00
6-8 Children	0.89 (0.65,1.23)	1 (0.75,1.33)	1.12 (0.88,1.45)	0.88 (0.64,1.21)
9+ Children	1.09 (0.53,2.22)	1.18 (0.64,2.15)	0.95 (0.53,1.71)	0.91 (0.46,1.8)
Age at First Birth 18 - 24 (ref)	1.00	1.00	1.00	1.00
Age at first Birth >= 25	1.09 (0.87,1.38)	0.86 (0.7,1.06)	0.89 (0.74,1.07)	0.79 (0.64,0.99)
Age at Last Birth < 35 (Ref)	1.00	1.00	1.00	1.00
Age at Last Birth 35 - 39	0.81 (0.62,1.06)	0.79 (0.62,1.01)	0.82 (0.67,1.02)	0.83 (0.64,1.08)
Age at Last Birth >= 40	0.87 (0.65,1.17)	0.95 (0.73,1.23)	0.78 (0.62,0.98)	0.92 (0.7,1.21)
Mother of Twins	1.00	1.00	1.00	1.00
One or More Short Birth Intervals	1.12 (0.87,1.43)	1.02 (0.81,1.28)	0.92 (0.75,1.13)	1.06 (0.83,1.36)
One or More Long Birth Intervals	1.12 (0.9,1.39)	1.08 (0.89,1.31)	1.05 (0.88,1.25)	1.15 (0.93,1.41)
One or More Infant Deaths	1.33 (0.9,1.96)	1.27 (0.89,1.81)	1.31 (0.95,1.8)	1.07 (0.72,1.59)
Age in 1992 (Centered)	1.07 (1.03,1.12)	1.11 (1.08,1.15)	1.11 (1.08,1.15)	1.14 (1.1,1.18)

