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Secular Trends in Life Expectancy by Diet Status Among Never Smoking Seventh-day Adventists

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SECULAR TRENDS IN LIFE EXPECTANCY BY DIET STATUS AMONG NEVER SMOKING SEVENTH-DAY ADVENTISTS

by

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Each person whose signature appears below certifies that this dissertation, in his/her opinion, is adequate in scope and quality as a dissertation for the degree Doctor of Public Health.

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ABSTRACT OF THE DISSERTATION

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To evaluate how life expectancy changed by age and secular time from 1960 through 1988, two cohort studies, the Adventist Mortality Study (AMS, 1960-1985, n = 27,530) and the Adventist Health Study (AHS, 1976-1988, n = 34,192) were combined. The life expectancy of omnivores was compared to vegetarians separately in never-smoking males and females for all-cause mortality, and where the cause of death was cardiovascular disease or all site-cancer. Life expectancies were calculated for subjects who had survived to ages 30, 50, 70, and 80 during six calendar periods: 1960-1964, 1965-1969, 1970-1974, 1975-1979, 1980-1984, and 1985-1988. Ten-year calendar periods were used for the specific causes of death: heart disease and all-sites cancer, because of the small number of events. The basis for the life table calculations was the age-specific mortality rates, which were calculated using the Multiple Decrement Life Table Analysis Program (MDLTAP) taking into account competing causes of death and

allowing for the control of confounders. Both univariate and multivariate analyses were performed controlling for the potential confounders: education, body mass index (BMI), and exercise. Secular trends in life expectancies were examined using weighted linear regression, where inverse variances obtained from the MDLTAP program were used as weights for the respective calendar periods.

The life expectancy for both males and females increased with secular time from 1960 to 1988 for all ages, and the linear trend was significant at most ages. The trend tended to be steeper in omnivores compared to vegetarians and in females as compared to males. The life expectancy of vegetarian females who had survived to 30, 50, and 70 years of age was about two years higher than that of omnivores for the calendar periods 1965-1969, 1975-1979, and 1980-1984. The life expectancy of vegetarian males up to 80 years of age was 1-4 years higher than that of omnivores for all calendar periods.

The life expectancy at all ages of both females and males who eventually died from heart disease or cancer increased with secular time from 1960-1988, irrespective of their type of diet. This increase was 2-10 years in females and 2-7 years in males. The life expectancy at all ages for vegetarian females who died from heart disease or cancer was 1-2 years higher than that of omnivores in the calendar period 1970-1979. The difference in life expectancy that was attributed to a vegetarian status in males who died of heart disease or cancer was 1-4 years. This difference was statistically significant at most ages.

In conclusion, the life expectancy for both males and females increased with secular time from 1960 to 1988, irrespective of type of diet and cause of death. The life expectancy of vegetarians at all ages was 1-4 years higher than that of omnivores. Females had a higher life expectancy than males. The gender differences in life expectancy were less in vegetarians compared to omnivores. A vegetarian diet does contribute to greater longevity, and this lifestyle decreases the gender gap in life expectancy.

TABLE OF CONTENTS

LIST OF TABLES

PUBLISHABLE PAPER I

PUBLISHABLE PAPER II

LIST OF FIGURES

CHAPTER 3 (PUBLISHABLE PAPER I)

APPENDIX B

ADDITIONAL FIGURES (PUBLISHABLE PAPER II)

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CHAPTER 1

INTRODUCTION

At the end of the 19^{th} century, about one in 100,000 Americans were 100 years old or more. In the year 2000, the figure was one in 4,235 and rising (1). The growing number of older adults increases the demands on the public health and medical systems, and social services. In the year 2000, it has been estimated that nearly half of Americans suffered from at least one chronic disease (125 million) and one-fifth of Americans had two or more chronic diseases. In the same year, the total annual health care cost for someone with one chronic illness was more than five times higher than for a healthy person ($6032 vs. $1105)(2). Gazzaniga et al (3) reported that $5.3 billion are lost in productivity due to mortality caused by heart diseases. Risk factor modification through the reduction of potentially detrimental behaviors such as smoking and sedentary life-style has the potential to substantially postpone mortality from chronic diseases (3).

Since the early 1970's, declines in mortality from chronic diseases at older ages have caused sharp increases in life expectancy (4-6). From 1980 to 1998, life expectancy for males and females rose 2.7 years resulting in a life expectancy of 74.2 years for males and 79.5 years for females (7). Because behaviors that place persons at risk often originate early in life, the public health system should support healthy behaviors throughout a person's lifetime (8). Diet is believed to be a major determinant of many causes of death, particularly cardiovascular disease and cancer (9, 10). Epidemiological studies investigating the association of diet and health have often related individual foods or nutrients to health outcomes (11). Ecological, case-control, and prospective studies have also shown that a dietary pattern largely based on plant foods is associated with decreased risk of mortality in both men and women (12-16).

Members of the Seventh-day Adventist (SDA) church adhere to church prescriptions on the use of tobacco, alcohol, and pork. The church recommends, moreover, that members practice a vegetarian lifestyle. Regarding diet, Adventists are quite heterogeneous. The church only recommends abstinence from flesh foods and allows the eating of eggs and dairy products with no restrictions. Consequently, about 3% of the Adventists are vegans; about 27% are lacto-ovo vegetarians; about 20% eat meat less than once per week; and the remainder eat meat more than four times a week on average (17). The low prevalence of cigarette smoking and alcohol use among this study population, who still exhibit a wide variety of food habits and other lifestyle factors, provides a unique opportunity to study the independent relationship between diet and longevity, and to examine the secular trends in life expectancy among healthy adults.

California Adventists adopted life-style characteristics that predict improved health and longevity decades before these characteristics were considered desirable by the general population. This suggests that the relationships between selected lifestyle characteristics and health and longevity outcomes among California Adventists can provide insights into the future of the United States general population. The Adventist Mortality Study (AMS) and the Adventist Health Study (AHS) cohorts are an excellent source of data to test the effect of diet on mortality patterns and changes in life expectancy from 1960 through 1988 because of similar age structure and risk factor distributions in the two studies.

To date, the relationship between diet and mortality (all cause mortality, cardiovascular mortality, and mortality from cancer) has been reported among men and women in the Adventist Mortality Study and the Adventist Health Study. Fraser et al (18) also reported that a vegetarian diet, past smoking habits, lean body mass index, regular physical activity, and nut consumption were each associated independently with longer median life expectancy in the AHS.

The two studies of this dissertation evaluate the following hypotheses:

1. The life expectancies of Seventh-day Adventist non-smoking males and females who survived to 30, 50, 70, and 80 years of age will increase from 1960 through 1988.
2. The life expectancies will increase similarly in vegetarians and omnivores.
3. The life expectancies of vegetarians will be higher than those of omnivores at all ages from 1960 through 1988.
4. Subjects with favorable health habits (exercise, highly educated, and with low body mass index) will have higher life expectancies at all ages from 1960 through 1988.
5. The life expectancies of subjects who died from specific causes (cardiovascular heart disease and all sites cancer) will increase from 1960 through 1988.
6. The life expectancies of vegetarians who died from specific causes will be higher than that of omnivores at all ages from 1960 through 1988.

CHAPTER 2

REVIEW OF THE LITERATURE

A. Background and Significance

In the United States, the number of persons aged 65 and older is expected to increase from approximately 35 million to an estimated 71 million in 2030, and the number of persons aged greater or equal to 80 years is expected to increase from 9.3 million in 2000 to 19.5 million in 2030 (19). At the end of the 19^{th} century, about one in 100,000 Americans was 100 or more years old. In the year 2000, the figure is one in about 9,000 and climbing (20). The increase in centenarians has been accompanied by substantial changes in the age-at-death and cause-of-death patterns (21). Changes in the cause-of-death pattern from mainly infectious diseases to chronic diseases were accompanied by a shift in the age pattern of mortality from younger to older ages (22). It has been estimated that in the year 2000: a) nearly half of Americans suffer at least one chronic disease (125 million); b) one-fifth of Americans have two or more chronic illnesses (60 million), and these figures will reach 157 and 81 million respectively by 2020 as the population ages; c) total annual health cost for someone with one chronic illness is more than five times higher than for a healthy person ($6,032 vs. $1,105); d) the annual medical bills will be doubled to $1.07 trillion by 2020 (23). The growing number of older adults increases demands on the public health system and on medical and social services. Chronic diseases contribute to disability, diminished quality of life, and increased health care costs (24). Ten years ago, the United States spent 440 billion dollars per year on health care and only one fourth of 1 percent was invested in prevention (25). Whereas "curing" a disease might cost approximately $100,000 per disease cured, preventing a case of lung cancer might cost $2,000 (25). In the United States, nursing homes and home health-care expenditures doubled during 1990-2001, reaching approximately $132 billion (26). Direct and indirect medical costs are strongly affected by adverse health habits such as cigarette smoking and inactivity (27). Gazzaniga et al (3) reported that $5.3 billion are lost in productivity due to mortality caused by heart diseases. Risk factors' modification through the reduction of potentially detrimental behaviors (e.g., smoking and sedentary lifestyle) has the potential to postpone morbidity and mortality of chronic diseases (28).

B. Factors Affecting Longevity

Because behaviors that place persons at risk for disease originate early in life, the public health system should support healthy behaviors throughout a person's lifetime (8). The most significant trend now affecting longevity in industrialized societies is the decline of death rates among the elderly (29). Since about 1970, however, some of the most rapid declines in death rates are occurring at older ages (30, 31). The most significant reasons for the mortality decline at older ages is the reduction of death rates due to heart disease (29). From 1950 to 1996 age-adjusted death rates declined by 56% for heart disease and 70% for stroke (32). It is estimated that 73% of the decline in total death rates over this time period was due to the reduction in cardiovascular mortality (32). The factors contributing to the decline in CVD mortality are: (1) a decline in cigarette smoking among adults; (2) a decrease in blood pressure levels; (3) increasing control of hypertension through treatment; (4) changes in diet, especially a reduction in the consumption of saturated fat and cholesterol; (5) improvements in medical care (32).

In most developed countries, cancer mortality has started to decline only within the last 10-15 years (33). There is strong evidence that a high consumption of fruit and vegetables reduces the risk of developing many cancers which may result in a gain in life years at no additional cost to the healthcare sector (34). Doll and Peto (35) reported that about 35% (CI: 10%;70%) of cancer deaths in the United States were attributable to dietary practices. In 1995, Willet indicated that about 32% (CI:20%;42%) of all cancer deaths in the United States may be associated with diet (36). Since the early 1970s, declines in mortality from chronic diseases at older ages have caused sharp rises in life expectancy of the elderly population (21, 22, 37). Nusselder (21) reported that life expectancy at age 60 increased from 16.95 to 18.22 years in men and from 20.87 to 23.14 years in women in the period 1970/74-1990/94 in the Netherlands. Life expectancy at age 85 increased from 4.46 to 4.63 years in men and from 4.96 to 5.82 years in women in the same period (21).

C. Trends in Life Expectancy

Life expectancy for newborns has increased over the past 70 years, from 57.1 years for babies born in 1929 to 77.4 years for babies born in 2000 (38). From 1980 to 1998, life expectancy at birth rose at a rate of 0.15 year per year, for an increase of 2.7 years, to 76.6 years (39). Life expectancy increased by more than one and a half years, from 75.8 years in 1995 to 77.4 years in 2000 (38). Life expectancy from age 65 rose at a rate of 0.07 year per year, for an increase of 1.2 years over 18 years to a life expectancy of 82.7 years (39). For age 85, life expectancy rose by 0.017 year per year for an increase of 0.3 years over 18 years (39). Average life expectancy is higher among females than among males. In the year 2002, the average life expectancy for males was 74.7 years, compared to 79.9 for females (38).

D. Relationship Between Lifestyle and Life Expectancy

Many studies including our own, have assessed the relationship between people's lifestyle and the risk factors for ischaemic heart disease, cancer, and all cause mortality in order to determine how people can live longer and healthier (18, 28, 40-42). The main behavioral factors of concern, namely diet, physical activity, and smoking are modifiable and are a major focus of national health improvement strategies (43). Haveman-Nies et al (43), reported that even at ages 70-75 years, smoking, having a low-quality diet, and being physically inactive were singly related to an increased mortality risk (hazard ratios ranged from 1.2 to 2.1). Men and women with all three unhealthy behaviors had a 3-4 fold increase in mortality risk (43). Choices regarding diet, exercise, cigarette smoking and body weight combined seem to change life expectancy by many years (18). In Adventist women, combinations of diet, exercise, body mass index, past smoking habits, and hormone replacement therapy can account for differences of up to 10 years of life expectancy (18).

There are historical accounts of populations that have experienced greater longevity because of the low meat content of their diet (44). The life expectancy of Agrarian peoples (i.e. Hunzakuts, Vilcarbambas, mountain dwellers of Turkey, Russian Caucasus) who follow plant based diets exceeds 10 years difference (45-49). Nestle (16) reported that the life expectancy of adults in Japan and certain Mediterranean countries is up to 2 years longer than their peers in Western nations in which the meat intake has been much higher in the past few decades.

E. Association Between Diet, All-Cause Mortality, Mortality From Specific Causes of Death

Three prospective studies have examined the mortality of vegetarians in Britain. The Health Food Shoppers Study (50-52) and the Oxford Vegetarian Study (53) were established in the 1970s and 1980s, respectively. Each included about 11,000 subjects that completed a food frequency questionnaire. The European Prospective into Cancer and Nutrition-Oxford (EPIC-Oxford) Study was established in 1990s and included 56,000 subjects who completed a food frequency questionnaire (54). The death rate ratios (DRRs), adjusted for age, sex, and smoking, in vegetarians compared with non-vegetarians was 1.03 (0.95, 1.13) in the Health Food Shoppers Study, 1.01 (0.89, 1.14) in the Oxford Vegetarian Study, and 1.05 (0.86, 1.27) in the EPIC-Oxford Study. For ischemic heart disease (IHD), DRRs in vegetarians compared with non-vegetarians were 0.85 (0.71, 1.01) in the Health Food Shoppers Study, 0.86 (0.67, 1.12) in the Oxford Vegetarian Study, and 0.75 (0.41, 1.37) in the EPIC-Oxford Study. Comparisons within three cohorts suggest that vegetarians have a moderately lower mortality from IHD than non-vegetarians, but there is little difference in mortality from other major causes of death. All-cause mortality was not significantly different between vegetarians and non-vegetarians in all 3 studies, and this could be due to the relatively small number of deaths from individual causes, hence, important differences might not be observed because of lack of established power (55).

Singh et al (56), in a review of 6 cohort studies, namely the Oxford Vegetarian Study, Health Food Shoppers Study, German Vegetarianism, Adventist Mortality Study, Adventist Health Study, and the Study of Italians, reported that all the studies, except for the Health Food Shoppers Study indicated a decrease (25% decrease up to almost 2-fold decrease) in risk for subjects with very low meat intake compared to higher meat consumption. It is noteworthy that in the Oxford Vegetarian Study, in which a significant 25% decrease in mortality risk for subjects with zero meat intake was reported at 12 years of follow-up (57), the mortality ratio attenuated to a weak association after an additional 10 years of follow-up (58). In both the German and the Adventist vegetarians, decreases in mortality risk were detected for those indicating long term (17 years and more or equal to 20 years, respectively) adherence to a very low meat intake diet compared to those indicating short adherence to a very low meat intake diet (44). Long term vegetarians with estimated life expectancy of 86.5 years experience 3.6 years (95% CI: 1.4, 5.8) increase in life expectancy over short-term vegetarians with estimated life expectancy of 82.9 years (56). The protective effect of very low meat intake seems to attenuate after the ninth decade (56). Among vegetarian Adventists, Kahn et al (59) reported a decreased mortality risk for higher consumption of green salads, and Fraser et al (60) reported a decreased coronary artery disease mortality risk for higher consumption of nuts.

In a population-based prospective cohort study of Swedish women, Michels et al (11) found a strong association between nutritional quality and longevity during 9.9 years of follow-up. Women who consumed a diet characterized by a great variety of vegetables, fruit, whole grain breads and cereals, fish, and low-fat dairy products had a significantly lower mortality than women who consumed few of those foods (11). For each additional healthy food consumed, the risk of death was decreased about 5% (95% CI: 4-6%). Cardiovascular mortality was particularly low among women who consumed a high variety of healthy foods (11). Women who consumed many less healthy foods, (high variety of red meats, refined carbohydrates and sugar, high in saturated or trans fats), however, were significantly more likely to die from cancer than those who consumed less healthy foods (11). In a case-control study conducted in Greece, individuals who followed a Mediterranean diet (high in fruit, vegetables, legumes, cereals, low in meat, milk and dairy products) had a low mortality (61). In a recent prospective study (62) involving 22,043 adults in Greece that had a median of 44 months of follow-up, Trichopoulou et al (62) found that greater adherence to the Mediterranean diet is associated with a significant reduction in total mortality. In the same study, an inverse association with greater adherence to this diet was observed for both death due to coronary heart disease, and death due to cancer (62). Results from other previous studies involving elderly persons indicated that reduction in overall mortality was associated with greater adherence to the Mediterranean diet (61, 63-65).

Many of the foods that would replace meat in the vegetarian diet may be causally protective against fatal disease (60, 66, 67). Many epidemiological studies have already shown that abundant consumption of essential food components of the vegetarian diet, such as fruits and vegetables, (68-70) legumes and unrefined cereals, (60, 71-73) and nuts (60, 74, 75) has been associated with a lower risk for many chronic diseases, and in some cases with greater longevity. High vegetable intake is always found to be a protective factor (76-80).

F. Effects of a Vegetarian Diet on Mortality From Heart Disease and Cancer

Key et al (81) in a collaborative analysis of five prospective studies (the Adventist Mortality Study, the Health Food Shoppers Study, the Adventist Health Study (AHS), the Heidelberg Study, and the Oxford Vegetarian Study) reported that mortality from ischemic heart disease was 24% lower in vegetarians than in non-vegetarians (DRR = 0.76; 95% CI: 0.62-0.94, $p < 0.01$). The lower mortality from IHD among vegetarians was greater at a younger age and was limited to those who followed their current diet for more than 5 years. In comparison with regular meat eaters, mortality from IHD was 20% lower in occasional meat eaters, 34% lower in people who ate fish but not meat, 34% lower in lacto-ovo vegetarians, and 26% lower in vegans. Based on the results of this analysis, there was no significant different between vegetarians and non-vegetarians in mortality from cerebrovascular disease, stomach cancer, colorectal cancer, lung cancer, breast cancer, prostate cancer, or all causes combined. Findings from the AHS strongly suggest that dietary factors influence longevity and the risk of chronic diseases (28). Results from the multivariate analyses showed that there are significant associations between beef consumption and fatal ischemic heart disease in men (relative risk (RR) = 2.31) for subjects who ate beef ≥3 times/week (28). The lifetime risk of IHD was reduced by 37% in male vegetarians compared to non-vegetarians (28). Cancers of the colon were significantly more likely in non-vegetarians (RR of 1.88 and 1.54 respectively) (28). There was a positive association between colon cancer risk and red meat consumption (RR = 2.68; 95% CI: 1.24-5.78) in subjects who consumed legumes infrequently (28). Singh et al (82) reported that findings from the AHS cohort identify both red and white meat intake as important dietary risk factors for colon cancer, and further suggest that the increased risk due to red meat intake occurred only in subjects with lower legume intake and higher body mass index. Intake of legumes was negatively associated with risk of colon and pancreatic cancers in non-vegetarians (28). Higher consumption of all fruits or dried fruits was associated with lower risk of lung, prostate, and pancreatic cancers after adjustment for age, sex and smoking status (28). Lung cancer risk was decreased 74% in those who frequently consumed fruit (83). There was a weak association between consumption of animal products and breast cancer risk after controlling for age at first menstrual period, age at first full-term pregnancy, and body weight (84).