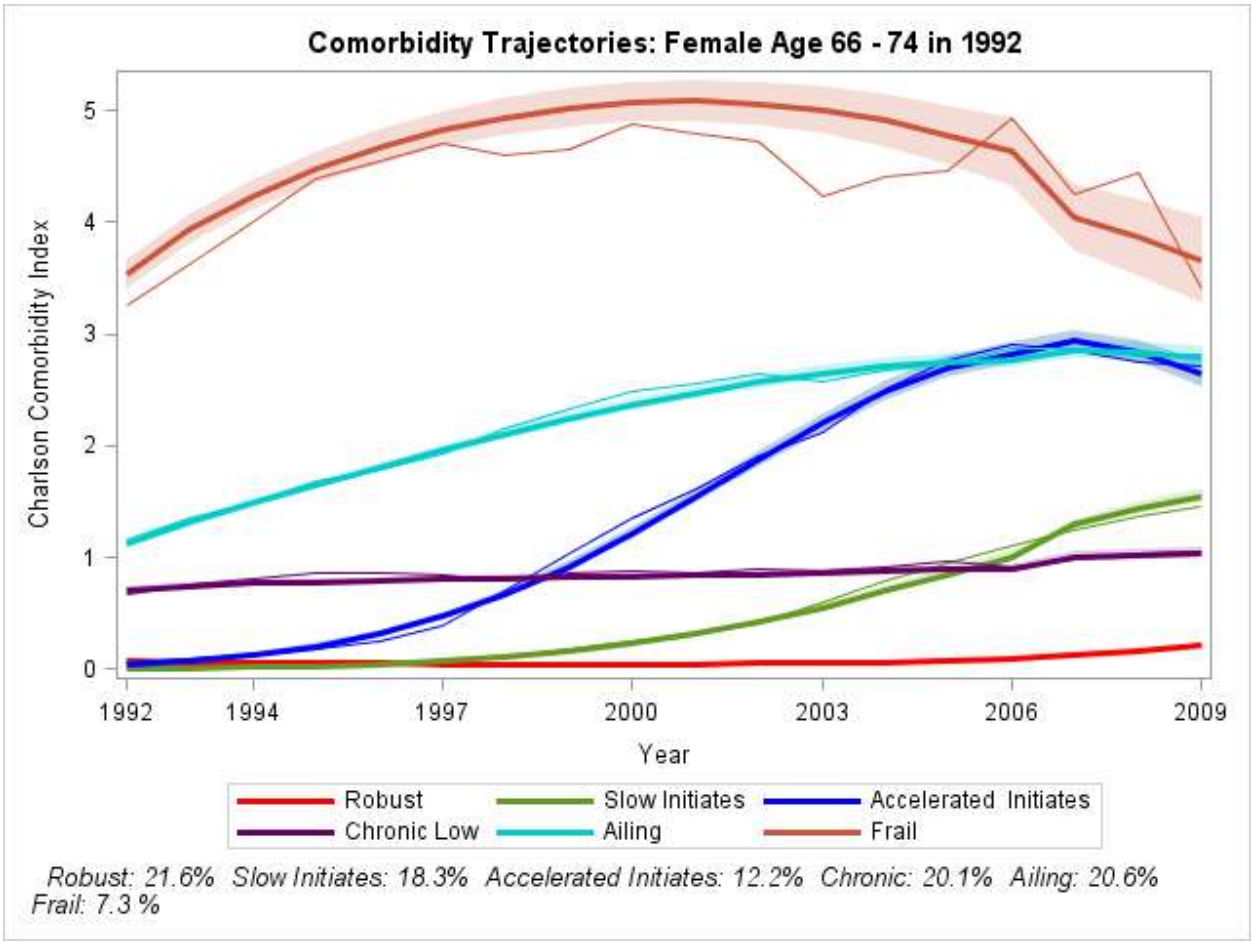

Figure 1. Comorbidity Trajectories for Females 66-74 in 1992

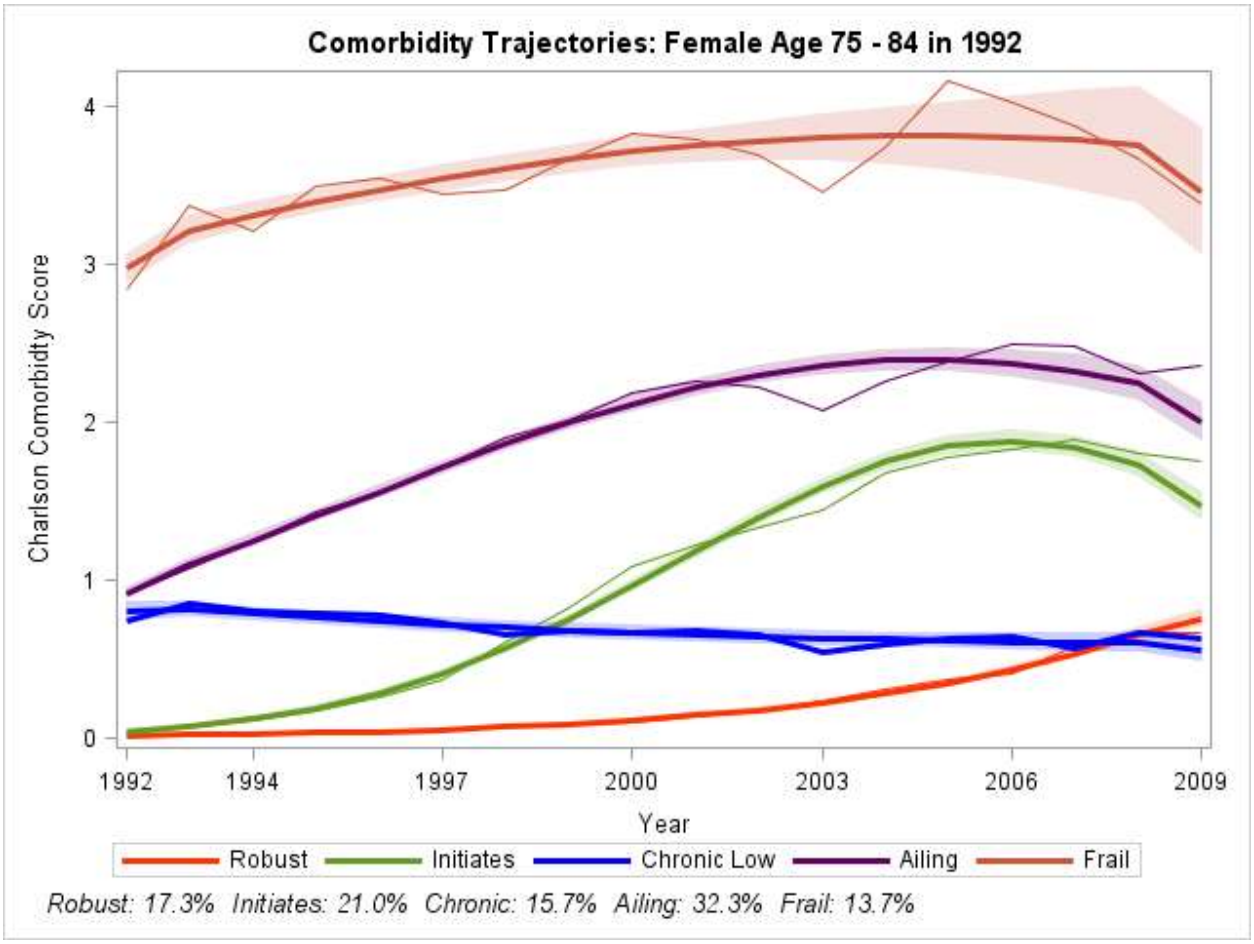

Figure 2. Comorbidity Trajectories for Females 75-84 in 1992