A review based on 206 human epidemiologic studies and 22 animal studies concluded that fruits and vegetables were effective in the prevention of several forms of cancer, including stomach, esophagus, lung, oral cavity, pharynx, endometrium, pancreas and colon cancer (85). In the Adventist mortality study, among males it was shown that risk of colon cancer was elevated in those in the highest meat/poultry consumption categories (86). Prostate cancer was not strongly associated with meat consumption (87). Risk of fatal prostate cancer, however, was found to be elevated threefold in men with a combined high intake of milk, cheese, eggs, and meat (87). Among women, breast cancer was not strongly associated with intake of animal products (88). After controlling for age at menarche, age at menopause, weight, and education, increasing consumption of meat was unrelated to fatal breast cancer risk (88). Animal product consumption was more strongly associated with ovarian cancer deaths (89).

G. Effect of a Vegetarian Diet on Longevity

Although there is a large body of evidence that many risk factors affect the risk of specific diseases, and of all-cause mortality at a particular age, there is very little published information about how these factors may influence longevity. Individual factors typically contribute 1.1 to 2.7 years difference in life expectancy (18). Seccareccia et al (90), in analyses that examined the 30-year long term experience of middle-aged men, reported that those eating more than 60 grams of vegetables per day lived about 2 years longer than subjects who ate less than 20g/day. The increase in survival was more striking in smokers than nonsmokers (2.1 vs. a 1.0 year gain). Fraser (18) reported that 80% of both the California Adventist men and women lose two years or more due to their choices, (such as being omnivores, not exercising, and having a high body mass index), about 50% lose four years or more, and about 10% lose seven to eight years.

Nusselder (4) reported that eliminating heart disease adds 4 years of life for men and 2.9 years for women in Holland. Elimination of heart disease and arthritis/back complaints leads to an increase in disability-free life expectancy (2.5 and 2.8 years for heart disease, and 1.9 and 1.4 years for arthritis in men and women, respectively). It has been estimated that eliminating all coronary heart disease and cancers in the United States would increase life expectancy by only 7.0 years in females, and 8.1 years in males (91). The differences due to choice of lifestyle, however, exceed these numbers. Through most of the twentieth century, the gains in adult life expectancy for subjects aged 50 years were only 9.4 years for women and 5.0 for men (92). Seventh-day Adventist vegetarians had a relative risk for all-cause mortality of 0.80 (95% CI: 0.74,- 0.87) compared with non-vegetarians (28). Findings from the same study showed that vegetarian Seventh-day Adventist women live 2.5 years longer than non-vegetarian (meat ≥ once/wk) women ($p < 0.001$), and that vegetarian men live 3.2 years longer than non-vegetarian men ($p < 0.001$).

Besides the Adventist Health Study, few studies have dealt with the effects of different risk factors on life expectancy. Tsevat et al (93) used data from United States Vital Statistics and the Framingham Heart Study to estimate increases in life expectancy that occurred when those who initially had elevations of a particular risk factor changed the elevation to an ideal value. Tsevat et al (93) predicted how male and female smokers would gain 2.3 and 2.8 years, respectively, from quitting smoking; male and female hypertensives would gain 1.1-5.3 and 0.9-5.7 years, respectively, by reducing diastolic levels to 88 mm Hg. Men and women with high cholesterol values would gain 0.5-4.2 and 0.5-1.1 years, respectively, by reducing cholesterol values to 200 mg/dl, and by maintaining ideal weight. Grover et al (94) reported similar estimates from the Lipid Research Clinic Study. An analyses of five large cohort studies compared hypothetical low-risk individuals with blood cholesterol levels less than 200 mg/dl, systolic and diastolic blood pressures less than and equal to 120/80, and who were not current smokers, with all other individuals who had one or more of these risk factors (95). It was estimated that low-risk individuals had 5.8 to 9.5 more years of life expectancy. One weakness of the analytic approach by Stamler et al (95) is that no account was taken of the different effects of individual risk factors at different ages.

H. Future Implications in Life Expectancy

It is controversial whether the mortality rates at older ages will continue to decline and result in a continuing increase in life expectancies. Proponents of a fixed life span hypothesis believe that the average life expectancy will not increase substantially above 85 years of age in the near future (91, 96, 97). It is hypothesized that future reductions in death rate will be constrained by biological, social, or environmental conditions (96). Other investigators argue that the observed reductions in mortality rates will continue or will accelerate (98-102). A life expectancy at birth above 100 years is plausible in the foreseeable future (18, 99, 100, 103-105). The observed decrease in mortality rates at advanced ages of 1-2% per year, and the low mortality rates in certain population groups are seen as supporting sustained future increases in life expectancies (98, 101, 103). Several studies have found large decreases in mortality rates at older ages (98, 106-109). Recent data from Holland, however, suggest that life expectancy has decreased in this age group or stagnated (21). The upper limit of lifespan is unlikely to be homogenous, even if environmental differences among individuals are reduced (110). Variations around the maximum lifespan will still be observed due to genetic variation (111). A fixed maximum human lifespan must result in a continued compression of mortality if life expectancy increases; hence, the failure to observe such a compression suggests that either no limit exists or that it is not currently in sight (6). Some have suggested that the rectangularization is "a myth" (112) or an "ill-posed question", (110) or that mortality is undergoing an expansion, rather than compression, at the oldest ages (109). Rothenberg et al (109) in the analyses of ages at death in the United States population between 1962 and 1984, reported a shift of deaths into the upper ages with an increasing variability of age at death suggesting a sort of "partial compression of mortality". Arguments against compression of mortality come from Australia (113), and France (114). Myers and Manton (115) reported an increase in both the mean age at death and its variability as measured by the standard deviation, based on the period 1962-1979 (115). Fries criticized the restriction of the analysis of the standard deviation of age of death at above 60 years (116). Based on analyses from several contemporary populations, Manton and Stallard (101), conclude that the effect of compression is not yet seen, and available data do not support a fixed life span (98, 103).

Himes in 1994 indicated that the pattern of old age mortality in the United States and to a lesser extent in Canada differs from that in other low mortality countries (117), making it difficult to compare the results. Paccaud et al (118) after analyzing the recent trends in the distribution of age at death among old people in Switzerland, reported that there is a sustained increase in age at death. There was also a shift in distribution toward the right, and the rate of secular increase diminished with increasing percentiles indicating a continuing reduction in the variability of age at death (118). Paccaud (118) indicated that the median age at death at age 50 and over is lower in the United States than Switzerland, which might indicate that an expansion in mortality is still dominant in the United States, while a compression of mortality is emerging in other European countries (118). Nusselder et al (119) reported that the discrepancies between the studies could be due to a difference in the methods used to assess rectangularization, or due to environmental and social differences between the populations and periods studied (119). Nusselder et al (21) found a lack of improvement in life expectancy at advanced ages.

Wilmoth et al (6) indicated that beyond the debate about compression of mortality, it is important to investigate long-term trends, to identify periods of rectangularization, and to identify the causes of rectangularization. Wilmoth et al (6) noted that previous work did not consider differences across contemporary populations in the variability of age at death. Populations with comparable mortality levels might still differ in the variability of age at death, due to differences in social structure and/or disease environments. Fries (120) stated that based on a fixed life span, further gains in longevity are unlikely. Some researchers suggest that improvements in mortality due to social and medical factors have occurred by increasing the time that a person survives with disability (121). Manton (110) suggest that improvements in mortality have occurred because of the improved ability to manage the progression and severity of disease.

CHAPTER 3

PUBLISHABLE PAPER I: SECULAR TRENDS IN LIFE EXPECTANCY BY DIET STATUS AMONG NEVER SMOKING SEVENTH-DAY ADVENTISTS

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ABSTRACT

To evaluate how life expectancy changed by age and calendar time from 1960 through 1988, we combined two overlapping cohorts, the Adventist Mortality Study (AMS, 1960-1985, n = 27 530) and the Adventist Health Study (AHS, 1976-1988, n = 34 192). After combining both cohorts, a total of 38,237 subjects were identified with 10 329 deaths. In order to determine the impact of diet on life expectancy, we compared the life expectancy of omnivores to vegetarians separately in never smoking males and females at different ages and different calendar periods. We calculated life expectancies for subjects who had survived to ages 30, 50, 70, and 80 during six calendar periods: 1960-1964, 1965-1969, 1970-1974, 1975-1979, 1980-1984, and 1985-1988. The basis for the life table calculations was the age-specific mortality rates, which were calculated using the Multiple Decrement Life Table Analysis Program (MDLTAP) allowing for the control of confounders for competing causes of death. We conducted both univariate and multivariate analyses controlling for the potential confounders: education, body mass index (BMI), and exercise. We examined the secular trends in life expectancies using weighted linear regression, where inverse variances obtained from the MDLTAP program were used as weights for the respective calendar periods.

Life expectancy for both males and females increased with secular time from 1960 to 1988 for all ages. There was a significant linear trend for both males and females at most ages. The trend tended to be steeper in omnivores compared to vegetarians, and females as compared to males. The life expectancy of vegetarian females who had survived to 30, 50, and 70 years of age was 1-2 years higher than that of omnivores for

the calendar periods 1965-1969, 1975-1979 and 1980 -1984. The life expectancy of vegetarian males up to 80 years of age was 1-4 years higher than that of omnivores for all calendar periods. Females had a higher life expectancy than males. The gender differences in life expectancy were much less in vegetarians compared to omnivores. We conclude that the life expectancy increased with secular time from 1960 to 1988 in both males and females, and for both vegetarians and omnivores. A vegetarian diet does contribute to greater longevity, and this lifestyle decreases the gender gap in life expectancy.

INTRODUCTION

In the past century, populations in industrialized countries experienced a sharp increase in life expectancy due to successful public health interventions (1). The number of persons aged 65 years or more is expected to increase from approximately 35 million in 2000 to an estimated 71 million in 2030 (2). The increase in life expectancies has been accompanied by substantial changes in age at death and cause-of-death patterns (3). The world has experienced an epidemiologic transition in the leading causes of death from nutrient deficiencies, infectious diseases and acute illness to chronic and degenerative diseases (4). Despite the medical progress during the past few decades, the last years of life are still accompanied by increasing ill health and disability, and huge medical and social costs (5). From 1980 to 1998, life expectancy in the United States rose 2.7 years, at a rate of 0.15 year per year (6). This resulted in a life expectancy at birth of 76.7 years in 1998 for both sexes combined. Life expectancy in 1998 at age 65 rose at a rate of 0.07 year per year, and increased 1.2 years over 18 years (6). This resulted in a life expectancy beginning at age 65 years of 82.7 years for both genders in 1998 (6). The growing number of older adults increases demands on the public health system and on medical and social services.

Behaviors that place persons at risk often originate early in life. The public health system, therefore, should support healthy behaviors throughout a person's lifetime (7). Many studies, including our own, have assessed the relationship between people's lifestyle and the risk factors for ischemic heart disease, cancer, and all-cause mortality in order to determine how people can live longer and healthier (8-12). The main modifiable lifestyle factors of concern are diet, physical activity, and smoking, and these are a major focus of national health improvement strategies (13). Choices regarding diet, exercise, cigarette smoking, and body weight combined seem to change life expectancy by many years (12). Fraser et al. (12) reported that in Adventists, combinations of diet, exercise, body mass index, past smoking habits, and hormone replacement therapy (in women) can account for differences of up to 10 years of life expectancy. Ecological, case-control, and prospective studies have shown that diets largely based on plant foods are associated with decreased risk of mortality in middle-aged men and women (14-17). Indeed, there are historical accounts of populations that had greater longevity, possibly because of low meat consumption (18-22). Life expectancy of adults in Japan and some Mediterranean countries is up to two years longer than their peers in Western nations, where the meat intake is higher (23).

Seventh-day Adventists present a unique opportunity to study the relationship between diet and longevity, and to examine the secular trends in life expectancy. This is because of their wide variety of food habits and lifestyle factors. The purposes of our study were: 1) to examine the 28-year secular trends in life expectancy of Adventists, and 2) to determine the potential impact of a vegetarian diet on life expectancy. We combined two cohorts, the Adventist Mortality Study (AMS, 1960-1985, n = 27,530) and the Adventist Health Study (AHS, 1976-1988, n = 34,192). In the combined cohort, life expectancy changes by age and calendar time from 1960 to 1988 were evaluated. To determine the effect of a vegetarian diet on life expectancy, we compared the life expectancy of omnivores to vegetarians separately in never smoking males and females at different ages and different calendar periods.

METHODS

A. Study Population

1. The Adventist Mortality Study Cohort (1960-1985)

In 1960, 27,530 California Seventh-day Adventists, age 30 years and older, completed a four page American Cancer Society (ACS) questionnaire, which included questions on personal health, exercise level, the frequency of use of 21 different foods and beverages, and other lifestyle factors. These individuals were followed for 26 years (1960-1985). The details of this population and the validity of death ascertainment have been described previously (24-27). In summary, deaths were ascertained by record linkage with the California Death Certificate File, record linkage with the National Death Index, and through church records.

We calculated body mass index (BMI) from the height and weight values that the subjects reported in the baseline questionnaire. The meat index was determined from the response to questions on the intake of meats. Vegetarians were defined as those eating meats never or less than once per week, all others were considered omnivores. Other variables included in the analysis were obtained from responses to questions on exercise level (none, slight, moderate, heavy), and educational level (no schooling, grammar school, some high school, high school graduate, some college, college, technical or trade school). Physical activity was not available for females in this study.

2. The Adventist Health Study Cohort (1976-1988)

In 1976, a lifestyle questionnaire was sent to 59,081 non-Hispanic white California Seventh-day Adventist adults, who were identified during a census that was taken between 1974 and 1976. Mailed questionnaires that included questions on demographics, diet, physical activity, psychosocial factors, and medical history were completed by 34,192 subjects. Details of the study design have been previously published (28). Direct follow-up was conducted to ascertain all deaths for the years 1976 to 1982. In addition, for the years 1976 to 1988, death ascertainment used computerized matching to California State Death Tapes and to the National Death Index, when this last data became available in 1979. These sources were supplemented by church records and short mailed annual surveys between the years 1976 and 1983 (29).

Body Mass Index was determined from questionnaire items about current weight in pounds and height in inches. The validity of the anthropometric data was tested earlier and the correlation between self-reported and measured weight was 0.94 for women and 0.96 for men (30). The dietary section of the questionnaire included 55 semi-quantitative food frequency questions (8 frequency categories from "never consumes" to "more than once each day"), and 10 qualitative dietary questions. The meat index was determined from the response to six questions on the intake of meats (beef, poultry, pork, and fish). A dietary validity study compared food frequency results and five unannounced 24-hour recalls, and the correlation between measurements of meat frequency and the 24-hour recalls (corrected for within person error on the recalls) was 0.83 (31).Vegetarians were defined as those eating meats never or less than once per week; all others were considered omnivores.

In the AHS Cohort, educational level was obtained from the response to a question on education (high grade or less, some high school, high school graduate, some college, college graduate or above). A physical activity index was calculated from subjects' responses to questions regarding vigorous leisure-time and occupational activities, and was considered "high" for frequent ($\geq$ 15 minutes per session and $\geq$ 3 times per week) participation, which reflects a positive response to either or both of the occupational or leisure activity questions, and was considered "none/low" for "Rarely or never" participation in both occupational and leisure activities. Subjects who were not included in either of the above categories were considered "moderate" exercisers. This index was shown to be a significant predictor of all-cause and CHD mortality in the study population (32, 33).

3. *Analytic Cohort (1960-1988)*

The combined cohorts had a total of 38,237 never-smokers, with 10,329 deaths from 1960 to 1988. There was an overlap of about 10,000 subjects, who were members of both the AMS and AHS cohorts. These subjects contributed person time only once for a particular calendar date in the combined cohort.

A validity study of subjects' ability to recall their dietary choices over 20 years has been described (31). Food frequency data in 1976 was compared to their responses in 1960. Results indicated good agreement.

As in AHS, vegetarians were defined as those eating meats less than once per week, all others were considered omnivores. When the cohorts were combined for the life table analysis, subjects were classified into high (some college or higher) and low (high school graduate or less) educational achievement. For physical activity, subjects in the combined cohort were divided into high (moderate and high) and low (none and low) exercise levels. We categorized BMI into three categories: low (BMI < 23.96 kg per m^2), mid ($23.96 \leq$ BMI < 26.68 kg per m^2), and high (BMI ≥ 26.68 kg per m^2). The study endpoint was all-cause mortality (International Classification of Diseases, 9th Revision (ICD-9) codes 0-999).

Subjects with some college or higher, a BMI less than 23.96 pounds and a moderate to high level of exercise were considered to have a favorable lifestyle. Subjects with high school degree or less, a BMI greater or equal to 26.68 pounds, and a low to none level of exercise were considered to have an unfavorable lifestyle. We compared life expectancies between vegetarians and omnivores for subjects with favorable lifestyle and for subjects with unfavorable lifestyle.

B. Analyses Methods

The Multiple Decrement Life Table Analysis Program (MDLTAP)(34) was used to calculate life expectancies by diet status for various calendar periods (1960-1964, 1965-1969, 1970-1974, 1975-1979, 1980-1984, and 1985-1988) for subjects who had survived to ages 30, 50, 70, and 80 years at these calendar periods. This multivariate method, where the time variable is attained age, uses proportional hazards modeling to produce maximum likelihood estimates for the exposure coefficients. A product term with age accommodated differences in effects by age, where such coefficients were statistically significant. These were needed for diet status, exercise level, and BMI levels. The hazards, which are conditional on exposure values, were used to calculate age-specific probabilities for a life table (34). Variance estimates, confidence intervals, and tests of significance have been described previously (34).

The method produced estimates of life expectancy comparing vegetarians with omnivores. We conducted both univariate and multivariate analyses using the MDLTAP program to determine life expectancy by diet status and age in males and females, separately. We also evaluated life expectancies for vegetarians and omnivores with otherwise favorable lifestyle (low BMI, highly educated, and exercised) and compared them to subjects with otherwise unfavorable lifestyle (high BMI, low education, and low exercise level).

In the univariate analysis, the model included diet status (vegetarians vs. omnivores) and the interaction of diet status with attained age. In the multivariate analysis, the model included diet status (vegetarians vs. omnivores), exercise level (high vs. low), educational level (high vs. low), medium BMI (coded as 1 if $23.96 \leq \text{BMI} < 26.68$ and 0 otherwise), and high BMI (coded as 1 is $\text{BMI} \geq 26.68$, 0 otherwise). The following product terms, education by exercise and high BMI by exercise, were included because they were statistically significant. We also included the interaction of exercise level, diet status, medium BMI, and high BMI with attained age because these interactions contributed significantly in the univariate analysis.

We formally examined secular trends in life expectancies using weighted linear regression, where the inverse of the variances obtained from the MDLTAP program were used as weights for the respective calendar periods. Life expectancy was regressed on calendar time separately for vegetarians and omnivores in males and females. In the weighted regression analysis, calendar year was centralized to the midpoint of the interval. The effects of diet status on life expectancy were evaluated for each calendar period, as well as by comparing the regression slopes for vegetarians and omnivores.

RESULTS

A. Demographic Characteristics

During 28 years of follow-up (1960-1988), 10,329 deaths were identified. Baseline characteristics of the population by diet status are presented in Table 1. Omnivores were more obese (32.9%with BMI ≥26.7 vs. 18.8% in males, and 27.5% vs. 18.3% in females), less educated (48.7% vs. 54.7% in males, and 35.8% vs. 42.6% in females had some college or higher), and omnivores exercised at a similar level to vegetarians (70.0% vs. 73.9% were high exercisers). Exercise was measured in males only because the data on the exercise level for females had not been entered into the database for the older mortality study. Because of the differences according to diet status, in body mass index, educational level, and possibly exercise, these variables were potential confounders that were controlled for in the multivariate analyses. In the multivariate analysis in females, only education and BMI were controlled for.

B. Secular Trends in Females

The results of the univariate analyses for the effect of meat intake in females are shown in Table 2a. Results of the multivariate analysis for females with otherwise favorable lifestyles are displayed in Table 2b, and for females with otherwise unfavorable lifestyles in Table 2c. In females, life expectancy increased with secular time from 1960 to 1988 for all ages (Tables 2a-c) in both vegetarians and omnivores, irrespective of otherwise favorable or unfavorable lifestyle, this increase being between 4-8 years. Linear trends over calendar time were significant at ages 30, 50, and 70 years of age.