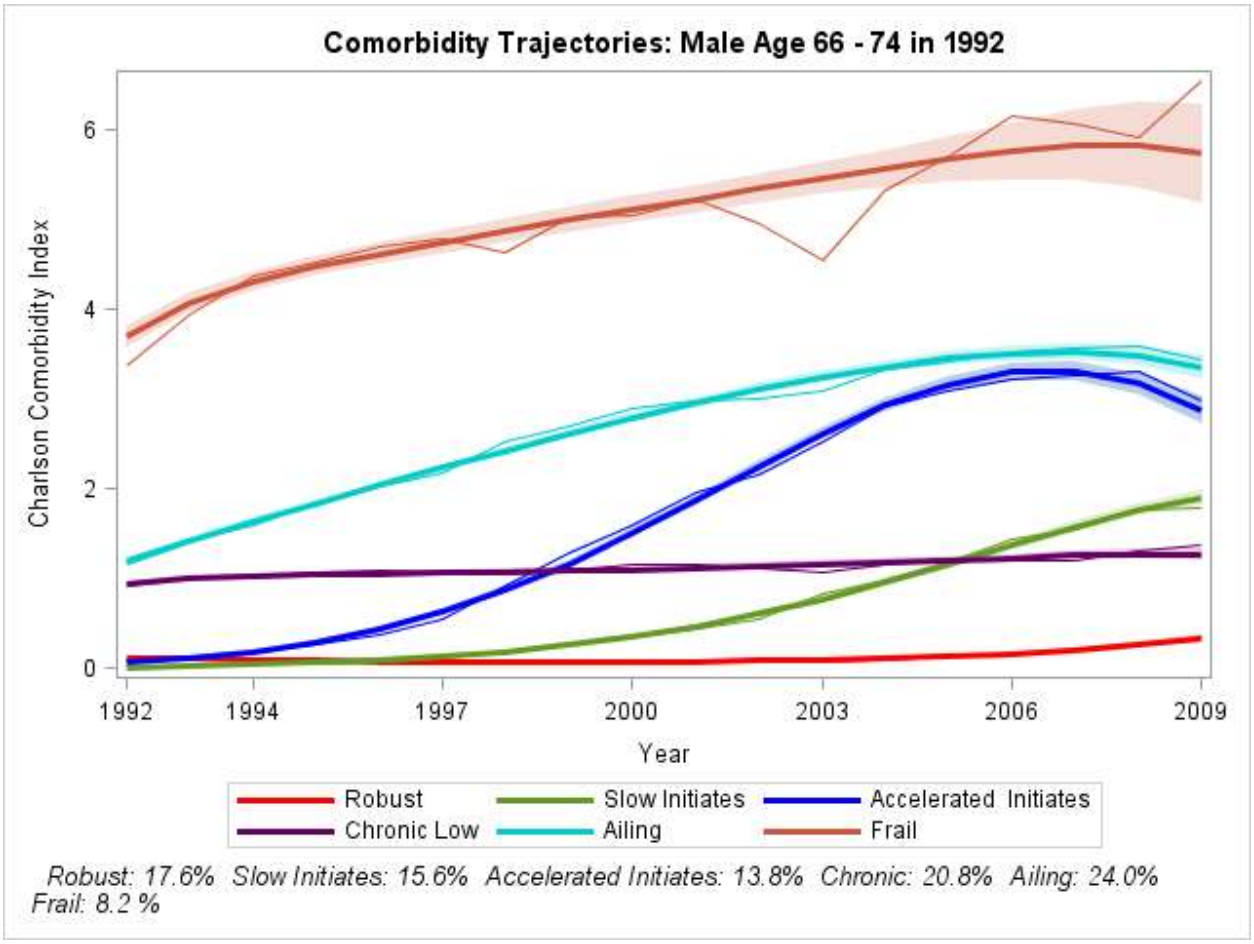

Figure 3. Comorbidity Trajectories for Males 66-74 in 1992

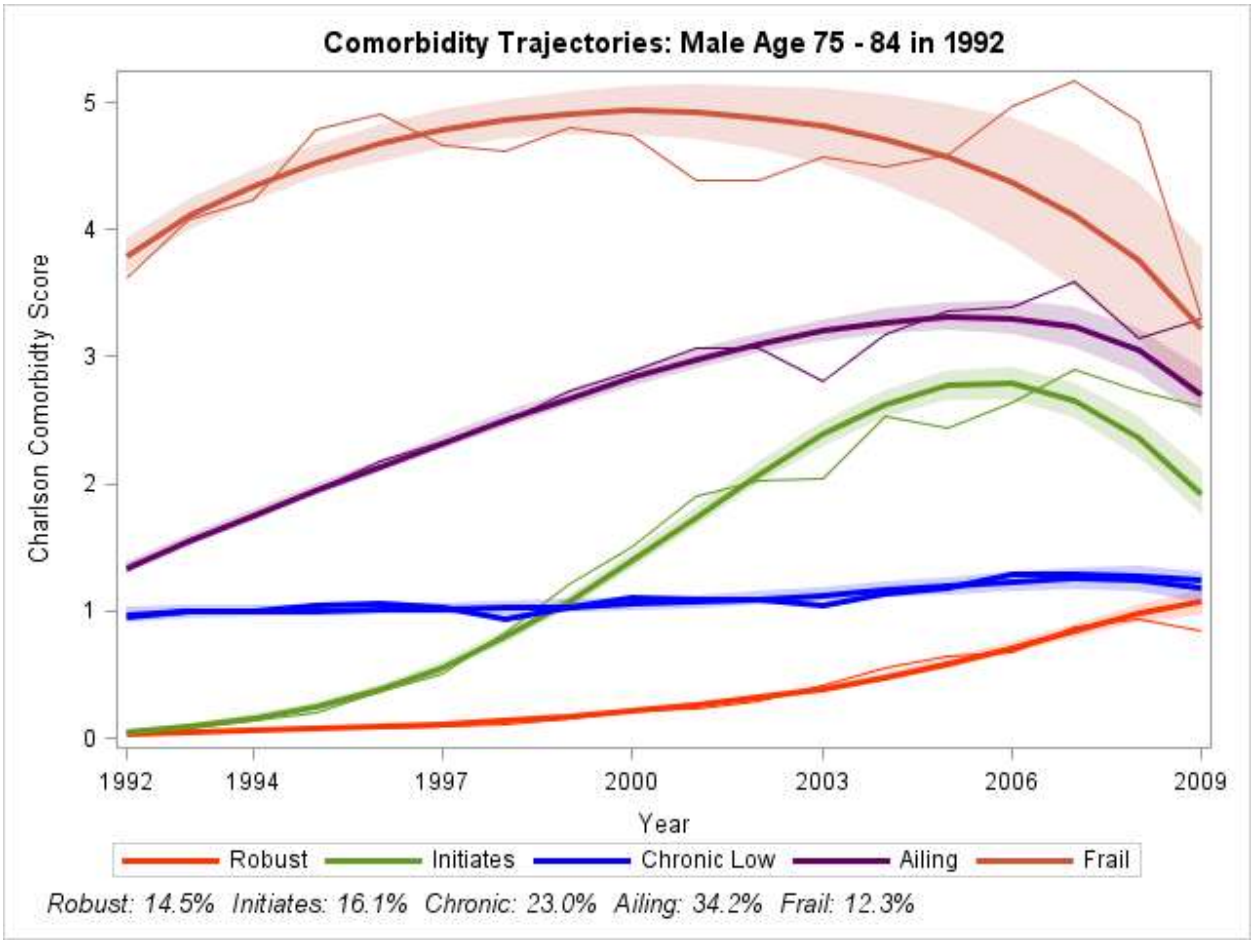

Figure 4. Comorbidity Trajectories for Males 75 – 84 in 1992

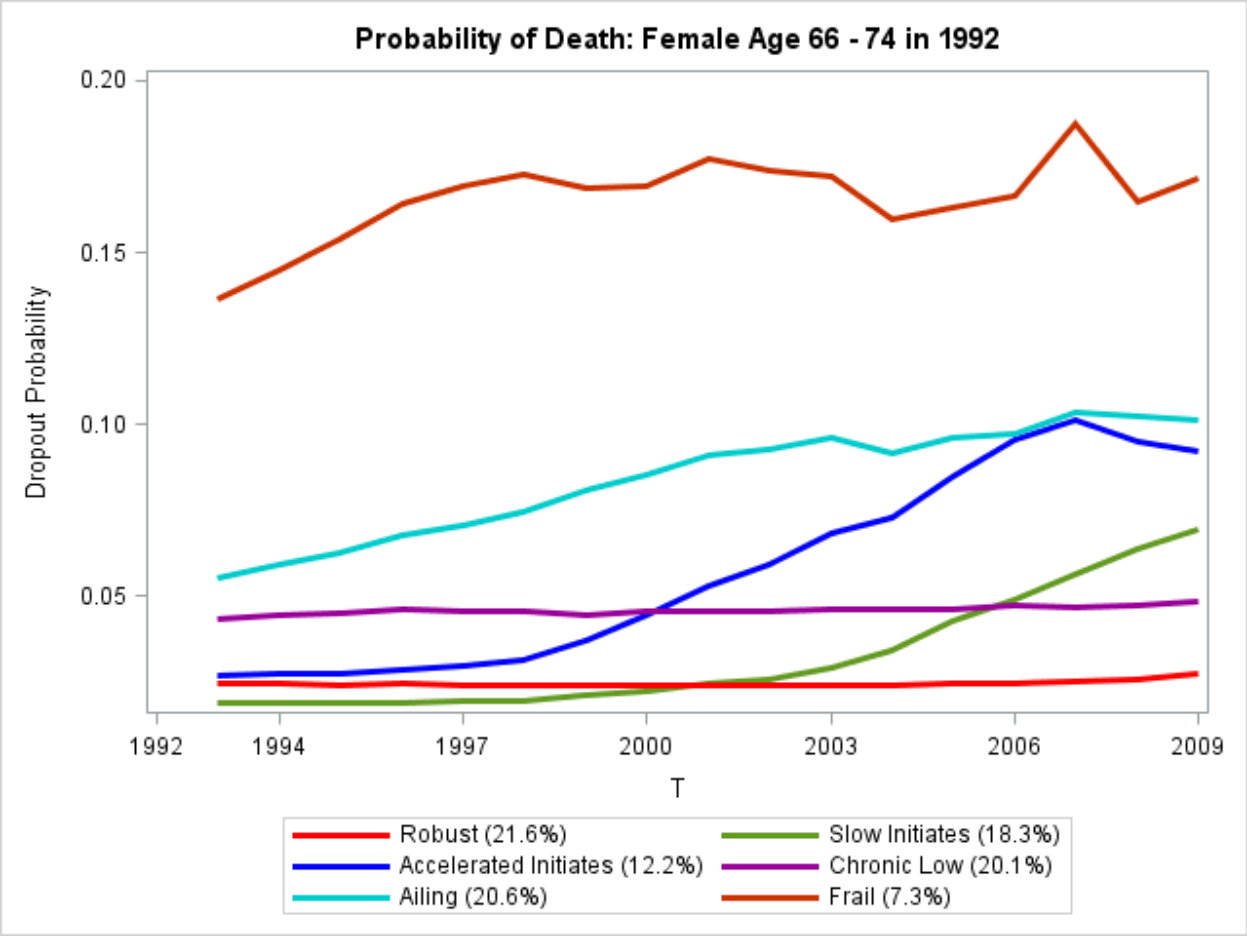

Figure 5. Morbidity trajectories for Females age 66 – 74 in 1992

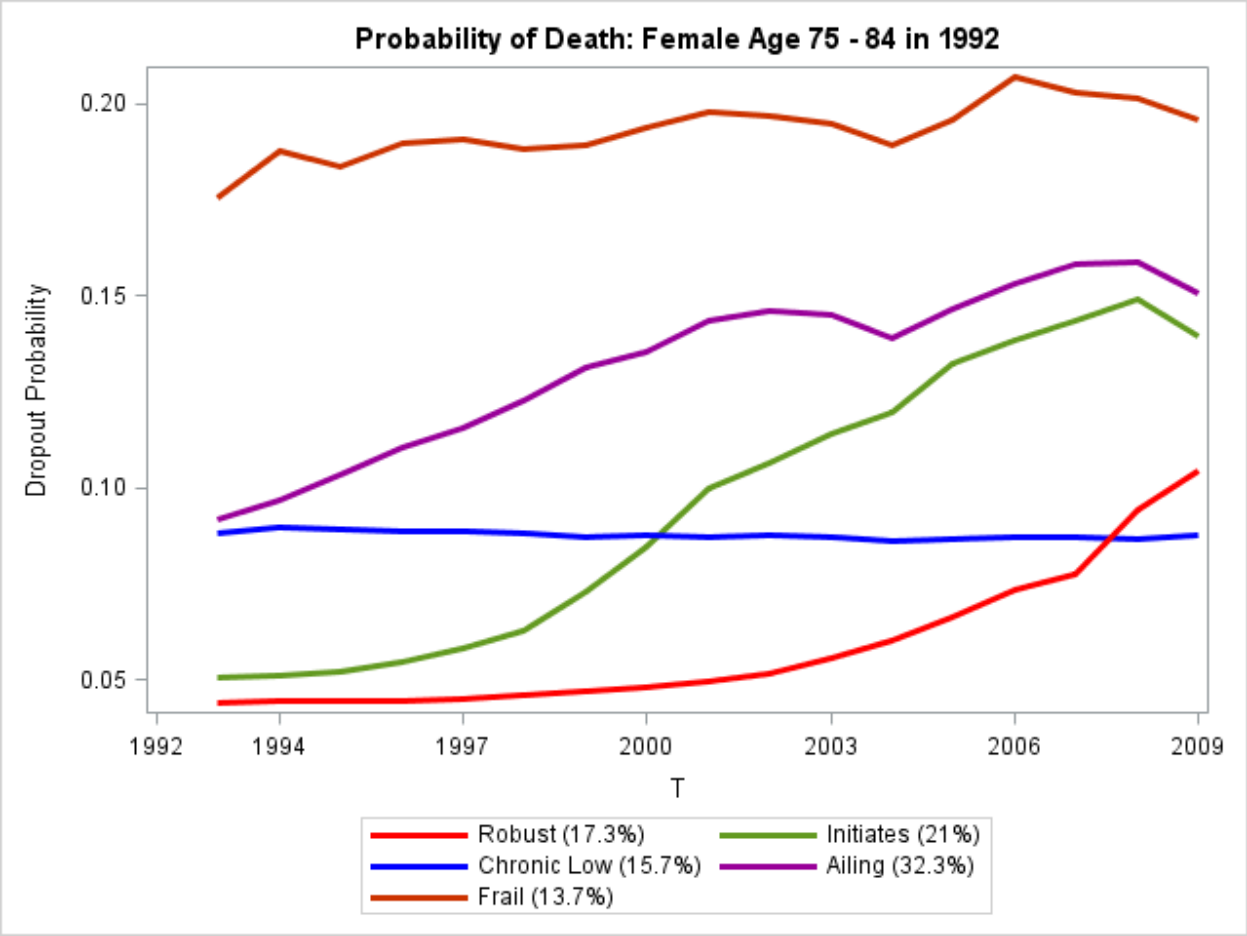