Some of this data is shown graphically in Figures 1 and 2 for females who survived to 50 or 70 years of age. The linear trend with calendar time is quite evident.

The slopes of the regression lines with calendar time (Tables 4 and 5) were consistently higher for omnivores at all ages. Irrespective of lifestyle choices, the difference in slopes was significant for females who survived to 50, 70, and 80 years of age. Over time, the life expectancy of omnivores approached the life expectancy of vegetarians.

C. Secular Trends in Males

The results of the univariate analyses for the effect of meat intake in males are shown in Table 3a. Results of the multivariate analysis for males with otherwise favorable lifestyles are displayed in Table 3b, and for males with otherwise unfavorable lifestyles in Table 3c. In both vegetarian and omnivorous males, life expectancy also increased with secular time from 1960 to 1988 for all ages (Tables 3a-c). For males with otherwise favorable lifestyles, the increase in life expectancy was 5-6 years in vegetarians compared to an increase of 6-8 years in omnivores (Table 3b). For males with unfavorable lifestyle, the increase was 3-7 years in vegetarians compared to an increase of 4-10 years in omnivores (Table 3c). For males with otherwise favorable lifestyles, the linear trends over calendar time were significant at ages 30 and 50 years, and the trend at age 70 was not significant, irrespective of type of diet. Some of this data is shown graphically in Figures 3 and 4 for males who survived to 50 and 70 years of age. The linear trend with calendar time is quite evident. Among males with otherwise unfavorable lifestyles, however, the linear trends over calendar time were not significant at ages 30, 50, and 70 years of age.

The slopes of the regression lines with calendar time (Tables 4 and 5) were consistently higher for omnivore males at all ages. The difference in slopes was significant for males with an otherwise favorable lifestyle who survived to 30, 50, and 70 years of age. For males with an otherwise unfavorable lifestyle, the differences in slopes were significant among subjects who survived to 30 and 70 years of age. Over time, the life expectancy of omnivores approached the life expectancy of vegetarians (Tables 4 and 5).

D. Gender Differences in Life Expectancy

Females had a higher life expectancy than males. Over the calendar period 1960-1988, the life expectancies of females, both vegetarian and omnivore, with otherwise favorable lifestyles were 1-3.5 years higher than those of males with otherwise favorable lifestyles (Tables 2b and 3b), and among subjects with otherwise unfavorable lifestyles, the life expectancy advantage among females compared to males was 3-5 years (Tables 2c and 3c). In fact, in those with otherwise favorable lifestyles who were also vegetarians, the life expectancy for males approached that for females (56 vs. 57 for age 30; 36 vs. 38 for age 50; 18 vs. 20 for age 70; and 12 vs. 13 for age 80) (Tables 2b and 3b). The gender gap was higher in omnivores and also in those with otherwise unfavorable lifestyles (Tables 2c and 3c).

E. Effects of Vegetarian Status

Regardless of their lifestyle otherwise, the life expectancy of vegetarian females who had survived to 30, 50 or 70 years of age was 1-2 years higher than that of omnivores for the calendar periods 1965-1969, 1975-1979, and 1980-1984 (Tables 2a-c). Vegetarian and omnivorous females at all ages had similar life expectancies in the calendar period 1960-1964 (Tables 2a-c). In the last calendar period 1985-1988, the life expectancy of omnivorous females was 1.5 years higher than that of vegetarians, and this was statistically significant at older ages (although this does not account for multiple testing). The life expectancy of vegetarian males who had survived to 30, 50, 70 and 80 years of age was 1-4 years higher compared to omnivores in all calendar periods (Tables 3a-c). The number of years gained were higher at younger ages. Overall, the life expectancy of vegetarians at all ages was 1-4 years higher than the life expectancy of omnivores regardless of other lifestyle factors. This suggests that a vegetarian diet does contribute to greater longevity.

F. Comparison Between Favorable and Unfavorable Lifestyle (Aside From Vegetarian Status)

At 30 years of age, the life expectancy of both vegetarian and omnivorous females with otherwise favorable lifestyles was 2-4 years higher than that of females with otherwise unfavorable lifestyle. At 70 years of age, this difference was almost 1 year, and by 80 years of age, the life expectancy of females with otherwise favorable lifestyles was similar to those with otherwise unfavorable life styles. At ages 30, 50 and 70, the life expectancy of vegetarian and omnivorous males with otherwise favorable lifestyles was 2-10 years higher than that of males with otherwise unfavorable lifestyle, and about 2 years higher at age 80 (Tables 3b-c). In summary, the life expectancies of males and females with otherwise favorable lifestyles were 2-10 years higher than those with otherwise unfavorable lifestyles across all calendar periods. Differences were greater when the life table started at younger ages.

DISCUSSION

Our study cohorts, with a combined follow-up of 28 years and a total of 10,329 deaths from all causes, showed a linear increase in life expectancy with secular time for all ages; although the trend was not always significant. This was true irrespective of type of diet, gender, and other lifestyle choices. The life expectancy of Adventist males and females who survived to age 30 increased almost 10 years between 1960 and 1988. In our cohort, the increase in life expectancy for those surviving to age 70 was 4.5 years for both genders. The increase in life expectancy at birth in the general population was 4.4 years for males and 5.8 years for females between 1960 and 1990. The life expectancy at birth, however, is not directly comparable to life expectancy at age 30. In the same time interval, the increase in life expectancy at age 65 years of non-Adventist men and women were 2.3 and 3.3 years, respectively (35).

The probable increase in life expectancy of Adventists over calendar time is 2-5 years greater than that of the general population. Possible explanations for the higher life expectancies among Adventists are that they may adhere to more favorable health habits (avoidance of cigarettes and alcohol, higher intake of fruits and vegetables, higher levels of physical activity, and a high awareness of personal health). In addition to their favorable habits, Adventists have also benefited from positive influences in society, such as improved medical care, that have led to greater longevity over calendar time in the United States population.

The overall life expectancy of vegetarians at all ages was higher than that of omnivores. This effect was observed in both males and females for most time periods studied. The adjustment for different health habits (BMI, education, and exercise) did not change the difference in life expectancy between vegetarians and omnivores substantially. This implies that a vegetarian diet has an independent effect on life expectancy.

It is noteworthy that in the calendar period 1985-1988, among females, the life expectancy at all ages of omnivores was about two years higher compared to vegetarians, irrespective of their lifestyle. This may, however, be a chance finding, considering the multiple testing involved.

Results from our data are quite similar to the findings by Mazess (19), who found that there was a significant 3.6 years increase in life expectancy among subjects who adhered to a diet very low in meat. Seccareccia et al. (36) reported that middle–aged men eating more than 60 grams of vegetables per day lived about 2 years longer than men who ate less than 20 grams per day. Singh et al. (37), in a review of data from six prospective studies, reported that a very low meat intake contributed to greater longevity. Results from the Oxford vegetarian Study (38, 39), the Germans Study (40, 41), the Adventist Mortality Study (42), and the Adventist Health Study (8, 12) indicate a decrease in risk of death for very low meat intake relative to high meat consumption. In addition, longitudinal studies in different populations have consistently shown fruit and vegetable consumption is inversely related to mortality (43-48). The Health Food Shoppers Study (49), however, showed only a small and non-significant decrease in risk of death.

The reduction in mortality in vegetarians may be due in part to their lower serum cholesterol concentration (50). The protective effects of fruits and vegetables may also be mediated through their effects on lowering blood pressure or their antioxidant effects

(51). Fruits and vegetables are rich sources of vitamins and minerals, such as potassium and magnesium, and other nutrients, such as folate and fiber (51). Potassium has been shown to increase the ability to relax the blood vessels, thereby lowering blood pressure (50-53). Magnesium, calcium, and other minerals may also play a role in preventing hypertension (54). High folate levels may lower serum homocysteine levels, a risk factor for arterial endothelial dysfunction, (55, 56) and fiber may have a role in lowering cholesterol (57, 58). Three randomized controlled trials have shown fruit and vegetable consumption to significantly lower systolic and diastolic blood pressure (59-61).

Other studies have also shown that the life expectancy advantage over calendar time due to low meat consumption decreases with age (62-64). This may be caused at least in part by older omnivores changing to a vegetarian diet since study baseline, when diet habits were assessed. If they made this switch, such changes would decrease the apparent difference due to diet habits (62).

The life expectancies of subjects with a favorable lifestyle (aside from vegetarian status) were consistently 2-10 years higher regardless of diet status. This indicates that the other factors (body mass index, exercise, and education) add to the effects of vegetarianism. In line with these results, Fraser et al. (12) reported that Adventists may experience up to 10 years difference in life expectancy as a result of their choices. In addition, Stamler et al. (65) estimated that low-risk individuals had a 6 to 10 years higher life expectancy.

The life expectancy advantage of males attributed to vegetarian diet was larger than that of females. This may be related in part to the high risk of cardiovascular disease in males, which tends to be attenuated by a vegetarian diet (8, 14, 36, 66). Based on data reported by Friedland (67), the gender gap in life expectancy widened from 2 years in the year 1900 to 7 years in 1970. The difference in life expectancy at birth between the sexes was about 6.6 years in the year 1960 (66.6 in males vs. 73.2 in females), 7.6 years in 1970 (70.1 vs.77.7), and 7.1 years in 1990 (71.9 vs. 79.0). Based on our data, the difference in life expectancy from 1960 to 1988 between Adventist males and females at ages 30, 50, and 70 is about 3 years. This reduced difference in life expectancy between Adventist men and women indicates that the gender gap is at least in part due to lifestyle choices.

A strength of this analysis is that it examines the 28-year follow-up of never-smoking non-Hispanic Adventists 30 years or older, and evaluates the effects of selected baseline health habits. Results are presented in terms of increased life expectancy rather than mortality rates. Another strength of this study is the great diversity in food and lifestyle factors (30). Regarding diet, in particular, Adventists are quite heterogeneous. Only about 3% in the Adventist Studies are vegans; about 27% are lacto-ovo vegetarians; about 20% eat meat 1-3 times a week; and the remainder eat meat more than four times a week (68). Fewer than 10% of the subjects in our studies drank even small quantities of alcohol, making this an unlikely confounder (68). We restricted the analysis to never-smokers and adjusted for available key lifestyle factors that may be confounding factors. Vegetarians have significantly lower BMI, but this was controlled in this analysis. Adjustment for different health indicators did not substantially change the relationship between diet status and life expectancy, implying that a vegetarian diet has an independent effect on life expectancy.

Limitations of the study include the dietary assessment at baseline only. Undocumented changes in diet after the study baseline would weaken the associations between diet and life expectancy (68). Willett (68) and others have reported that in a cohort study measurement error in dietary assessment usually tends to bias the effect estimate toward the null hypothesis. Thus, the effects of a vegetarian diet may have been under-estimated here. Assessment of vegetarian status, however, is probably more accurate than measuring individual foods. Our validity correlation coefficient of 0.82 for meat consumption is consistent with this conjecture (31). Another limitation of this analysis was the need to dichotomize most of the exposure variables to ensure sufficient numbers of events in each category. This will tend to obscure effects in the extreme values of the distributions.

In conclusion, life expectancy at all ages usually showed significant strong linear trends with secular time between 1960 and 1988 in both males and females. The life expectancy of vegetarians was 1-4 years higher when compared to omnivores. The effects of low BMI and high educational level further increased this advantage in life expectancy among vegetarians. Life expectancy was substantially lower in males compared to females, but this gender difference was less in vegetarians with favorable lifestyle compared to omnivores. These results strongly suggest that a vegetarian diet does contribute to greater longevity, and that choosing a favorable lifestyle decreases the gender gap in life expectancy. Secular gains in life expectancy, moreover, are seen equally in this healthy subgroup, and are presumably due to other factors.

TABLE 1: Frequency of selected variables by gender and diet status for never-smokers

	Males (N = 11 717)				Females (N = 26 520)			
	Vegetarians		Omnivores		Vegetarians		Omnivores	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Number of study subjects	6344	54.1	5373	45.9	13317	50.2	13203	49.8
Number of deaths	1643	25.9	1294	24.1	3874	29.1	3518	26.7
Education*								
Low†	2849	45.3	2731	51.3	7536	57.4	8396	64.2
High‡	3444	54.7	2598	48.7	5601	42.6	4689	35.8
BMI*								
BMI < 23.96	2974	50.1	1617	32.1	7333	60.2	5940	48.8
23.96 ≤BMI < 26.68	1842	31.1	1763	35.0	2618	21.5	2886	23.7
BMI ≥ 26.68	1117	18.8	1655	32.9	2234	18.3	3349	27.5
Exercise*§								
Low (none/low)	1646	26.1	1599	30.0				
High (moderate/high)	4652	73.9	3732	70.0				

* The percentages for the variables Education, BMI and Exercise are based on the number of study subjects (first row of results)
† High school graduates or less
‡ Some college or higher education
§ The data on the exercise level of females had not been entered in the database for the mortality study.

TABLE 2a. Univariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking females

Age		Calendar Year† 60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarians	52.3	53.9	54.5	56.9	58.4	62.4	55.8
	Omnivores	52.0	51.6	53.7	54.3	56.5	63.7	54.5
30+	Difference	0.3	2.3	0.8	1.6	1.9	-1.3	1.3
	95% CI	(-1.1, 1.7)	(1.0, 3.6)	(-0.5, 2.1)	(0.3, 2.8)	(0.5, 3.1)	(-3.1, 0.4)	(0.7, 1.8)
	p-values	0.70	< 0.001	0.25	< 0.01	<0.01	0.13	< 0.001
	Vegetarians	33.3	34.9	35.4	37.6	39.3	43.0	36.6
	Omnivores	33.4	33.0	34.7	36.1	37.8	44.6	35.6
50+	Difference	-0.1	1.9	0.7	1.5	1.5	-1.6	1.0
	95% CI	(-1.3, 1.2)	(0.8, 3.0)	(-0.4, 1.9)	(1.4, 2.5)	(0.3, 2.6)	(-3.2, 0.1)	(0.5, 1.5)
	p-values	0.92	< 0.001	0.18	< 0.01	<0.01	0.06	< 0.001
	Vegetarians	16.3	17.3	17.8	20.1	21.3	25.0	19.1
	Omnivores	16.3	15.8	17.3	18.8	20.6	26.8	18.4
70+	Difference	0.0	1.5	0.5	1.3	0.7	-1.8	0.7
	95% CI	(-1.1, 1.1)	(0.5, 2.4)	(-0.5, 1.5)	(0.4, 1.3)	(-0.3, 1.8)	(-3.3, -0.3)	(0.2, 1.1)
	p-values	0.99	< 0.01	0.36	< 0.01	0.16	0.02	< 0.01
	Vegetarians	9.5	9.6	10.6	12.8	13.8	17.5	11.9
	Omnivores	9.9	9.2	10.2	11.8	13.7	19.7	11.7
80+	Difference	-0.4	0.4	0.4	1.0	0.1	-2.2	0.2
	95% CI	(-1.6, 0.8)	(-0.5, 1.3)	(-0.6, 1.4)	(0.0, 1.2)	(-0.9, 1.1)	(-3.7, -0.7)	(-0.3, 0.6)
	p-values	0.55	0.42	0.64	0.05	0.89	<0.01	0.25

* Model includes diet status and product term between diet status and attained age.

† Separate analyses were performed for each calendar year period.

TABLE 2b. Multivariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking females. Non-dietary covariates were set at low BMI and high educational level (otherwise favorable lifestyle)

Age		Calendar Year†						
		60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarians	52.5	54.3	55.7	57.8	60.4	63.4	57.2
	Omnivores	52.4	52.3	55.2	56.4	59.1	64.9	56.3
30+	Difference	0.1	2.0	0.5	1.4	1.3	-1.5	0.9
	95% CI	(-1.3, 1.5)	(0.8, 3.2)	(-0.8, 1.7)	(0.4, 2.6)	(0.1, 2.6)	(-3.0,0.0)	(0.4, 1.4)
	p-values	0.86	<0.01	0.48	0.03	0.04	0.06	< 0.01
	Vegetarians	33.6	35.2	36.5	38.5	41.0	43.3	37.9
	Omnivores	33.7	33.5	36.0	37.2	40.0	44.9	37.2
50+	Difference	-0.1	1.7	0.5	1.3	1.0	-1.4	0.7
	95% CI	(-1.5, 1.1)	(0.6, 2.7)	(-0.6, 1.6)	(0.1, 2.4)	(-0.1, 2.3)	(-2.8, -0.0)	(0.2, 1.2)
	p-values	0.81	<0.01	0.40	0.03	0.07	0.05	< 0.01
	Vegetarians	16.7	17.1	19.1	20.7	22.5	25.3	20.1
	Omnivores	16.8	15.7	18.8	19.4	21.9	26.9	19.6
70+	Difference	-0.1	1.4	0.3	1.3	0.6	-1.6	0.5
	95% CI	(-1.3, 1.1)	(0.5, 2.3)	(-0.8, 1.3)	(0.2, 2.3)	(-0.5, 1.8)	(-3.2, -0.2)	(0.0, 0.9)
	p-values	0.91	<0.01	0.63	0.02	0.26	0.03	< 0.04
	Vegetarians	10.6	9.3	11.5	12.7	14.6	17.3	12.5
	Omnivores	10.9	8.8	11.2	11.8	14.5	19.2	12.3
80+	Difference	-0.3	0.5	0.3	0.9	0.1	-1.9	0.2
	95% CI	(-1.7, 1.0)	(-0.4, 1.4)	(-0.8, 1.3)	(-0.1, 2.0)	(-1.0, 1.2)	(-3.4, -0.4)	(-0.3, 0.6)
	p-values	0.64	0.27	0.63	0.08	0.84	0.01	0.37

* Model includes diet status, educational level, medium Body Mass Index (BMI), high BMI and product terms between diet and attained age, medium BMI and attained age, and high BMI and attained age. † Separate analyses were performed for each calendar year period.

TABLE 2c. Multivariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking females. Non-dietary covariates were set at high BMI and low educational level (otherwise unfavorable lifestyle)

Age		Calendar Year†						
		60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarians	50.6	51.4	51.8	55.5	57.4	59.6	53.3
	Omnivores	50.4	48.6	51.3	54.0	55.9	61.5	52.0
30+	Difference	0.2	2.8	0.5	1.5	1.5	-1.9	1.3
	95% CI	(1.5, 2.0)	(1.0, 4.7)	(-1.3, 2.4)	(0.1, 2.8)	(-0.7, 3.5)	(-4.3, 0.5)	(0.6, 2.1)
	p-values	0.79	<0.01	0.57	0.04	0.18	0.12	< 0.001
	Vegetarians	32.2	33.3	33.7	36.2	38.5	41.4	35.0
	Omnivores	32.4	31.1	33.0	34.9	37.5	43.7	34.0
50+	Difference	-0.2	2.2	0.7	1.3	1.0	-2.3	1.0
	95% CI	(-1.6, 1.2)	(0.8, 3.6)	(-0.8, 2.0)	(0.1,2.6)	(-0.6, 2.7)	(-4.2, -0.4)	(0.3, 1.6)
	p-values	0.79	0.01	0.39	0.04	0.20	0.02	< 0.01
	Vegetarians	16.5	17.3	17.1	19.2	26.7	24.8	18.8
	Omnivores	16.8	15.8	16.8	18.0	26.1	26.5	18.3
70+	Difference	-0.3	1.5	0.3	1.2	0.6	-1.1	0.5
	95% CI	(-1.8, 1.3)	(0.3, 2.7)	(-0.9, 1.5)	(0.1, 2.2)	(-0.6, 1.9)	(-3.0, -0.5)	(-0.1, 1.0)
	p-values	0.74	0.01	0.62	0.02	0.27	<0.01	0.07
	Vegetarians	11.4	10.2	10.6	12.1	15.0	18.0	12.2
	Omnivores	11.1	9.7	10.3	11.1	14.8	19.7	12.1
80+	Difference	0.3	0.5	0.3	1.0	0.2	-1.7	0.1
	95% CI	(-1.7,2.3)	(-0.5,1.4)	(-0.8, 1.4)	(0.0,1.9)	(-0.7, 1.1)	(-2.8, -0.7)	(-0.4, 0.6)
	p-values	0.75	0.33	0.63	0.04	0.67	<0.01	0.77

* Model includes diet status, educational level, medium Body Mass Index (BMI), high BMI and product terms between diet and attained age, medium BMI and attained age, and high BMI and attained age. † Separate analyses were performed for each calendar year period.