Figure 6. Morbidity trajectories for Females age 75 – 84 in 1992

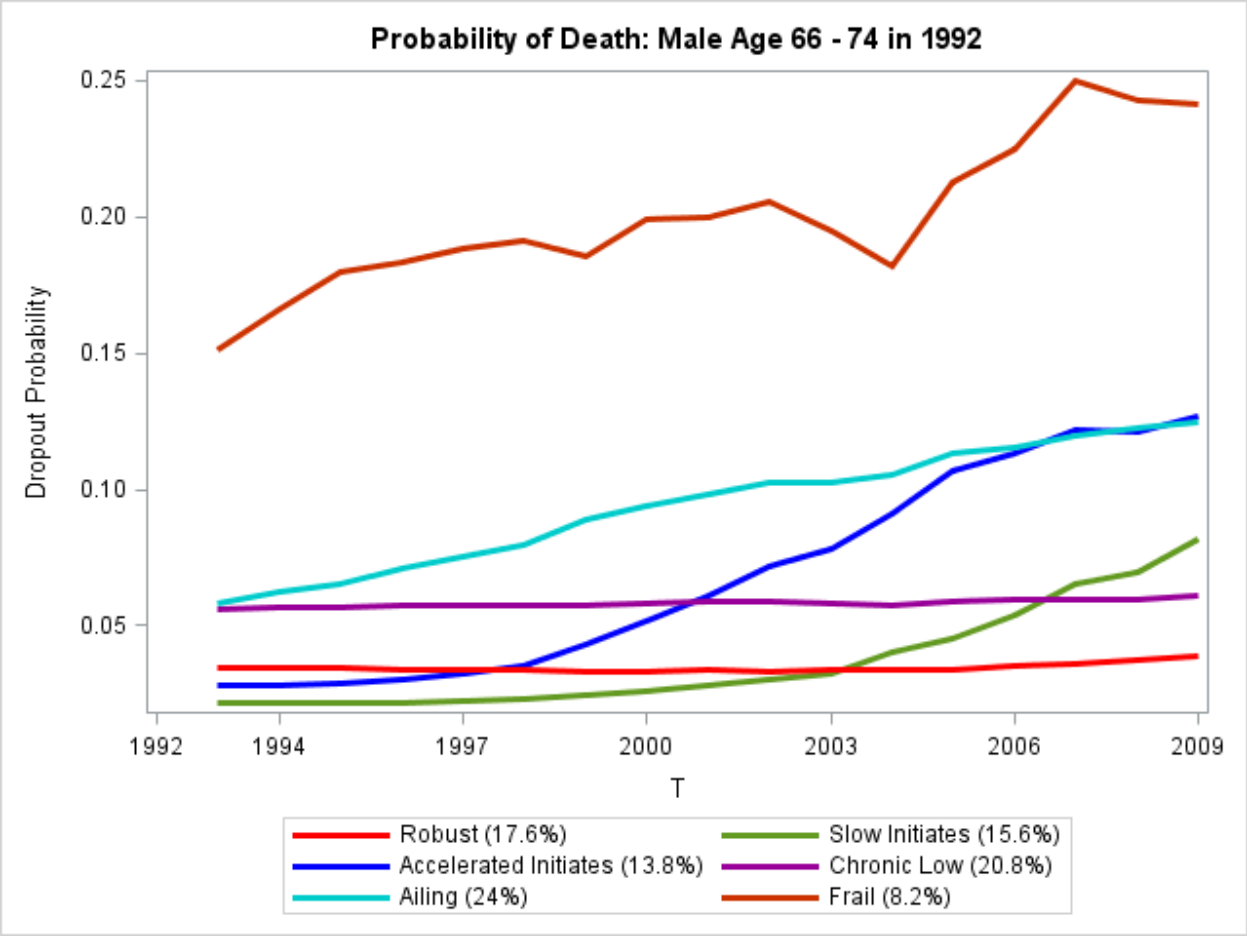

Figure 7. Morbidity trajectories for Males age 66 - 74 in 1992