TABLE 3a. Univariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking males

Age		Calendar Year†						
		60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarians	51.0	50.7	53.2	54.5	54.7	58.7	53.2
	Omnivores	47.3	48.6	49.3	51.1	53.4	57.1	50.8
30+	Difference	3.7	2.1	3.9	3.4	1.3	1.6	2.4
	95% CI	(3.8, 5.9)	(0.0, 4.2)	(1.8, 6.0)	(1.3, 5.2)	(-0.5, 3.1)	(-0.7, 3.9)	(1.7, 3.3)
	p-values	< 0.001	0.05	< 0.001	< 0.001	0.15	0.18	< 0.001
	Vegetarians	32.1	31.9	33.9	35.3	35.7	39.2	34.1
	Omnivores	29.1	29.7	30.2	32.4	34.3	37.8	32.0
50+	Difference	3.0	2.2	3.7	2.9	1.4	1.4	2.1
	95% CI	(1.1, 4.8)	(0.3, 4.2)	(1.7, 5.5)	(1.1, 4.6)	(-0.3, 3.1)	(-0.8, 3.6)	(1.4, 2.9)
	p-values	< 0.01	0.02	< 0.001	< 0.01	0.10	0.22	< 0.001
	Vegetarians	14.4	15.8	17.0	17.6	18.9	21.4	16.7
	Omnivores	13.2	13.9	13.4	15.7	17.0	20.4	15.3
70+	Difference	1.2	1.9	3.6	1.9	1.1	1.0	1.4
	95% CI	(-0.2, 2.7)	(0.0, 3.7)	(1.9, 5.3)	(0.2, 3.5)	(-0.4, 2.7)	(-1.2, 3.1)	(1.8, 2.1)
	p-values	0.11	0.05	< 0.001	0.03	0.16	0.37	< 0.001
	Vegetarians	8.1	9.1	10.6	11.0	11.6	14.3	10.2
	Omnivores	6.9	8.4	8.2	9.6	10.7	13.4	9.1
80+	Difference	1.2	0.7	2.4	1.4	0.9	0.9	1.1
	95% CI	(-0.1, 2.5)	(-1.3, 2.7)	(0.8, 3.9)	(0.2, 2.7)	(-0.7, 2.5)	(-1.4, 3.8)	(0.4, 1.7)
	p-values	0.07	0.56	<0.01	0.03	0.25	0.45	< 0.01

* Model includes diet status and product term between diet status and attained age.

† Separate analyses were performed for each calendar year period.

TABLE 3b. Multivariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking males. Non-dietary covariates were set at low BMI, high educational level and exercise (otherwise favorable lifestyle)

Age		Calendar Year†						
		60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarians	52.3	52.1	56.4	57.9	56.6	58.6	55.5
	Omnivores	49.0	49.9	52.9	55.9	55.8	57.3	53.7
30+	**Difference**	3.3	2.2	3.5	2.0	0.8	1.3	1.8
	95% CI	(1.1, 5.6)	(-0.0, 4.4)	(1.3, 5.6)	(-0.1, 4.1)	(-0.8, 2.5)	(-0.9, 3.6)	(1.0, 2.6)
	p-values	<0.01	0.05	<0.01	0.06	0.34	0.24	< 0.001
	Vegetarians	33.1	33.3	36.8	38.5	37.3	39.0	36.3
	Omnivores	30.4	31.1	33.7	36.9	36.4	37.8	34.7
50+	**Difference**	2.7	2.2	3.1	1.6	0.9	1.2	1.6
	95% CI	(0.6,4.7)	(0.2, 4.3)	(1.2, 5.1)	(-0.4,3.7)	(-0.7, 2.4)	(-0.9, 3.3)	(08, 2.3)
	p-values	0.01	0.03	<0.01	0.11	0.27	0.25	< 0.001
	Vegetarians	14.8	17.3	18.8	21.1	18.7	20.7	18.2
	Omnivores	13.8	15.6	15.7	19.1	17.9	19.7	17.1
70+	**Difference**	1.0	1.7	3.1	2.0	0.8	1.0	1.1
	95% CI	(-0.5,2.5)	(-0.3, 3.7)	(1.2,4.9)	(0.2,3.8)	(-0.7, 2.3)	(-1.1,3.0)	(0.4, 1.8)
	p-values	0.20	0.10	<0.01	0.03	0.30	0.36	< 0.01
	Vegetarians	7.5	11.3	13.1	14.3	12.0	12.9	11.6
	Omnivores	6.6	10.9	11.0	11.6	11.7	12.2	10.7
80+	**Difference**	0.9	0.4	2.1	2.7	0.3	0.7	0.9
	95% CI	(-0.4,2.2)	(-2.3,3.0)	(0.1, 4.1)	(0.9,4.5)	(-1.4, 2.1)	(-1.3,2.6)	(0.1, 1.6)
	p-values	0.16	0.79	0.04	<0.01	0.71	0.50	0.02

* Model includes diet status, educational level, exercise level, medium Body Mass Index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age. † Separate analyses were performed for each calendar year period.

TABLE 3c. Multivariate* comparison of life expectancy for all cause mortality by diet status for different calendar years and ages in the Adventist Studies for never smoking males. Non-dietary covariates were set at high BMI, low educational level and do not exercise (otherwise unfavorable lifestyle)

Age		Calendar Year†						
		60-64	65-69	70-74	75-79	80-84	85-88	60-88
	Vegetarian	45.7	50.4	49.4	54.3	48.1	53.5	49.6
	Omnivores	41.6	48.7	46.5	51.5	47.8	51.8	47.6
30+	Difference	4.1	1.7	2.9	2.8	0.3	1.7	2.0
	95% CI	(1.5, 6.9)	(-0.3, 3.8)	(0.5, 5.2)	(-0.4, 6.1)	(-1.9, 2.6)	(-0.7, 4.2)	(1.1, 3.0)
	p-values	<0.01	0.09	0.01	0.09	0.76	0.17	< 0.001
	Vegetarian	27.8	31.0	29.5	35.3	29.1	34.0	30.6
	Omnivores	24.9	29.0	26.9	32.6	28.5	32.7	28.8
50+	Difference	2.9	2.0	2.6	2.7	0.6	1.3	1.8
	95% CI	(0.7, 5.1)	(-0.0, 4.2)	(0.4, 4.8)	(0.1, 5.2)	(-1.4, 2.7)	(-0.9, 3.5)	(0.9, 2.6)
	p-values	0.01	0.05	0.02	0.04	0.53	0.25	< 0.0001
	Vegetarian	10.0	19.9	13.4	10.4	13.6	17.4	14.0
	Omnivores	9.4	16.8	10.4	10.7	13.0	16.4	12.9
70+	Difference	0.6	3.1	3.0	-0.3	0.6	1.0	1.1
	95% CI	(-1.2, 2.4)	(-0.6, 6.9)	(1.1, 4.9)	(-1.4, 0.8)	(-1.0, 2.2)	(-1.2,3.2)	(0.3, 1.8)
	p-values	0.51	0.10	<0.01	0.58	0.47	0.38	< 0.01
	Vegetarian	6.7	6.4	6.5	††	9.4	5.2	9.6
	Omnivores	5.9	6.0	5.1		9.1	5.3	8.6
80+	Difference	0.8	0.4	1.4		0.3	-0.01	1.0
	95% CI	(-0.5,2.1)	(-0.3, 1.1)	(0.0, 2.8)		(-1.4, 1.9)	(-0.7, 0.5)	(0.1, 1.8)
	p-values	0.22	0.23	0.05		0.76	0.75	0.02

* Model includes diet status, educational level, exercise level, medium Body Mass Index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age

† Separate analyses were performed for each calendar year period. †† Insufficient number of events.

TABLE 4. Comparison of gender-specific regression lines of life expectancy as a function of calendar year and diet status in the Adventist Studies (aside from vegetarian status a favorable lifestyle)

	Slope (p for trend)		p-value for testing $\beta_1 \neq \beta_2$*
	Vegetarians	**Omnivores**	
Females			
30	0.44 (p<0.01)	0.48 (p<0.01)	0.05
50	0.39 (p<0.01)	0.44 (p<0.01)	<0.01
70	0.35 (p<0.01)	0.40 (p=0.01)	<0.01
80	0.29 (p=0.13)	0.39 (p=0.15)	0.02
Males			
30	0.27 (p=0.02)	0.36 (p<0.01)	0.01
50	0.25 (p=0.01)	0.33 (p<0.01)	0.03
70	0.21 (p=0.40)	0.23 (p=0.15)	0.02
80	0.18 (p=0.09)	0.18 (p=0.03)	1.00

* β_1 : slope of regression line of life expectancy of vegetarians as a function of calendar year.
β_2 : slope of regression line of life expectancy of omnivores as a function of calendar year.

TABLE 5. Comparison of gender-specific regression lines of life expectancy as a function of calendar year and diet status in the Adventist Studies (aside from vegetarian status an unfavorable lifestyle)

Age (years)	Slope (p for trend)		p-value for testing $\beta_1 \neq \beta_2$*
	Vegetarians	Omnivores	
Females			
30	0.39 (p<0.01)	0.46 (p<0.01)	<0.01
50	0.37 (p<0.01)	0.45 (p=0.02)	<0.01
70	0.42 (p=0.02)	0.47 (p=0.03)	0.02
80	0.28 (p=0.01)	0.34 (p=0.03)	<0.01
Males			
30	0.21 (p=0.26)	0.31 (p=0.13)	0.01
50	0.18 (p=0.25)	0.25 (p=0.09)	0.06
70	0.08 (p=0.66)	0.36 (p=0.86)	0.04
80	0.01 (p=0.01)	0.05 (p=0.08)	0.11

* β_1 : slope of regression line of life expectancy of vegetarians as a function of calendar year.
β_2 : slope of regression line of life expectancy of omnivores as a function of calendar year.

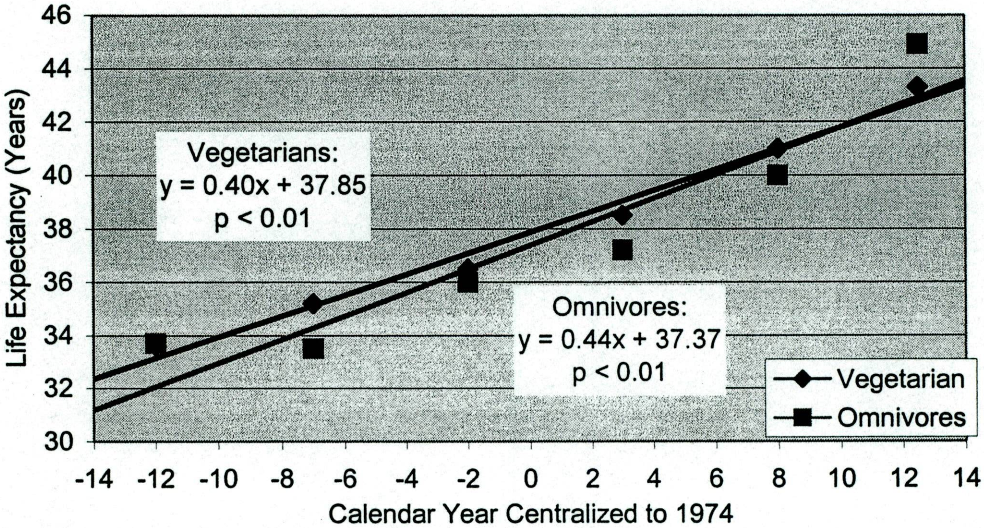

FIGURE 1. Comparison of change in life expectancy by calendar year (1960-1988) and diet status of females with otherwise favorable lifestyles at age 50 in the Adventist Studies.

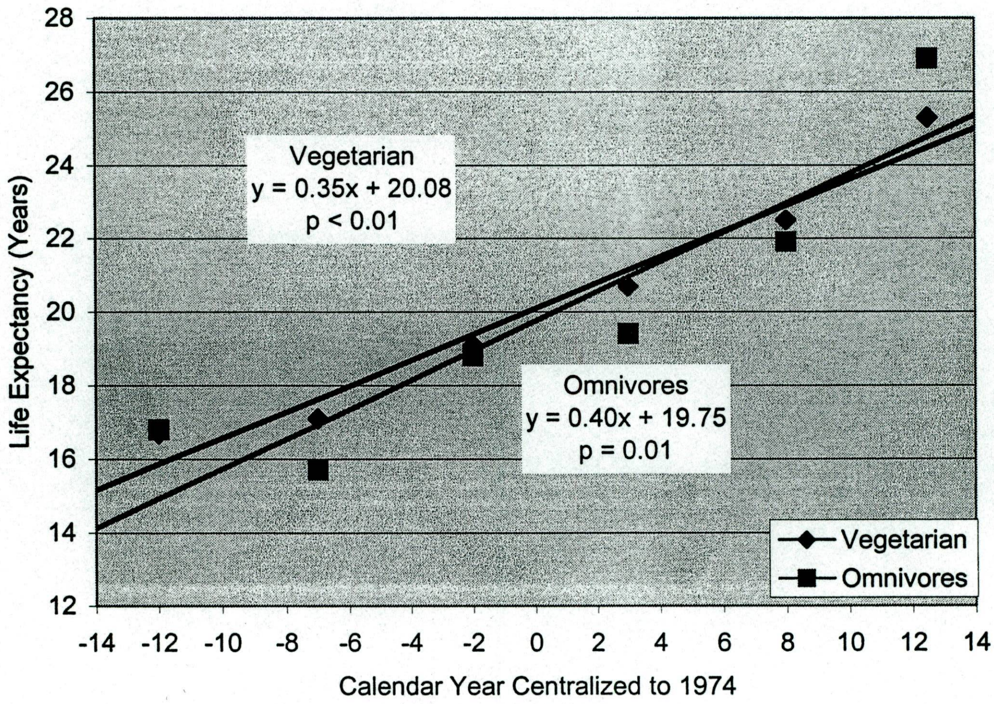

FIGURE 2. Comparison of change in life expectancy by calendar year (1960-1988) and diet status in females with otherwise favorable lifestyles at age 70 in the Adventist Studies.

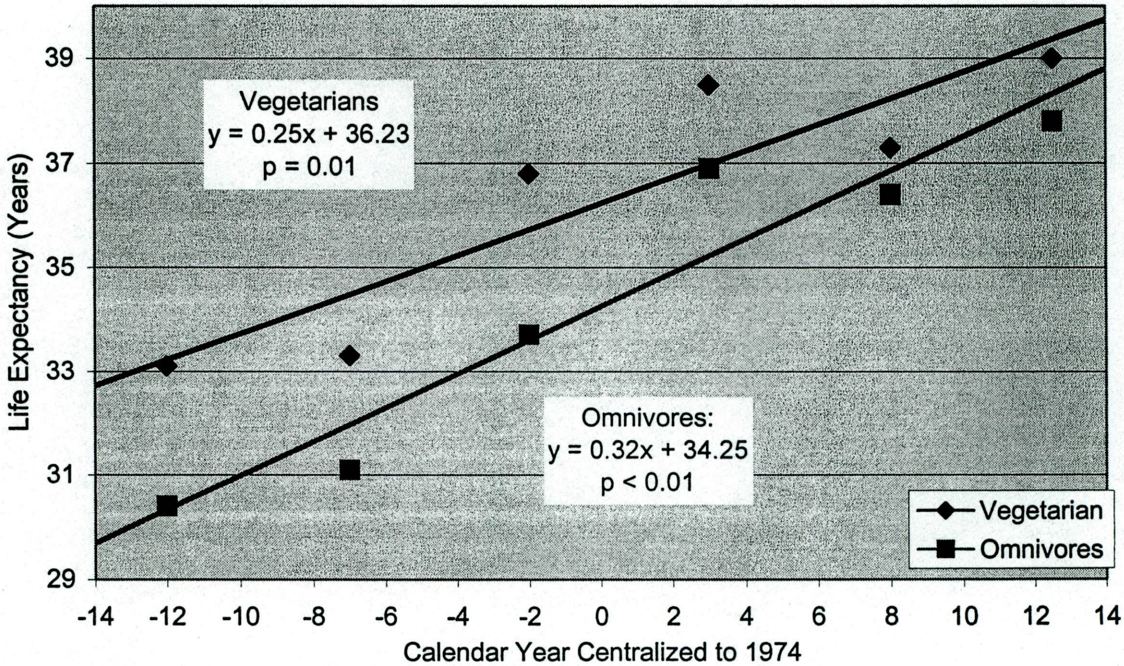

FIGURE 3. Comparison of change in life expectancy by calendar year (1960-1988) and diet status in males with otherwise favorable lifestyles at age 50 in the Adventist studies.

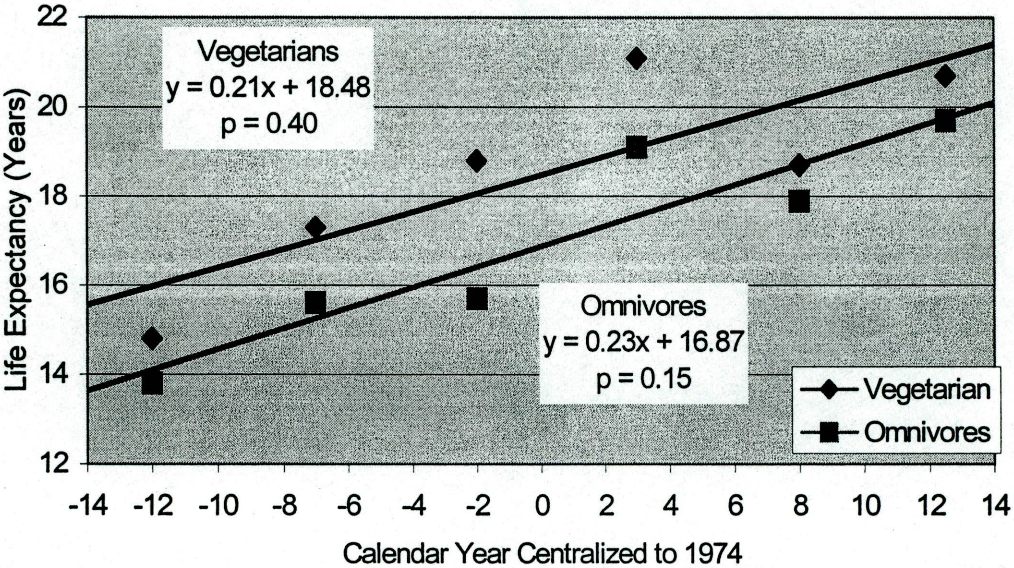

FIGURE 4. Comparison of change in life expectancy by calendar year (1960-1988) and diet status of males with otherwise favorable lifestyles at age 70 in the Adventist Studies.

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CHAPTER 4

PUBLISHABLE PAPER II: SECULAR TRENDS IN LIFE EXPECTANCY FOR SUBJECTS WHO DIED FROM HEART DISEASE AND CANCER BY DIET STATUS IN NEVER-SMOKING SEVENTH-DAY ADVENTISTS

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ABSTRACT

The objectives of the study were: 1) to evaluate how life expectancies changed in subjects who died from heart disease and all-site cancer from 1960 through 1988 using the Adventist Studies; 2) to compare the life expectancies from heart disease and all-site cancer between vegetarians and omnivores for different ages and calendar times, and separately in males and females. We combined the two cohort studies, the Adventist Mortality Study (AMS, 1960-1985; n = 27,517), and the Adventist Health Study (AHS, 1970-1988; n = 34,192). Life expectancies from specific causes were calculated for subjects who had survived to ages 30, 50, 70, and 80 during three calendar periods: 1960-1969, 1970-1979, and 1980-1988. The basis for the life table calculations was the age disease-specific mortality rates, which were calculated using the Multiple Decrement Life Table Analysis Program (MDLTAP), taking into account competing causes of death and allowing for the control of confounders. We conducted both univariate and multivariate analyses controlling for the potential confounders: education, body mass index (BMI), and exercise. We examined the secular trends in life expectancies using weighted linear regression, where inverse variances obtained from the MDLTAP program were used as weights for the respective calendar periods.

During 28 years of follow-up, 2,646 deaths from coronary heart disease, and 1,549 deaths from cancer were identified. The life expectancy for vegetarian and omnivorous males and females who eventually died from heart disease increased with secular time from 1960 to 1988 for all ages. This increase was 4-10 years in females and 2-6 years in males. The life expectancy at all ages of vegetarian females who died from

heart disease was 0.5-2.0 years higher than that of omnivores for all the calendar periods. This difference was statistically significant at younger ages during the calendar period 1960-1988. The life expectancy of vegetarian males who died from heart disease was 2-4 years higher than that of omnivores for the calendar periods 1960-1969 and 1970-1979 and this difference was statistically significant at most ages.

The life expectancy at all ages of both females and males who eventually died from cancer increased with secular time from 1960-1988, irrespective of their type of diet. This increase was 2-9 years in females and 3-7 years in males. The life expectancy at all ages of vegetarian females who died from cancer was 1-2 years higher than that of omnivores in the calendar period 1970-1979. The difference in life expectancy that was attributed to a vegetarian status in males who died of cancer was 1-4 years.

In conclusion, the life expectancy from specific causes of death, increased with secular time from 1960 to 1988, irrespective of gender and type of diet. Vegetarians had 1-4 years greater life expectancy from these causes when compared to omnivores. The gender differences in life expectancy of subjects who died from heart disease or cancer were less in vegetarians compared to omnivores. Among those subjects, a vegetarian diet contributes to greater longevity, and this lifestyle decreases the gender gap in life expectancy in those dying from specific causes of death.

INTRODUCTION

Life expectancy has been increasing, not just in industrialized societies, but around the world. Since 1970, the main reason for continued gains in life expectancy in the industrialized countries is a reduction in the death rates among the elderly (1, 2). The most significant factor driving the mortality decline at older ages is the reduction of death rates due to cardiovascular disease and cancer (3). In the United States, heart disease has been the leading cause of death since 1921. From 1950 to 1996, the age adjusted death rate from heart disease declined by 56% (4). In the United States, it has been argued that new therapeutic interventions, decline in cigarette smoking, and changes in diet and life style contributed to this decline (4). In most developed countries, cancer mortality has begun to decline within the last two decades (5). The reasons for this decline are improvements in medical care and changes in diet and personal habits (3). Willett indicated that about 32% (95% CI; 20%- 42%) of all cancer deaths in the United States may be associated with diet (6). Many epidemiological studies have already shown that a vegetarian diet, rich in whole-grains, vegetables and nuts, has been associated with a lower risk for many chronic diseases (7-14).

Seventh-day Adventists present a unique opportunity to study the relationship between diet and expected age at death from specific chronic diseases. This is because of their wide variety of dietary habits, and because cohorts have been followed for twenty-eight years. In this study, we combined the Adventist Mortality Study (AMS)(1960-1985), and the Adventist Health Study (AHS)(1976-1988) cohorts of non-Hispanic white Seventh-day Adventists from California. In order to determine the potential impact of diet on the expected age at death from chronic diseases, we compared the life expectancies of those who died from heart disease and cancer in omnivores and vegetarians, separately for non-smoking males and females. We calculated life expectancies for these subjects who had survived to 30, 50, 70, and 80 years of age during three calendar periods: 1960-1969, 1970-1979, and 1980-1988.

METHODS

A. Study Population

1. The Adventist Mortality Study (AMS) Cohort (1960-1985)

In 1960, 27,530 California Seventh-day Adventists, age 30 years and older, completed a four page American Cancer Society (ACS) questionnaire, which included questions on personal health, exercise level, the frequency of use of 21 different foods and beverages, and other life-style factors. These individuals were followed for 26 years (1960-1985). The details of this population and the validity of death ascertainment has been described previously (15-18). In summary, deaths were ascertained by record linkage with the California Death Certificate File, record linkage with the National Death Index (after 1978), and through church records.

We calculated body mass index (BMI) from the height and weight values that the AMS subjects reported on the baseline questionnaire. The meat index was determined from the responses to questions on the intake of meats. Vegetarians were defined as those eating meats never or less than once per week. All others were considered omnivores. Other variables included in the analysis were obtained from responses to questions on exercise level (none, slight, moderate, heavy), and educational level (no schooling, grammar school, some high school, high school graduate, some college, college, technical or trade school).

2. The Adventist Health Study Cohort (AHS) (1976-1988)

In 1976, a lifestyle questionnaire was sent to 59,081 non-Hispanic white California Seventh-day Adventist adults, who were identified during a census that was taken between 1974 and 1976. Mailed questionnaires that included questions on demographics, diet, physical activity, psychosocial factors, and medical history were completed by 34,192 subjects. Details of the study design have been previously published (19). Direct follow-up was conducted to ascertain all deaths for the years 1976 to 1982. In addition, for the years 1976 to 1988, death ascertainment used computerized matching to California State Death Tapes and the National Death Index, when this last date became available in 1979. These sources were supplemented by church records and short mailed annual surveys between the years 1976 and 1983 (20).

Body Mass Index in AHS subjects was determined from items on current weight in pounds and height in inches. The validity of the anthropometric data had been tested and the correlation between self-reported and measured weight was 0.94 for women and 0.96 for men (21). The dietary section of the questionnaire included 55 semi-quantitative food frequency questions (8 frequency categories from "never consumes" to "more than once each day"), and 10 qualitative dietary questions. The meat index was determined from the response to six questions on the intake of meats (beef, lamb, processed meats, poultry, pork, and fish). A dietary validity study compared food frequency results to five unannounced 24-hour recalls, and the correlations between measurements of meat and the

24-hour recalls were 0.83 (22) . Vegetarians were again defined as those eating meats never or less than once per week; all others were considered omnivores.

In the AHS Cohort, educational level was obtained from the response to a question on education (high grade or less, some high school, high school graduate, some college, college graduate or above). A physical activity index was calculated from subjects' responses to questions regarding vigorous leisure-time and occupational activities, and was considered "high" for frequent ($\geq$ 15 minutes per session, $\geq$ 3 times per week) participation, which reflects a positive response to either or both of the occupational or leisure activity questions, "moderate" for less frequent (< 15 minutes per session, < 3 times per week) participation, or "none/low" for "rarely or never" participation in both occupational and leisure activities. This index was shown to be a significant predictor of all-cause and CHD mortality in the study population (23, 24).

3. *Analytic Cohort (1960-1988)*

The combined cohorts had a total of 38,237 never-smoking subjects. There was an overlap of about 10,000 subjects, who were members of both the AMS and AHS cohorts. These subjects contributed person time only once for a particular calendar date in the combined cohort. A validity study of subjects' ability to recall their dietary choices 20 years previous has been described. Recall data was compared to their responses in 1960 for "current" consumption. Results indicated good agreement between the recall data and the original 1960 data (22). We restricted the analysis to non-smokers (the huge majority). When the cohorts were combined for the life table analysis, subjects were classified into high (some college or more) and low (high school graduate or less) educational achievement. For physical activity, male subjects in the combined cohort were divided into high (moderate and high) and low (none and low) exercise levels. We categorized BMI into three categories: low (BMI < 23.96 kg per m^2), mid (23.96 ≤ BMI < 26.68 kg per m^2), and high (BMI ≥ 26.68 kg per m^2). The study endpoints were fatal cardiovascular disease (ICD-9 codes 390-398, 400-404, 410-414, 420-429, 430-438, 440-458) and cancer (ICD-9 codes 140-239).

Subjects with some college or higher, a BMI less than 23.96 kg/m^2, and a moderate to high level of exercise were considered to have a favorable lifestyle. Subjects with high school degree or less, a BMI greater than or equal to 26.68 kg/m^2, and a low to no exercise were considered to have an unfavorable lifestyle. We compared the life expectancies between vegetarians and omnivores, for subjects with favorable lifestyles and for subjects with unfavorable lifestyles.

B. Analyses Methods

The Multiple Decrement Life Table Analysis Program (MDLTAP) was used to calculate life expectancies for those who died from heart disease and cancer by diet status for three calendar periods (1960-1969, 1970-1979, and 1980-1988) for subjects who had survived to ages 30, 50, 70, and 80 years at these calendar periods. This multivariate method, where the time variable is attained age, uses proportional hazards modeling to produce maximum likelihood estimates for the exposure coefficients. A product term with age accommodated differences in effects by age, where such coefficients were statistically significant. The hazards, which are thus conditional on exposure values, were used to calculate age-specific probabilities for the life table (25). Variance estimates, confidence intervals, and tests of significance have been described previously (25).

The method produced estimates of life expectancies comparing vegetarians with omnivores.

We conducted both univariate and multivariate analyses using the MDLTAP program to determine how life expectancies for those who died from specific causes changed with secular time, age, and diet status in males and females, separately. We also evaluated the secular changes in these life expectancies for vegetarians and omnivores with otherwise favorable lifestyle (low BMI, highly educated, and exercised) and in subjects with otherwise unfavorable lifestyle (high BMI, not educated, and did not exercise).

In the univariate analysis, the model included diet status (vegetarians, omnivores) and the interaction of diet status with attained age. In the multivariate analysis, the model included diet status (vegetarians vs. omnivores), exercise level (high vs. low), educational level (high vs. low), medium BMI (coded as 1 if $23.96 \leq \text{BMI} < 26.68$ and 0 otherwise), and high BMI (coded as 1 if $\text{BMI} \geq 26.68$, 0 otherwise). The product terms, education by exercise and high BMI by exercise, were also included because they were statistically significant. We also included the interaction of exercise level, diet status, medium BMI, and high BMI with attained age because these interactions contributed significantly in the multivariate analysis.

We formally examined the secular trends in life expectancies using weighted linear regression, where the inverse of their variances obtained from the MDLTAP program were used as weights for the respective calendar periods. Life expectancy in those dying from specific causes was regressed on calendar time separately for vegetarians and omnivores in males and females. In the weighted regression analysis, calendar year was centralized to the middle of the interval. The effects of diet status on life expectancy were evaluated for each calendar period, as well as by comparing the regression slopes for vegetarians and omnivores.

RESULTS

A. Demographic Characteristics

During 28 years of follow-up, 2,646 deaths from coronary heart disease and 1,549 deaths from cancer were identified. Baseline characteristics of the population, according to diet status, are presented in Table 1. Omnivores were more obese (32.9% with BMI ≥26.7 vs. 18.8% in males, and 27.5% vs. 18.3% in females), less educated (48.7% vs. 54.7% in males, and 35.8% vs. 42.6% in females had some college or higher), but omnivores exercised at a similar level to vegetarians (70.0% vs. 73.9% were high exercisers). Exercise was available in males only, because the data on the exercise level for females had not been entered into the database for the older mortality study. Because of the differences according to diet status, body mass index, educational level, and possibly exercise in males, these variables were potential confounders that were controlled in the multivariate analyses.

B. Life Expectancy in Subjects Who Died From Heart Disease

1. Secular Trends in Subjects Who Died From Heart Disease

The results of the multivariate analyses for females with otherwise favorable lifestyles who eventually died from coronary heart disease (CHD) are displayed in Table 2a, and for females with otherwise unfavorable lifestyles in Table 2b. Life expectancies increased 4-10 years with secular time from 1960 to 1988 for all ages, irrespective of type of diet and other favorable or unfavorable lifestyles (Table 2a-b). Linear trends over secular time were not significant at most ages, irrespective of type of diet and other lifestyle choices. The linear trend for females with otherwise favorable lifestyles who had survived to age 80, however, was significant for omnivores, but not for vegetarians. The life expectancies for females who had survived to 50 years of age are shown graphically in Figure 1.

Results of the multivariate analyses for males with otherwise favorable lifestyles who eventually died from CHD are displayed in Table 3a, and for males with otherwise unfavorable lifestyles in Table 3b. Life expectancies increased with secular time from 1960 to 1988 for all ages, irrespective of type of diet and otherwise favorable or unfavorable lifestyles (Tables 3a-b). The increase in life expectancy over secular time, however, was consistently higher in omnivores, this increase being between 3-6 years in omnivores versus 2-4 years in vegetarians. Linear trends over secular time were not significant at most ages, irrespective of type of diet and lifestyle choices (Tables 3a-b). The linear trend for males with otherwise unfavorable lifestyles who had survived to age 30 was significant for vegetarians, but not for omnivores. The life expectancies for males who had survived to 50 years of age are shown graphically in Figure 2.

2. *Effects of Vegetarian Status in Subjects Who Died From Heart Disease*

Regardless of their lifestyle, the life expectancies at all ages of vegetarian females who died from heart disease were 0.1-2.7 years higher than that of omnivores for the calendar periods 1960-1969, 1970-1979 and 1980-1988, though not significant during particular calendar periods. In the calendar period 1960-1969, however, the life expectancy advantage at age 80 attributed to a vegetarian diet in females with otherwise unfavorable lifestyles was statistically significant (Table 2b). Over the calendar period

1960-1988, the life expectancies of vegetarian females with otherwise favorable lifestyles were 0.5-1.6 years higher than those of omnivores. This difference was statistically significant at younger ages (Table 2a).

In males with otherwise favorable lifestyles, the life expectancies of vegetarians who died from heart disease were 2-4 years higher than those of omnivores in the calendar periods 1960-1969 and 1970-1979. The life expectancy advantage across calendar years, that was attributed to a vegetarian diet, was statistically significant at most ages. In the calendar period 1980-1988, however, the life expectancies of vegetarians approached those of omnivores (Table 3a). The life expectancies of vegetarian males with otherwise unfavorable lifestyles were 1-3 years higher than those of omnivores in the calendar periods 1960-1969 and 1980-1988. This difference was significant in those who had survived to 30 or 50 years of age in the calendar period 1960-1969. In the calendar period 1970-1979, however, the life expectancies of vegetarians at 30 and 50 years of age were 1.5-2 years lower than those of omnivores, yet not significant. On the other hand, life expectancies of vegetarian males at 70 and 80 years of age were about 1-6 years higher than those of omnivores, though not statistically significant. During the calendar period 1960-1988, the life expectancies of vegetarian males at all ages were between 1.0-1.6 years higher than those of omnivores, irrespective of otherwise favorable or unfavorable lifestyles, but this difference was not statistically significant.

3. *Gender Differences in Life Expectancy of Subjects Who Died From Heart Disease*

Females who died of heart disease had a higher life expectancy than males. Over the calendar period 1960-1988, the life expectancies of both vegetarian and omnivore females with otherwise favorable lifestyles who eventually died from heart disease were 1-2 years higher than those of males with otherwise favorable lifestyles, irrespective of type of diet (Tables 2a and 3a). Among subjects with otherwise unfavorable lifestyles, the life expectancy advantage among females compared to males was 3-6 years (Tables 2b and 3b). The gender gap was higher in those with unfavorable lifestyles, irrespective of their diet.

4. *Comparison Between Favorable and Unfavorable Life Styles (Aside from Vegetarian Status): Effects on Life Expectancy of Subjects Who Died From Heart Disease*

At 30 and 50 years of age, the life expectancies of both vegetarian and omnivorous females with otherwise favorable lifestyles who eventually died from heart disease were 4-5 years higher than those of females with otherwise unfavorable lifestyles (Table 2a-b). At 70 and 80 years of age, the life expectancies of females with otherwise favorable lifestyles were 1-2 years higher than those of females with otherwise unfavorable lifestyles, irrespective of type of diet (Tables 2a-b).

At 30, 50, and 70 years of age, the life expectancies of both vegetarian and omnivorous males with otherwise favorable lifestyles, who eventually died from heart disease were 7-8 years higher than those of males with otherwise unfavorable lifestyles (Table 3a-b). At 80 years of age, the life expectancies of males with otherwise favorable lifestyles were about 5 years higher than those of males with otherwise unfavorable lifestyles, irrespective of type of diet (Table 3a-b). Thus a much greater effect is seen in males.

C. Life Expectancy of Subjects Who Died From Cancer

1. Secular Trends in Life Expectancy of Subjects Who Died From Cancer

The results of the multivariate analyses for females with otherwise favorable lifestyles who eventually died from cancer are displayed in Table 4a, and for females with otherwise unfavorable lifestyles in Table 4b. In females, life expectancy increased with secular time from 1960 to 1988 for all ages in both vegetarians and omnivores, irrespective of otherwise favorable or unfavorable lifestyles. The increase in life expectancy over calendar time, however, was consistently higher in omnivores (between 3-9 years in omnivores versus 2-6 years in vegetarians). Linear trends over calendar time were not significant at most ages, irrespective of type of diet and lifestyle choices (Tables 4a-b). The linear trend for females with otherwise unfavorable lifestyles, however, was significant (Table 4b). The life expectancies for females who had survived to 50 years of age are shown graphically in Figure 3.

The results of the multivariate analyses for males with otherwise favorable lifestyles who eventually died from cancer are displayed in Table 5a, and for males with otherwise unfavorable lifestyles in Table 5b. In males with otherwise favorable lifestyles, life expectancies increased 3-7 years with secular time from 1960 to 1988 for all ages, irrespective of type of diet. In males with otherwise unfavorable lifestyles, who had survived to 30 years of age, the increase in life expectancy was about 5 years in vegetarians compared to 8 years in omnivores. From the calendar period 1970-1979 to 1980-1988, however, the life expectancy of males with otherwise unfavorable lifestyles who had survived to 50, 70, and 80 years of age declined (between 3-6 years in omnivores versus 1-7 years in vegetarians). Linear trends over calendar time were not significant, irrespective of type of diet and lifestyle choices (Tables 5a-b). The linear trend for vegetarian males who had survived to 70 years of age, however, was significant. The life expectancies of males who survived to 50 years of age are shown graphically in Figure 4.

2. *Effects of Vegetarian Status on Life Expectancy of Subjects Who Died From Cancer*

The effects of a vegetarian status on life expectancies of females who died from cancer were similar, irrespective of otherwise favorable or unfavorable lifestyles. In the calendar periods 1960-1969 and 1980-1988, the life expectancies of vegetarian females who had survived to 30 years of age were slightly higher (0.5-0.8 years) than those of omnivores (Tables 4a-b). In the same calendar periods, however, the life expectancies of vegetarian females who died from cancer and who had survived to 50, 70, and 80 years of age were a non-significant 0.1-3.7 years lower than those of omnivores. In the calendar periods 1970-1979, the life expectancies of vegetarian females were 1-2 years higher than those of omnivores (Tables 4a-b).

In the calendar periods 1960-1969 and 1980-1988, the life expectancies at all ages of vegetarian males with otherwise favorable lifestyles who died from cancer were 2.3-3.8 years higher than those of omnivores (Table 5a). The life expectancy advantage due to a vegetarian diet was only significant for males who had survived to 70 years of age in the calendar period 1960-1969. In the calendar period 1970-1979, the life expectancies of vegetarians who had survived to 30 or 50 years of age were a non-significant 1.8-2.9

years higher than those of omnivores. The life expectancies of vegetarians who had survived to 70 or 80 years were a non-significant 0.3-1.7 years lower than those of omnivores (Table 5a).

In the calendar periods 1960-1969 and 1980-1988, the life expectancies of vegetarian males with otherwise unfavorable lifestyles were 0.4-3.4 years higher than those of omnivores (Table 5b). In the calendar period 1970-1979, the life expectancies at 30, 70, and 80 years of age were 0.2-1.1 years lower for vegetarians compared to omnivores. In the same calendar period, however, the life expectancies of vegetarians who had survived to 70 years of age were a non-significant 3.7 years higher than those of omnivores (Table 5b).

3. Gender Differences in Life Expectancy of Subjects Who Died From Cancer

Females who had survived to 30 or 50 years of age had a lower life expectancy till a cancer death than males. Over the calendar period 1960-1988, the life expectancies of these younger vegetarian and omnivorous females with otherwise favorable lifestyles, who eventually died from cancer were 1-3 years lower than those of males, irrespective of their lifestyle (Tables 4a-b and 5a-b). The life expectancies of older vegetarian or omnivore females with otherwise favorable or unfavorable lifestyles, (those who had survived to 70 or 80 years of age) approached or slightly exceeded those of males.