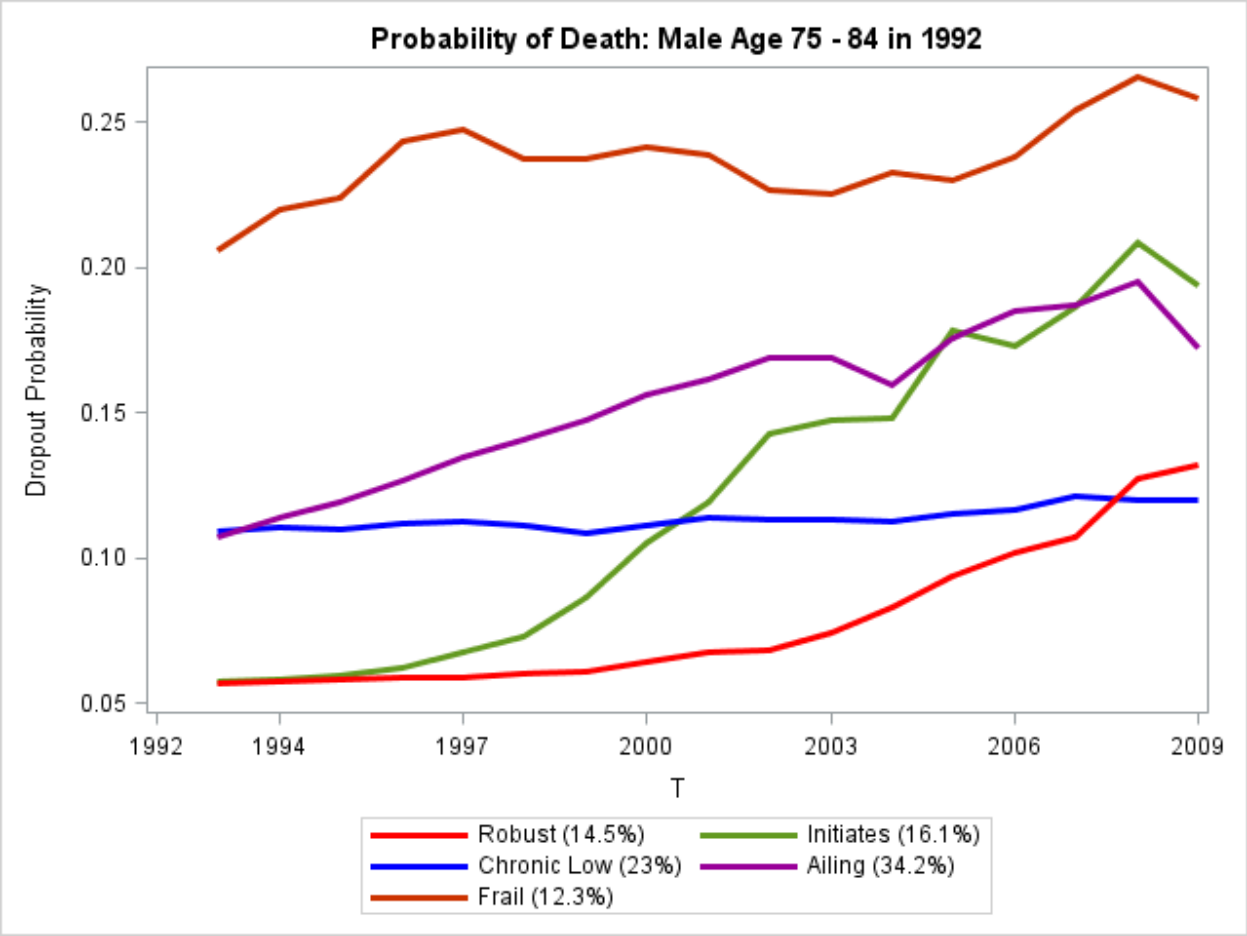

Figure 8. Morbidity trajectories for Males age 66 - 74 in 1992

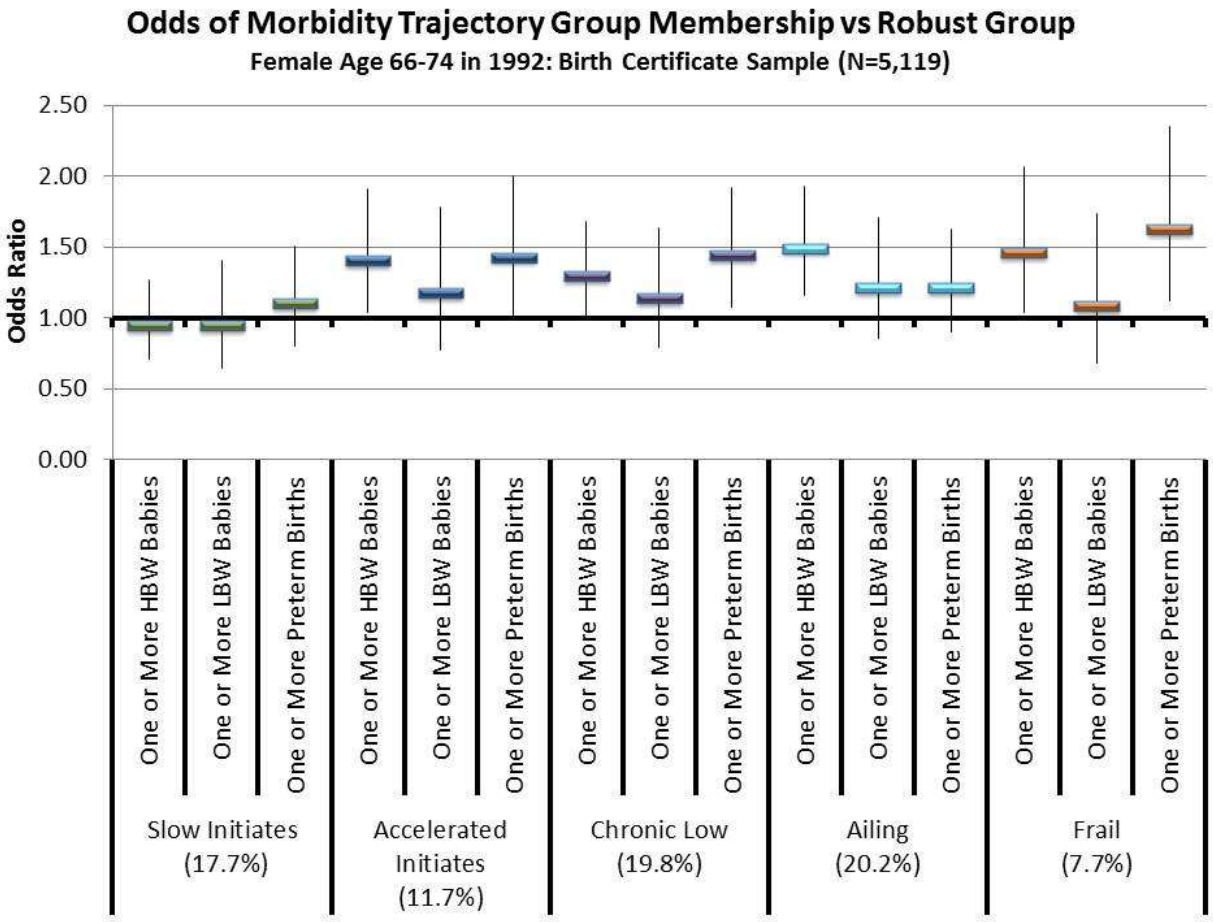

Figure 9. Female Birth Certificate Results

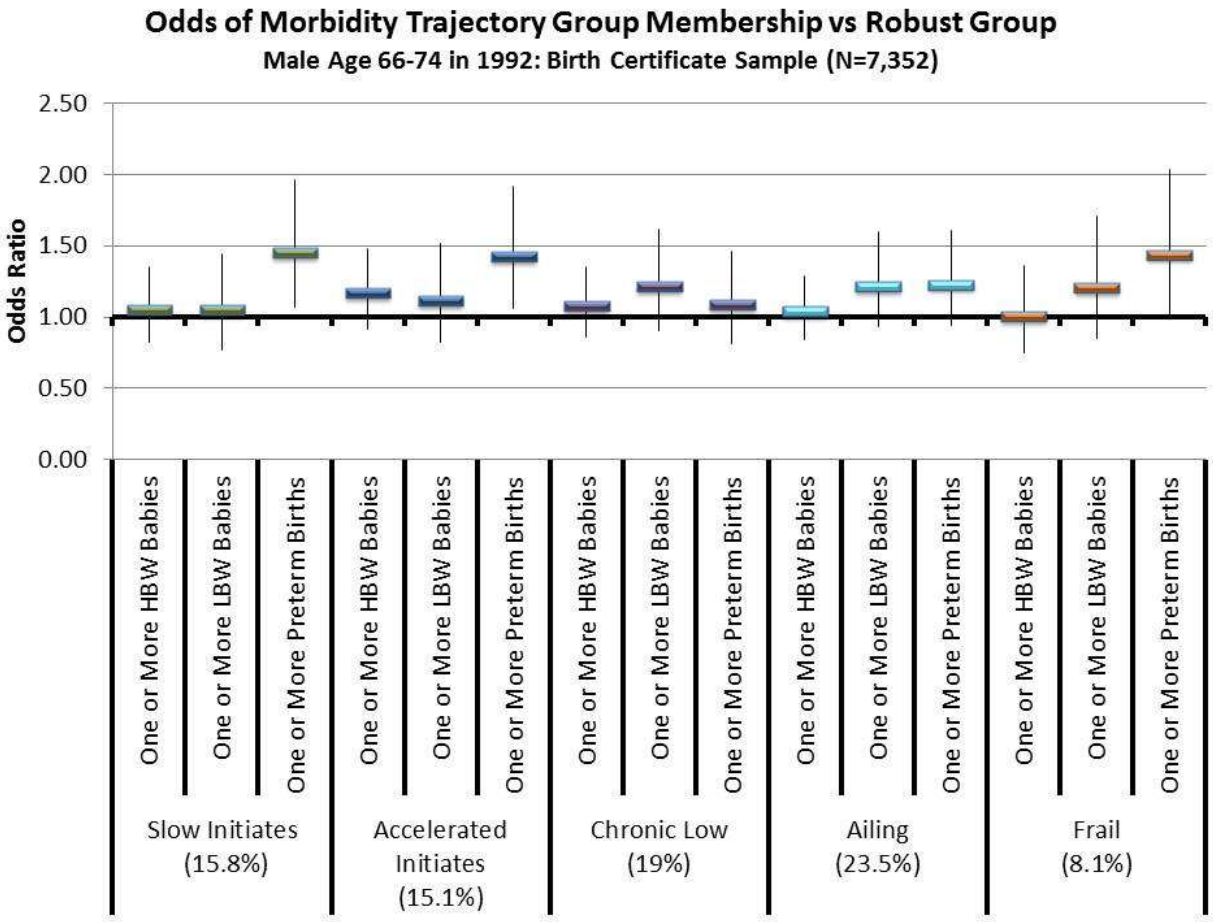

Figure 10. Female Birth Certificate Results

Acknowledgements:
We wish to thank the Pedigree and Population Resource of the Huntsman Cancer Institute, University of Utah for providing the data and valuable computing support. This work was also supported by NIH grant AG022095 (Early Life Conditions, Survival and Health; Smith PI).