4. Comparison between Favorable and Unfavorable Life Styles (Aside From Vegetarian Status): Effects on Life Expectancy of Subjects Who Died From Cancer

At 30 and 50 years of age, the life expectancies of females with otherwise favorable lifestyles who died from cancer were 3-5 years higher than those of females with otherwise unfavorable lifestyles, irrespective of their diet (Tables 4a-b). Life expectancies at 70 and 80 years of age were 1-2 years higher for females with otherwise favorable lifestyles than those of females with otherwise unfavorable lifestyles, irrespective of type of diet (Tables 4a-b).

At 30 and 50 years of age, the life expectancies of vegetarian and omnivorous males with otherwise favorable lifestyles, who eventually died from cancer, were about 4 years higher than those of males with otherwise unfavorable lifestyles (Tables 5a-b). At 70 and 80 years of age, the life expectancies of males with otherwise favorable lifestyles were 1-3 years higher than those of males with otherwise unfavorable lifestyles, irrespective of type of diet (Tables 5a-b).

DISCUSSION

This cohort study with a follow-up of 28 years and a total of 2,646 deaths from coronary heart disease and 1,549 deaths from cancer showed that life expectancy in those dying from these disorders increased with secular time for both vegetarians and omnivores. From the calendar period 1960 to 1988, the life expectancies of vegetarian and omnivorous females at all ages, who eventually died from heart disease, increased 4-10 years in different subgroups. Similar trends were also seen in males who survived to 30, 50, and 70 years of age (increases of 2-6 years). The life expectancies at all ages of vegetarians and omnivores who died from cancer increased 2-9 years with calendar time in males and females. Thus, the increase in life expectancies with secular time for subjects who died from specific causes of death was similar in magnitude to the increase in overall life expectancy (death from any cause), irrespective of the type of diet and lifestyle (26).

The life expectancy of males and females who eventually died from specific causes (heart disease or cancer) at all ages increased with secular time from 1960 to 1988. There was a significant linear trend for vegetarian males and females who eventually died from cancer at 70 years of age. Otherwise, the linear trend was not statistically significant. This might be due to the small number of events; the confidence intervals were wide, and power was insufficient in order to show a significant effect. Among our cohorts, we saw a reduction in cardiovascular mortality, therefore, age at death was postponed to higher ages. Between 1950 and 1985, Lopez (27) also found a delayed age at death due to cardiovascular disease and a rise in cancer mortality that was accompanied by a rise in age at death from cancer.

For both causes of death, the life expectancies of vegetarians at virtually all ages was higher than that of omnivores, but there was little difference at the older age in subjects who died from cancer. Adjustment for different health indicators (BMI, education, and exercise) did not change the relationship between diet status and life expectancy. This consistency implies that the additional years gained by following a vegetarian diet is probably a true effect, at least at younger ages.

The life expectancy advantage attributed to a vegetarian diet for males who died from heart disease (2-4 years) was larger than that of females (0.5-2 years). For females who died from coronary heart disease, the life expectancy advantage attributed to a vegetarian diet was higher at younger ages (30 and 50) compared to older ages (70 and 80) in the calendar period 1970-1979. This result is reminiscent of the findings reported by Lasheras et al. (28), who indicated that the protective effective effect of a Mediterranean diet among younger adults was not apparent among 80-95 year-old adults.

Key et al. (29), in a collaborative analysis of 5 prospective studies, namely the Oxford vegetarian Study (UK), the Heidelberg Study, the Adventist Mortality Study, the Adventist Health Study, and the Health Food Shoppers Study, reported that mortality from ischemic heart disease was 24% lower in vegetarians than in omnivores (death rate ratio = 0.76; 95% CI : 0.62- 0.94; $p<.001$), and that the lower mortality among vegetarians was greater at younger ages and was restricted to those who followed the diet for more than 5 years.

The delay in age at death among vegetarians who die of heart disease may be due to their lower serum cholesterol concentration (30). Soluble fiber plays a role in lowering cholesterol (31, 32). The potential protective effects of fruits and vegetables are probably also mediated by lowering blood pressure and/or their antioxidant effects (33). Fruits and vegetables are rich sources of vitamins, such as vitamin C and betacarotene, and minerals,such as potassium and magnesium, in addition to other nutrients, such as folate and fiber (33). Potassium has been shown to increase the ability to relax the blood vessels, thereby lowering blood pressure (30, 33-35). Magnesium, calcium, and other minerals may also play a role in preventing hypertension (36). Three randomized controlled trials have shown fruit and vegetable consumption to significantly lower systolic and diastolic blood pressure (37-39). High folate intake from these foods lowers serum homocysteine levels, a risk factor for arterial endothelial dysfunction (40, 41).

The life expectancy advantage attributed to the vegetarian diet was 1-4 years in males who eventually died from cancer in all the calendar periods. In the calendar period 1970-1979, the life expectancy advantage of vegetarian females who eventually died from cancer was 1-2 years higher than that of omnivorous females. Potter (42) has indicated that fruits and vegetables are associated with decreased frequency of many cancers. This protection may result from phytoestrogens (such as isoflavones and lignans), folic acid, or antioxidants (such as the flavonoids, carotenoids, vitamin C, and vitamin E). The consumption of legumes may decrease the risk of colon cancer, and may also protect against prostate and pancreatic cancer according to multivariate results from the Adventist Health Study (16, 43, 44). Key et al. (29), however, did not find significant differences between vegetarians and non-vegetarians in mortality from stomach cancer, colorectal cancer, lung cancer, or all other causes combined.

Several food chemicals, such as certain polycyclic aromatic hydrocarbons, nitrosamines and heterocyclic amines have been found to be carcinogenic in animals (45). High temperature cooking of meat generates heterocyclic amines, whereas the process of grilling and smoking of meat generates polycyclic aromic hydrocarbons. It has been suggested that N-nitroso compounds present in processed meat may induce G>A transitions at the second base of codon 12 or 13 of the K-*ras* gene in the human colon (46). Serveral different types of studies (case-control, case-cohort, and cross-sectional) with colon cancer patients have reported an association between meat consumption and K-*ras* mutilations (47-50).

We found an association between age at death from all site cancers and meat consumption. This may be influenced by specific types of cancer and their relationship to dietary components. Epidemiological studies have indicated that consumption of broiled, fried, barbequed, or smoked meats may increase the risk of colorectal cancer (51, 52). Satia et al. (53) and others (54-56) have reported a positive association between red meat consumption and increased risk of development of colorectal cancers. Consumption of chicken and fish, however, has not been associated with increased risk (54, 55). Dietary associations of meat and colon cancer were also found in the Adventist Health Study (43), and in two cohort studies (the Physician's Health Study (57) and the Nurses' Health Study (58)). Several other cohort studies (16, 59-61), however, did not find an association between meat intake and increased risk of colon cancer, but this may be related to measurement errors, and perhaps to a small range of meat consumption.

Dietary associations with the risk of prostate cancer have been revealed by the Adventist Health Study (62, 63). A relationship between meat consumption and prostate cancer has been reported by others (64, 65). Those who eat meat more frequently may have a greater risk of bladder cancer. Results from the Adventist Health Study have indicated that Adventists who ate meat three or more times per week had a relative risk of 2.38 (95% CI, 1.23-4.51), as compared with those eating meat less frequently (66). A Swedish study (67) has reported a relative risk of 2.2 (95% CI: 1.1-4.4) with a greater intake of pork and beef, and a study in Hawai by Chyou et al. (68) have indicated a relative risk of 1.5 (95% CI, 0.8-3.2) with higher consumption of meat. A recent case control study by Radosavljevic et al. (69) reported that consumption of liver, canned meat, and pork was a risk factor for bladder cancer.

Results from the Adventist Health Study have indicated a strong association between high meat intake and ovarian cancer among postmenopausal women (RR= 2.3; 95% CI, 1.1-4.7) (70). Schultz et al. (71), based on a review of 7 cohort studies and 27 case-control studies, reported that high meat consumption may be associated with an increased risk of ovarian cancer. Pan et al. (72), however, did not observe an association of ovarian risk with meat products, fish, and poultry. Two other studies have reported a positive association between meat consumption and ovarian cancer (73, 74).

In our study, the life expectancies of subjects with a favorable lifestyle (aside from vegetarian status) who died from heart disease or cancer were consistently higher (1-8 years) than of those with an unfavorable lifestyle. This indicates that other factors, such as body mass index, exercise, and education, may add to the effect of vegetarianism. In line with these results, Fraser et al. (75) reported that Adventists may experience up to 10 years difference in life expectancy as a result of their choices. In addition, Stamler et al.(76) estimated that low-risk individuals had a 6-10 years higher life expectancy. Knoops et al. (77) have also reported that, among individuals 70 to 90 years of age, adherence to a healthful lifestyle is associated with a more than 50% lower mortality rate from specific causes (heart disease and cancer), and lack of adherence to this lifestyle is associated with a considerable population attributable risk of death (54% from coronary heart disease and 60% from cancer).

Health related behaviors, such as physical activity, also impact life expectancy. In the Adventist Health Study, a high exercise level contributed 2.2 years difference in life expectancy (75). Three other studies have found greater physical activity to be associated with higher life expectancy (78-80). Increased physical activity has been associated with a reduction in the incidence and mortality for all-site cancer (81). In addition, excess body weight and physical inactivity have been associated with higher risk of colon cancer (82-85), and several studies have suggested an inverse association between physical activity and risk of prostate cancer (86-88). Simin et al. (89), however, have reported that increased physical activity may not reduce the risk of prostate cancer. In the Adventist

Health Study, regular physical activity has been associated with reduced risk for breast cancer, but not for colon cancer (90). Other studies have also found similar protective indications between physical activity and breast cancer (84, 91-94).

Overweight in adulthood has been linked to a decrease in life expectancy (75, 95, 96). Among 40-year old non-smokers without previously diagnosed cardiovascular disease, overweight was associated with a 3-year decrease in life expectancy, and obesity was associated with a 6-7 year decrease (96). Fraser et al. (75), in the Adventist Health Study, reported that Adventists with a high BMI may experience 1.5 -1.9 years decrease in life expectancy. Fontaine et al. (95) have reported that the effect of excessive body weight on life expectancy is especially great at younger ages.

There is also growing evidence for a link between high body mass index (BMI) and risk of death (97-101). McGee et al. (102) , in a meta-analysis that examined the relationship between BMI and mortality from heart disease and cancer, have reported that the relative risks among the heaviest individuals (BMI $\geq$30) for death from coronary heart disease and cancer were 1.56 and 1.07. Obesity has also been associated with an elevated risk of coronary heart disease and cancer (97, 103, 104). Further support of the relationship between overweight and cancer has been given by the Adventist cohorts, where overweight Adventists were at significantly greater risk of developing breast and colon cancer (16, 43, 90, 105). The association of colon cancer and BMI is stronger in men than in women (43, 106, 107). A completed meta analysis of prospective and case-control studies of specific cancers have reported increased risks from higher values of BMI for cancers of the breast, colon, prostate, endometrium, and kidney (108). In the Iowa Women's Health Study, Folsom et al. (109) also found a 30% higher risk of all cancers, and substantially increased risks for breast, colon, and uterine cancer for older women who were obese. Eichholzer et al. (110), however, have indicated that there is little evidence of an association between BMI and mortality from all cancers combined, cancer of the lung, the prostate, and the colon.

The life expectancies of older (beginning at 50, 70, and 80 years of age) omnivorous females who eventually died from cancer were a non-significant 0.1-3.7 years higher than those of vegetarian females. The attenuation of the effect of individual risk factors, such as diet and physical activity, with age had been reported by others (111, 112). A possible explanation could be that the elderly may have changed their diet due to age related pathologies. If they switched their diet to become vegetarian since study baseline, such changes would decrease the apparent beneficial effect of a vegetarian diet (111). The effect of diet could also be diminished at older ages.

Based on the data reported by Friedland (113), the difference in life expectancy at birth between the sexes was about 7 years in the years 1960, 1970, and 1990. In the Adventist Studies, the life expectancies from heart disease and cancer were lower in males compared to females, but the gender differences in life expectancy were much less in vegetarians compared to omnivores. Fraser (114) reported that vegetarians were more likely to never have smoked cigarettes, to not use alcohol, and to have no prevalent chronic disease. Also, it is well established that a diet rich in vegetables and fruits is associated with lower rates of smoking, higher levels of physical exercise, better health management, and a relatively low intake of cholesterol and saturated fat (115, 116).

A strength of this analysis is that it examines the 28-year follow-up of never-smoking non-Hispanic Adventists 30 years or older, and evaluates the effects of selected baseline health habits. Results are presented in terms of increased life expectancy rather than mortality rates. Another strength of this study is the great diversity in food and lifestyle factors (21). Regarding diet, in particular, Adventists are quite heterogeneous. Only about 3% in the Adventist Studies are vegans; about 27% are lacto-ovo vegetarians; about 20% eat meat 1-3 times a week; and the remainder eat meat more than four times a week (117). Fewer than 10% of the subjects in our studies drank even small quantities of alcohol, making this an unlikely confounder (26). We restricted the analysis to never-smokers and adjusted for available key lifestyle factors that may be confounding factors. Vegetarians have significantly lower BMI, but this was controlled in this analysis. Adjustment for different health indicators did not substantially change the relationship between diet status and life expectancy, implying that a vegetarian diet has an independent effect on life expectancy.

Limitations of the study include the dietary assessment at baseline only. Undocumented changes in diet after the study baseline would weaken the associations between diet and life expectancy (117). Willett (117) and others have reported that, in a cohort study, measurement error in dietary assessment usually tends to bias the effect estimate toward the null hypothesis. Thus, the effects of a vegetarian diet may have been under-estimated here. Assessment of vegetarian status, however, is probably more accurate than measuring individual foods. Our validity correlation coefficient of 0.82 for meat consumption is consistent with this conjecture (22). Another limitation of this analysis was the need to dichotomize most of the exposure variables to ensure sufficient numbers of events in each category. This will tend to obscure effects in the extreme values of the distributions.

In conclusion, the life expectancies at all ages from coronary heart disease and all-site cancer at all ages increased substantially with secular time from 1960 to 1988 in both males and females. The life expectancies of vegetarians were between 1-4 years higher in different subgroups when compared to omnivores, although this effect was not seen in older subjects dying of cancer. The effects of low BMI and high educational level further increased this advantage in life expectancy among vegetarians. The life expectancies were substantially lower in males compared to females, but the gender differences in life expectancy in those dying of these causes were much less in vegetarians compared to omnivores. These results strongly suggest that a vegetarian diet does delay onset of heart disease in those who will die from this cause. Possibly this is true also of younger subjects who will die from cancer. Finally, choosing a favorable lifestyle decreases the gender gap in the life expectancy in those dying from these two causes.

TABLE 1. Frequency of selected variables by gender and diet status for never-smokers

	Males (N = 11 717)				Females (N = 26 520)			
	Vegetarians		Omnivores		Vegetarians		Omnivores	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%
Number of study subjects	6344	54.1	5373	45.9	13317	50.2	13203	49.8
Number of deaths from heart disease*	430	6.8	38	7.1	962	7.2	873	6.6
Number of deaths from cancer*	271	4.3	199	3.7	531	4.0	548	4.2
Education*								
Low†	2849	45.3	2731	51.3	7536	57.4	8396	64.2
High‡	3444	54.7	2598	48.7	5601	42.6	4689	35.8
BMI*								
BMI < 23.96	2974	50.1	1617	32.1	7333	60.2	5940	48.8
23.96 ≤BMI < 26.68	1842	31.1	1763	35.0	2618	21.5	2886	23.7
BMI ≥ 26.68	1117	18.8	1655	32.9	2234	18.3	3349	27.5
Exercise*§								
Low (none/low)	1646	26.1	1599	30.0				
High (moderate/high)	4652	73.9	3732	70.0				

* The percentages for the variables Education, BMI and Exercise are based on the number of study subjects (first row of results), as are the percentages of those who died from heart disease or cancer † High school graduates or less ‡ Some college or higher education § The data on the exercise level of females had not been entered in the database for the mortality study.

TABLE 2a. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking females who eventually died from coronary heart disease. Non-dietary covariates were set at low BMI and high educational level (otherwise favorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	56.3	60.1	65.9	0.08	60.3
	Omnivores	55.1	59.0	65.7	0.12	59.3
30+	Difference	1.1	1.1	0.2		1.0
	95% CI	(-0.6, 2.8)	(-0.3, 2.6)	(-2.2, 2.5)		(-0.0, 2.0)
	p-values	0.20	0.11	0.88		0.05
	Vegetarians	36.9	40.2	45.9	0.11	40.6
	Omnivores	35.2	39.2	45.8	0.11	39.5
50+	Difference	1.7	1.0	0.1		1.1
	95% CI	(-0.1, 3.4)	(-0.4, 2.5)	(-2.2, 2.5)		(0.0, 2.1)
	p-values	0.06	0.14	0.92		0.04
	Vegetarians	17.8	21.1	26.3	0.10	21.3
	Omnivores	16.5	20.5	25.4	0.05	20.5
70+	Difference	1.3	0.6	0.9		0.8
	95% CI	(-0.4, 3.0)	(-0.9, 2.1)	(-1.7, 3.5)		(-0.2, 1.9)
	p-values	0.12	0.41	0.51		0.11
	Vegetarians	10.4	12.8	17.4	0.13	13.1
	Omnivores	8.7	12.9	17.3	0.02	12.6
80+	Difference	1.7	-0.1	0.1		0.5
	95% CI	(0.0, 3.6)	(-1.6, 1.5)	(-2.6, 2.8)		(-0.5, 1.6)
	p-values	0.05	0.94	0.93		0.34

* Model includes diet status, educational level, medium BMI, high BMI, and product terms between diet and attained age, medium body mass index (BMI) and attained age, and high BMI and attained age.

TABLE 2b. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking females who eventually died from coronary heart disease. Non-dietary covariates were set at high BMI and low educational level (otherwise unfavorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	55.9	56.3	60.5	0.08	56.2
	Omnivores	54.4	54.8	58.6	0.12	54.6
30+	**Difference**	1.5	1.5	1.9		1.6
	95% CI	(-0.7, 3.7)	(-0.3, 3.2)	(-1.5, 5.3)		(0.1, 3.0)
	p-values	0.19	0.09	0.27		0.03
	Vegetarians	36.9	36.3	40.7	0.11	36.7
	Omnivores	35.1	35.1	39.3	0.11	35.2
50+	**Difference**	1.8	1.2	1.4		1.5
	95% CI	(-1.0, 3.8)	(-0.4, 2.9)	(-1.9, 4.7)		(0.5, 2.8)
	p-values	0.06	0.14	0.40		0.02
	Vegetarians	19.6	18.1	22.5	0.76	18.7
	Omnivores	18.6	17.4	20.5	0.72	17.7
70+	**Difference**	1.0	0.7	2.0		1.0
	95% CI	(-1.4, 3.5)	(-0.8, 2.0)	(-1.9, 5.9)		(-0.1, 2.2)
	p-values	0.41	0.38	0.32		0.08
	Vegetarians	11.9	11.1	11.8	0.90	11.5
	Omnivores	9.2	10.9	10.2	0.61	10.9
80+	**Difference**	2.7	0.2	1.6		0.6
	95% CI	(0.1, 5.4)	(-1.0, 1.4)	(-1.2, 4.4)		(-0.4, 1.7)
	p-values	0.04	0.73	0.27		0.23

* Model includes diet status, educational level, medium BMI, high BMI, and product terms between diet and attained age, medium body mass index (BMI) and attained age, and high BMI and attained age.

TABLE 3a. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking males who eventually died from coronary heart disease. Non-dietary covariates were set at low BMI, high educational level and exercise (otherwise favorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	55.5	61.3	59.4	0.52	58.4
	Omnivores	52.6	58.9	58.8	0.34	57.3
30+	Difference	2.9	2.4	0.6		1.1
	95% CI	(0.5, 5.4)	(0.2, 4.8)	(-2.3,3.5)		(0.3, 2.5)
	p-values	0.02	0.03	0.69		0.13
	Vegetarians	35.6	41.3	39.0	0.57	38.3
	Omnivores	32.5	38.9	38.5	0.55	37.3
50+	Difference	3.1	2.4	0.5		1.0
	95% CI	(0.5, 5.8)	(0.03, 4.7)	(-2.3,3.4)		(-0.5, 2.5)
	p-values	0.02	0.04	0.71		0.18
	Vegetarians	16.9	22.8	20.5	0.55	19.8
	Omnivores	15.2	19.8	19.3	0.45	18.5
70+	Difference	1.7	3.0	1.2		1.3
	95% CI	(-0.6, 4.1)	(0.9, 5.2)	(-1.9,4.4)		(-0.3, 2.8)
	p-values	0.14	<0.01	0.44		0.11
	Vegetarians	9.1	16.4	13.4	0.56	12.9
	Omnivores	7.2	12.5	12.7	0.30	11.3
80+	Difference	1.9	3.9	0.7		1.6
	95% CI	(-0.6, 4.4)	(1.8, 5.9)	(-2.6, 4.1)		(-0.1, 3.4)
	p-values	0.13	<0.001	0.67		0.07

* Model includes diet status, educational level, exercise level, medium body mass index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age.

TABLE 3b. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking males who eventually died from coronary heart disease. Non-dietary covariates were set at high BMI, low educational level and do not exercise (otherwise unfavorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	49.1	50.9	52.1	0.03	50.5
	Omnivores	45.8	52.5	51.3	0.38	49.5
30+	Difference	3.3	-1.6	0.8		1.0
	95% CI	(0.6, 6.0)	(-7.4, 4.1)	(-1.9, 3.6)		(-0.7, 2.8)
	p-values	0.02	0.57	0.55		0.25
	Vegetarians	29.9	30.8	32.5	0.08	30.9
	Omnivores	26.7	32.7	31.6	0.37	29.8
50+	Difference	3.2	-1.9	0.9		1.1
	95% CI	(0.6, 5.7)	(-7.6, 3.7)	(-2.0, 3.7)		(-0.6, 2.8)
	p-values	0.01	0.50	0.55		0.22
	Vegetarians	11.7	16.6	14.2	0.69	13.2
	Omnivores	10.4	15.5	13.1	0.60	12.3
70+	Difference	1.3	1.1	1.1		0.9
	95% CI	(-1.0, 3.6)	(-2.4, 4.5)	(-1.0, 3.2)		(-0.6, 2.4)
	p-values	0.26	0.55	0.31		0.23
	Vegetarians	6.5	16.6	8.4	0.78	8.8
	Omnivores	5.4	11.0	7.9	0.59	7.6
80+	Difference	1.1	5.6	0.5		1.2
	95% CI	(-0.6, 4.4)	(-4.6, 15.7)	(-2.6, 4.1)		(-0.7, 3.1)
	p-values	0.13	0.28	0.67		0.21

* Model includes diet status, educational level, exercise level, medium body mass index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age.

TABLE 4a. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking females who eventually died from cancer. Non-dietary covariates were set at low BMI and high educational level (otherwise favorable lifestyle)

Age		Calendar Year 60-69	70-79	80-88	P for trend	60-88
	Vegetarians	46.5	48.1	49.9	0.03	48.5
	Omnivores	46.0	46.4	49.1	0.27	47.8
30+	**Difference**	0.5	1.7	0.8		0.7
	95% CI	(-3.1, 4.1)	(-1.7, 5.1)	(-2.3, 3.8)		(-1.5, 2.7)
	p-values	0.79	0.34	0.62		0.55
	Vegetarians	27.3	29.7	31.0	0.10	29.8
	Omnivores	27.4	27.8	31.4	0.30	29.5
50+	**Difference**	-0.1	1.9	-0.4		0.3
	95% CI	(-3.4, 3.2)	(-1.0, 4.9)	(-3.2, 2.3)		(-1.6, 2.2)
	p-values	0.94	0.20	0.75		0.74
	Vegetarians	12.8	14.2	15.5	0.02	15.0
	Omnivores	13.6	13.4	16.7	0.37	15.7
70+	**Difference**	-0.8	0.8	-1.2		-0.7
	95% CI	(-3.7, 2.0)	(-2.3, 3.9)	(-4.1, 1.7)		(-2.4, 1.1)
	p-values	0.57	0.63	0.99		0.46
	Vegetarians	7.9	9.1	9.8	0.10	10.0
	Omnivores	8.6	7.3	12.0	0.55	10.7
80+	**Difference**	-0.7	1.8	-2.2		-0.7
	95% CI	(-4.0, 2.6)	(-1.6, 5.2)	(-5.6, 1.2)		(-2.5,1.0)
	p-values	0.68	0.29	0.21		0.40

* Model includes diet status, educational level, medium Body Mass Index (BMI), high BMI and product terms between diet and attained age, medium BMI and attained age, and high BMI and attained age.

TABLE 4b. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking females who eventually died from cancer. Non-dietary covariates were set at high BMI and low educational level (otherwise unfavorable lifestyle)

		Calendar Year				
Age		**60-69**	**70-79**	**80-88**	**P for trend**	**60-88**
	Vegetarians	42.2	45.2	46.8	0.11	43.8
	Omnivores	41.6	43.4	46.0	0.07	43.0
30+	**Difference**	0.6	1.8	0.8		0.8
	95% CI	(-3.8, 5.0)	(-1.8, 5.5)	(-2.9, 4.5)		(-1.5, 3.1)
	p-values	0.80	0.33	0.66		0.50
	Vegetarians	23.8	27.8	29.5	0.14	26.4
	Omnivores	24.0	25.7	31.0	0.21	26.0
50+	**Difference**	-0.2	2.1	-1.5		0.4
	95% CI	(-3.8, 3.4)	(-1.1, 5.1)	(-5.2, 2.2)		(-1.5, 2.3)
	p-values	0.91	0.20	0.42		0.69
	Vegetarians	10.6	13.1	16.2	0.04	13.5
	Omnivores	11.5	12.4	18.4	0.31	14.0
70+	**Difference**	-0.9	0.7	-2.2		-0.5
	95% CI	(-3.7, 2.0)	(-2.1, 3.6)	(-6.0, 1.6)		(-2.2, 1.1)
	p-values	0.56	0.61	0.25		0.49
	Vegetarians	5.0	9.6	11.0	0.17	9.2
	Omnivores	5.6	7.7	14.7	0.23	9.9
80+	**Difference**	-0.6	1.9	-3.7		-0.7
	95% CI	(-2.8, 1.5)	(-1.9, 5.8)	(-8.6, 1.1)		(-2.4, 1.0)
	p-values	0.56	0.31	0.13		0.41

* Model includes diet status, educational level, medium Body Mass Index (BMI), high BMI and product terms between diet and attained age, medium BMI and attained age, and high BMI and attained age.

TABLE 5a. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking males who eventually died from cancer. Non-dietary covariates were set at low BMI, high educational level and exercise (otherwise favorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	49.2	54.1	53.4	0.32	50.3
	Omnivores	46.0	52.3	49.6	0.60	48.6
30+	**Difference**	3.2	1.8	3.8		1.7
	95% CI	(-2.1, 8.4)	(-4.0, 7.5)	(-0.8, 8.4)		(-0.8, 4.4)
	p-values	0.24	0.54	0.10		0.19
	Vegetarians	29.3	29.7	34.2	0.24	31.1
	Omnivores	26.0	26.8	31.8	0.27	29.6
50+	**Difference**	3.3	2.9	2.4		1.5
	95% CI	(-1.8, 8.4)	(-3.0, 8.8)	(-1.6, 6.3)		(-0.9, 3.8)
	p-values	0.2	0.33	0.24		0.22
	Vegetarians	12.1	16.2	17.6	0.02	15.0
	Omnivores	8.4	17.9	15.1	0.31	14.0
70+	**Difference**	3.7	-1.7	2.5		1.0
	95% CI	(0.3, 7.1)	(-7.8, 4.3)	(-1.6, 6.6)		(-1.3, 3.2)
	p-values	0.03	0.57	0.23		0.4
	Vegetarians	7.5	6.1	10.6	0.57	10.1
	Omnivores	5.2	6.4	7.7	0.03	9.5
80+	**Difference**	2.3	-0.3	2.9		0.6
	95% CI	(-0.5,5.2)	(-2.1, 1.5)	(-1.8, 7.7)		(-1.9, 3.2)
	p-values	0.11	0.31	0.13		0.64

* Model includes diet status, educational level, exercise level, medium body mass index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age.

TABLE 5b. Multivariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist Studies for never-smoking males who eventually died from cancer. Non-dietary covariates were set at high BMI, low educational level and do not exercise (otherwise unfavorable lifestyle)

Age		Calendar Year				
		60-69	70-79	80-88	P for trend	60-88
	Vegetarians	44.7	43.8	40.1	0.74	46.7
	Omnivores	41.8	44.0	39.7	0.85	45.0
30+	**Difference**	2.9	-0.2	0.4		1.7
	95% CI	(-1.4, 7.4)	(-4.7, 4.1)	(-3.9, 4.7)		(-0.5, 3.9)
	p-values	0.19	0.91	0.86		0.13
	Vegetarians	25.7	28.8	22.0	0.54	27.2
	Omnivores	22.6	25.1	21.6	0.78	25.8
50+	**Difference**	3.1	3.7	0.4		1.4
	95% CI	(-1.1, 7.3)	(-2.3,9.8)	(-2.8, 2.7)		(-0.5, 3.5)
	p-values	0.14	0.22	0.97		0.16
	Vegetarians	18.1	14.2	10.9	0.02	13.2
	Omnivores	14.7	15.0	9.0	0.32	12.1
70+	**Difference**	3.4	-0.8	1.9		1.1
	95% CI	(-0.4, 7.3)	(-4.2, 2.6)	(-0.9, 4.7)		(-1.0, 3.3)
	p-values	0.08	0.66	0.19		0.29
	Vegetarians	11.3	10.1	10.8	0.65	9.0
	Omnivores	10.0	11.2	7.8	0.55	8.3
80+	**Difference**	1.3	-1.1	3.0		0.7
	95% CI	(-2.4,5.0)	(-3.9, 1.7)	(-1.1, 7.3)		(-1.6, 3.0)
	p-values	0.49	0.45	0.15		0.54

* Model includes diet status, educational level, exercise level, medium body mass index (BMI), high BMI, and product terms between education and exercise, high BMI and exercise, diet and attained age, exercise and attained age, medium BMI and attained age, and high BMI and attained age.

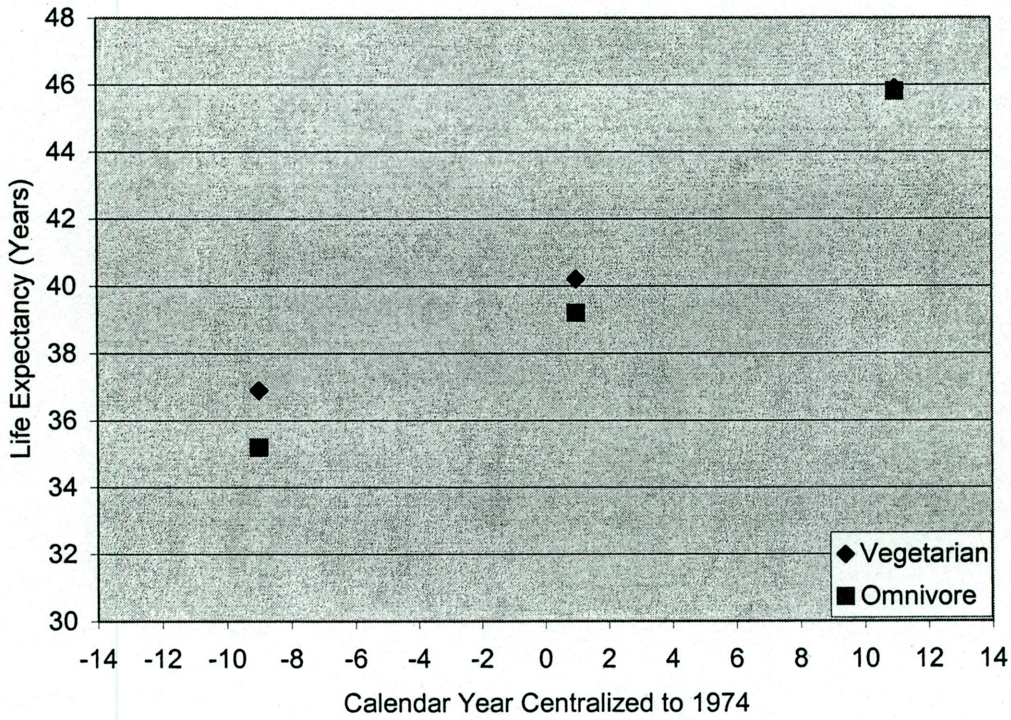

FIGURE 1. Comparison of change in life expectancy at age 50 by calendar year and diet status in females with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

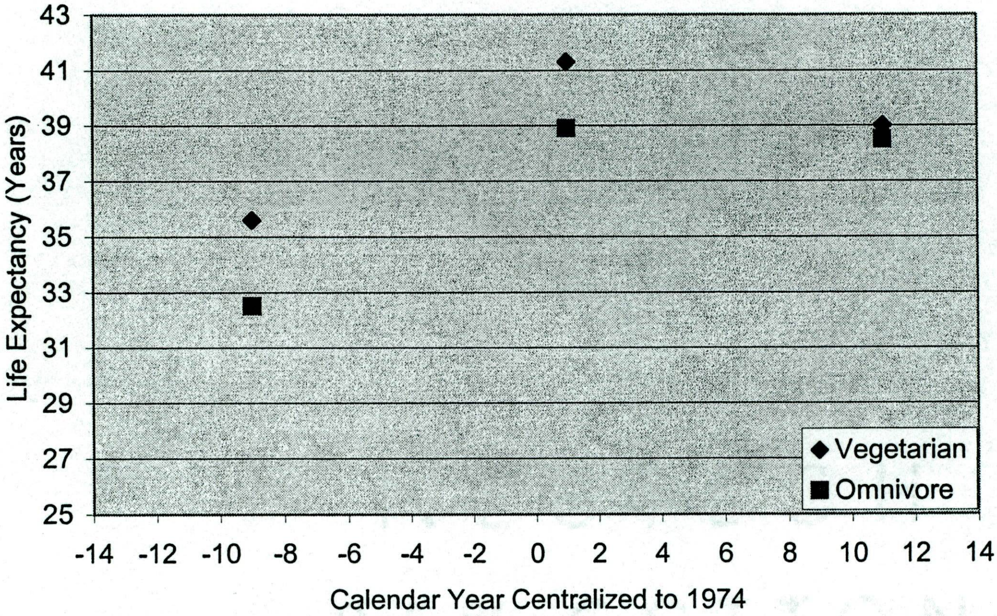

FIGURE 2. Comparison of change in life expectancy at age 50 by calendar year and diet status in males with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

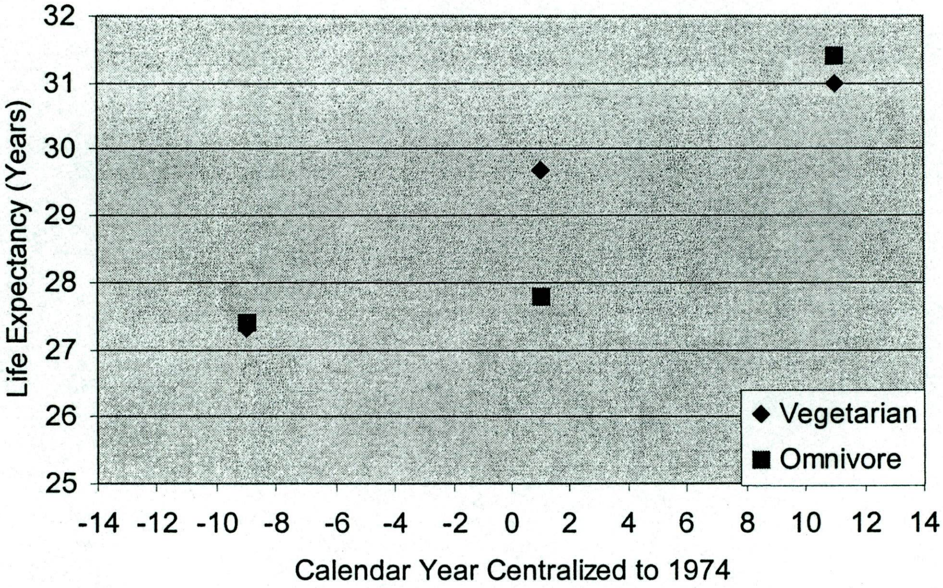

FIGURE 3. Comparison of change in life expectancy at age 50 at by calendar year and diet status in females with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

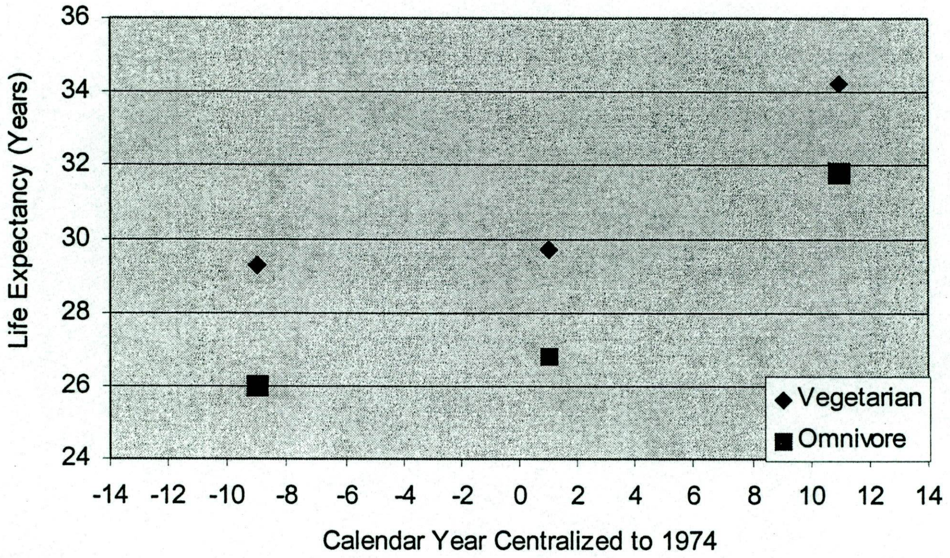

FIGURE 4. Comparison of change in life expectancy at age 50 by calendar year and diet status in males with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

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CHAPTER 5

SUMMARY AND CONCLUSIONS (PUBLISHABLE PAPER I and II)

A. Summary of Findings

1. *Publishable Paper I*

In study I, the study population included 38,237 never smoking Seventh-day Adventists with 10,329 deaths from all causes. There was a linear increase in life expectancy with secular time from 1960 to 1988 for all ages, although the trend was not always significant. This was true irrespective of type of diet, gender, and other lifestyle choices. The trend tended to be steeper in omnivores compared to vegetarians, and females as compared to males. The life expectancy advantage that was attributed to a vegetarian diet was 1-2 years in females up to 70 years of age for the calendar periods 1965-1969, 1975-1979, and 1980-1984, and 1-4 years in males up to 80 years of age for all calendar periods. This difference was statistically significant at most ages. Females had a higher life expectancy than males. The gender differences in life expectancy were much less in vegetarians compared to omnivores.

2. *Publishable Paper II*

In study II, the study population was comprised of 38,237 never smoking Seventh-day Adventists, with 2,646 deaths from coronary heart disease and 1,549 deaths from cancer. Life expectancy of subjects who died from heart disease or cancer at all ages increased with secular time from 1960 to1988 for both vegetarians and omnivores, although the linear trend was not always significant. The life expectancy advantage attributed to a vegetarian diet of females who died from heart disease was 0.5-2.0 years in all calendar periods. During the same calendar periods, males who died from heart disease had a life expectancy advantage of 2-4 years that was attributed to a vegetarian diet.

The life expectancy at all ages of vegetarian females who died from cancer was 1-2 years higher than that of omnivores in the calendar period 1970 to1979. The increase in life expectancy that was attributed to a vegetarian diet in males who died from cancer was 1-4 years. The life expectancy of females who died from heart disease was higher than that of males. The life expectancy of females who died from cancer approached or was slightly lower that of males. For the specific causes of death, the gender differences in life expectancy were less in vegetarians compared to omnivores.

B. Conclusions

The findings from the two studies of never smoking Seventh-day Adventists form the basis for the following conclusions:

- Life expectancy for both males and females increased with secular time from 1960 to 1988, irrespective of type of diet, cause of death and other lifestyle choices.
- The linear trend in life expectancy of subjects who died at most ages from all causes was statistically significant.
- The linear trend in life expectancy of subjects who died at most ages from specific causes (heart disease; all site-cancer) was strong but not statistically significant.
- The life expectancy of vegetarian females up to 70 years of age was 1-2 years higher than that of omnivores.

- The life expectancy of vegetarian males was 1-4 years higher than that of omnivores for all the calendar periods.
- Among subjects who died from heart disease, the life expectancy advantage that was attributed to a vegetarian diet was 0.5-2.0 years in females and 2-4 years in males.
- Among subjects who died from cancer, the life expectancy advantage that was attributed to a vegetarian diet was 1-2 years in females and 1-4 years in males.
- Vegetarians had 1-4 years greater life expectancy when compared to omnivores irrespective of gender and cause of death.
- Females, who died from all causes or from heart disease, had a higher life expectancy than males regardless of type of diet.
- Females who died from cancer had similar or lower life expectancy than males regardless of type of diet.
- The gender differences in life expectancy were much less in vegetarians compared to omnivores. This was true for subjects who died from all causes or who died from heart disease or cancer.
- A vegetarian diet does attribute to greater longevity, and this lifestyle decreases the gender gap in life expectancy, irrespective of cause of death.

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APPENDIX A

Additional Figures (Publishable Paper I)

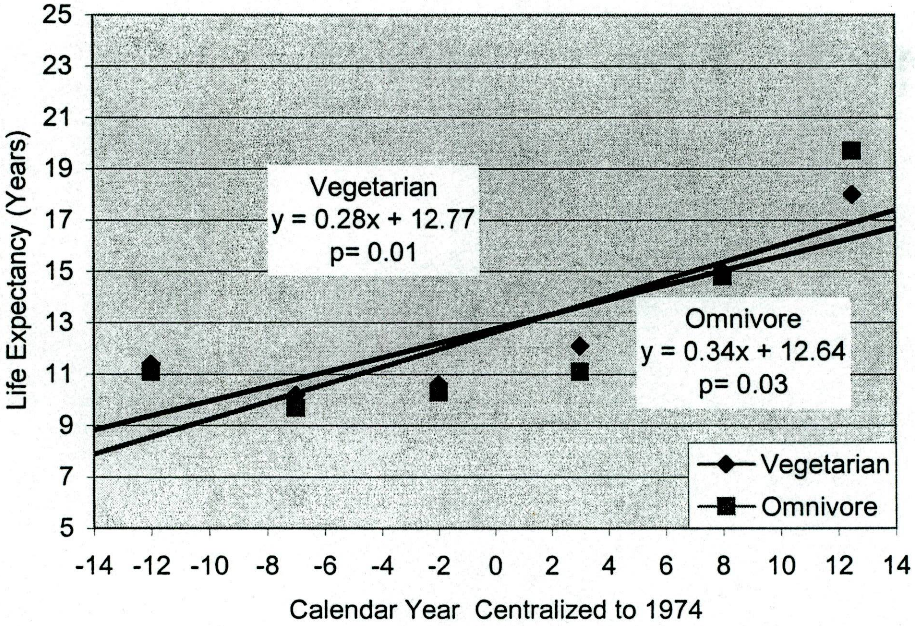


FIGURE 1. Comparison of change in life expectancy by calendar year and diet status in females with otherwise favorable lifestyle at age 30 in the Adventist Studies.

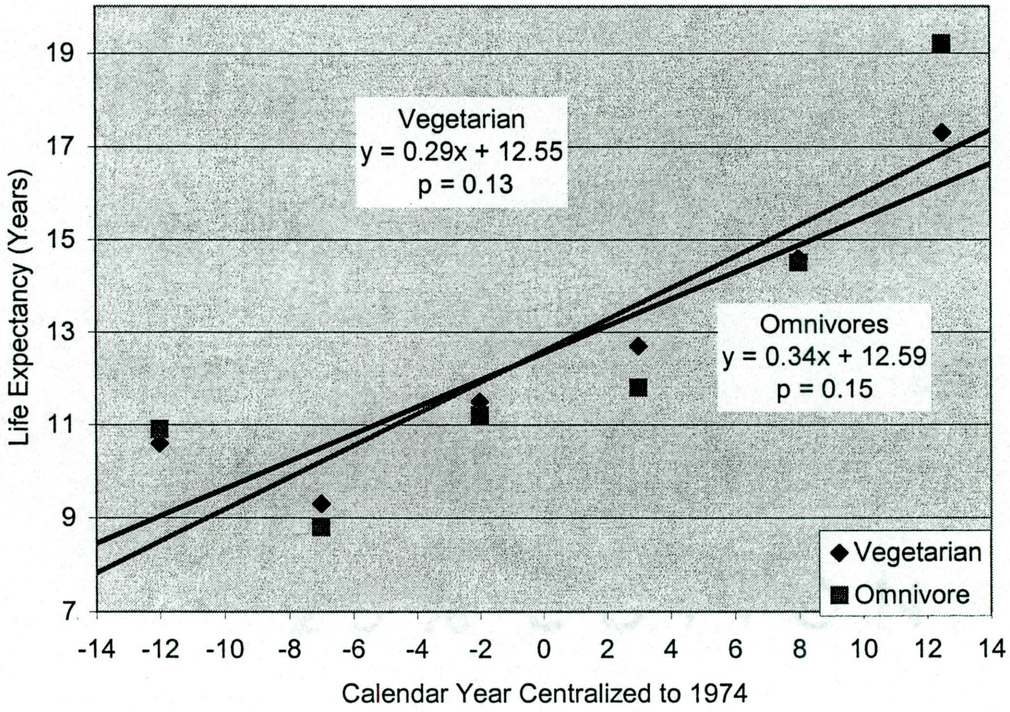


FIGURE 2. Comparison of change in life expectancy by calendar year and diet status in females with otherwise favorable lifestyle at age 80 in the Adventist Studies.

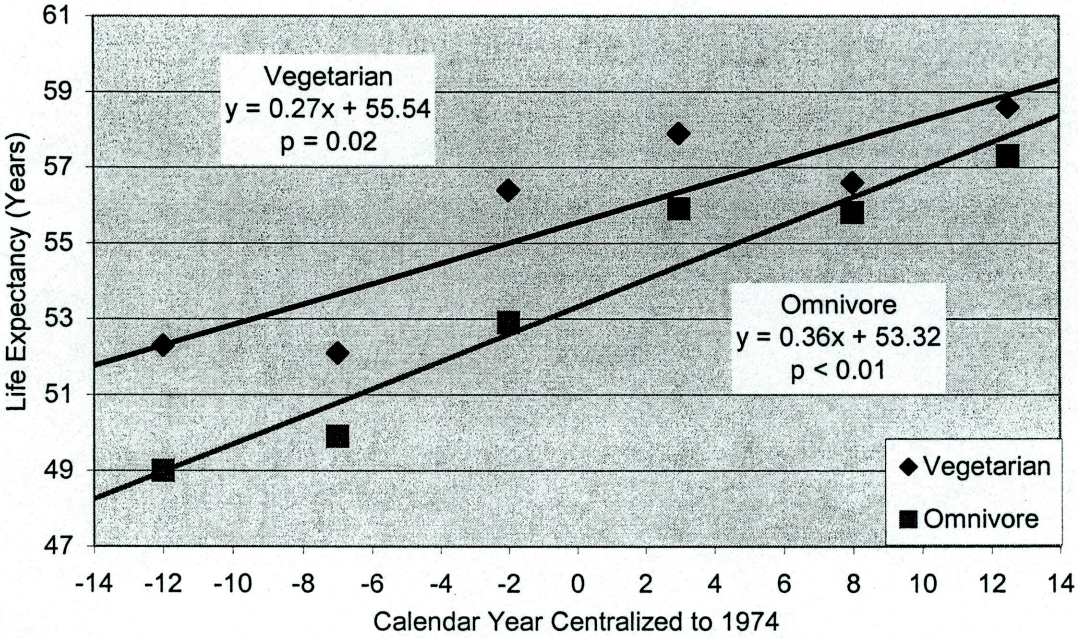
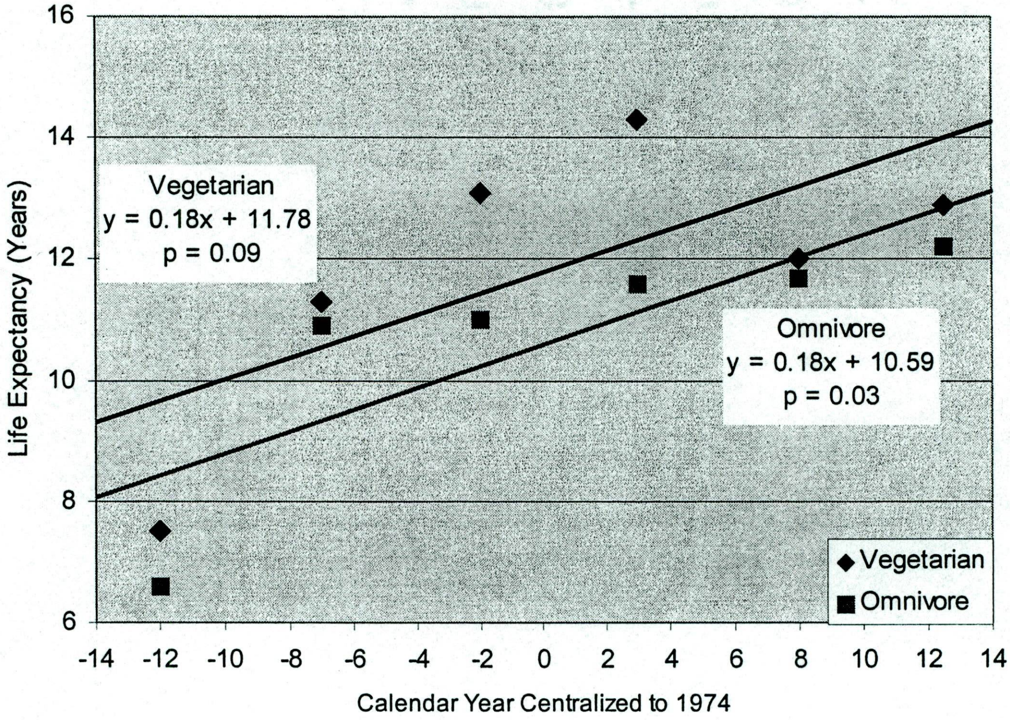


FIGURE 3. Comparison of change in life expectancy by calendar year and diet status in males with otherwise favorable lifestyle at age 30 in the Adventist Studies.



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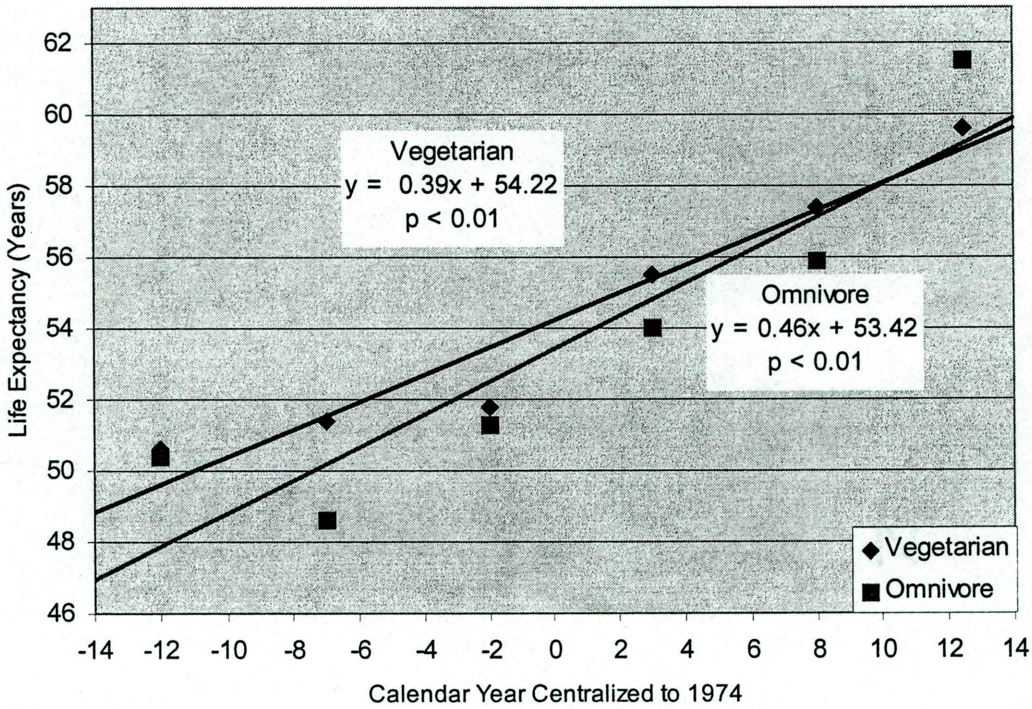

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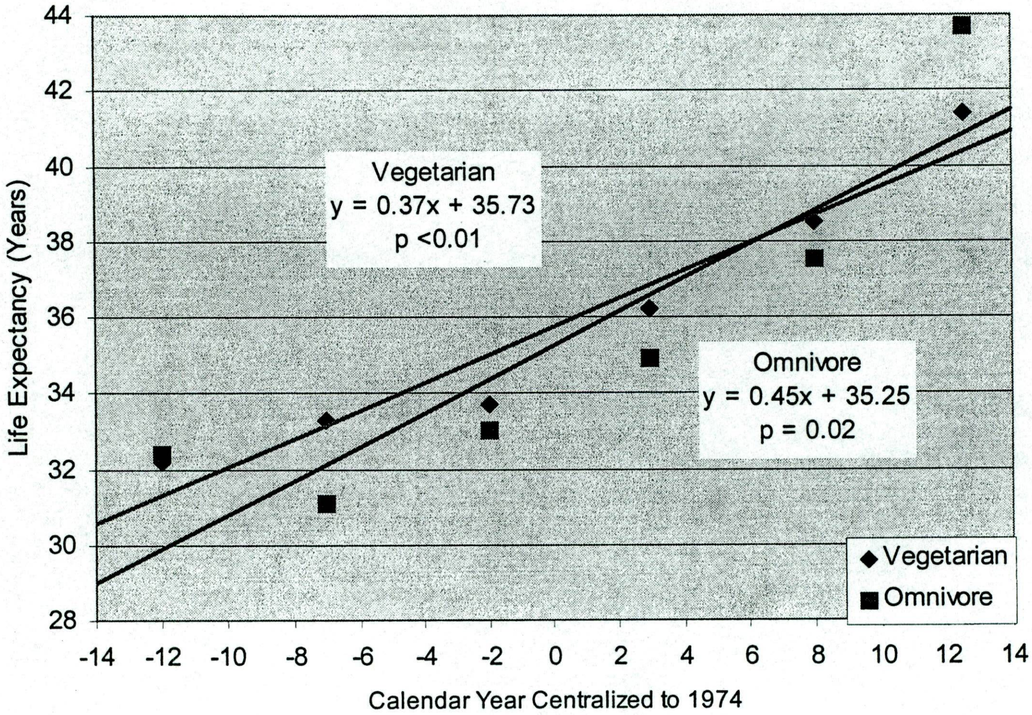

FIGURE 6. Comparison of change in life expectancy by calendar year and diet status in females with otherwise unfavorable lifestyle at age 50 in the Adventist Studies.

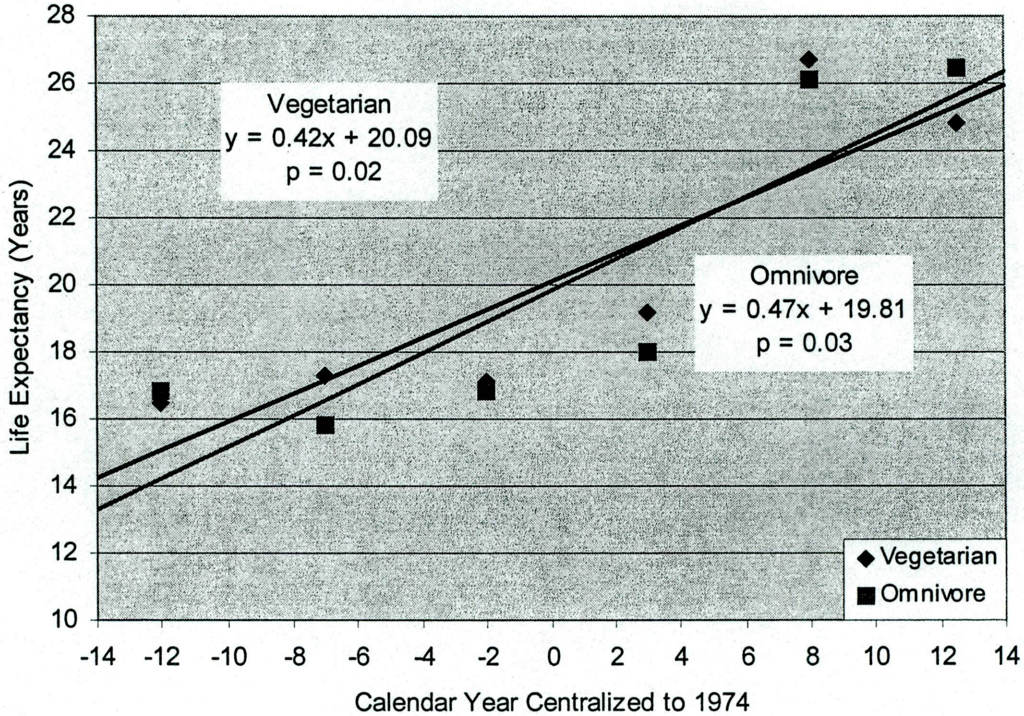

FIGURE 7. Comparison of change in life expectancy by calendar year and diet status in females with otherwise unfavorable lifestyle at age 70 in the Adventist Studies.

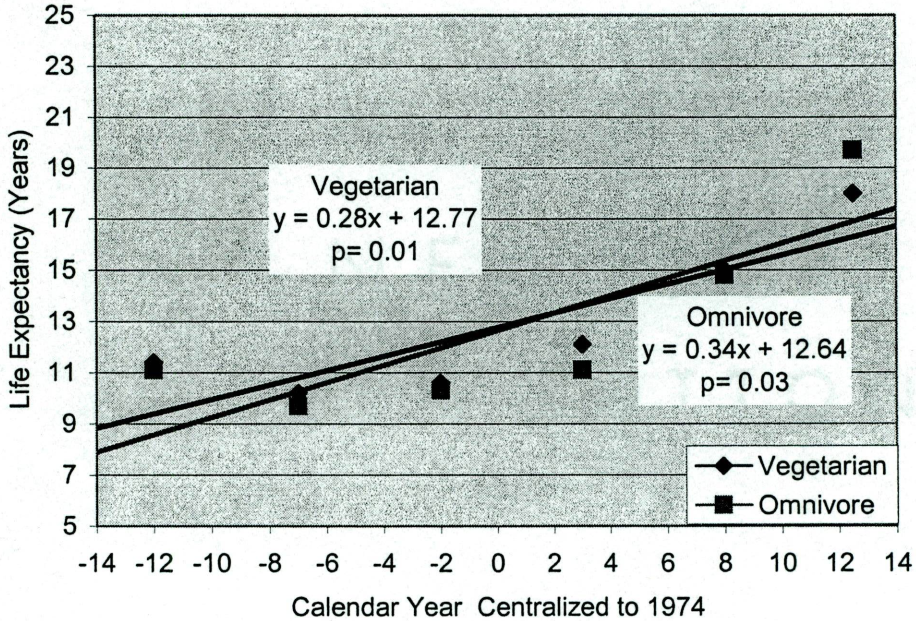

FIGURE 8. Comparison of change in life expectancy by calendar year and diet status in females with otherwise unfavorable lifestyle at age 80 in the Adventist Studies.

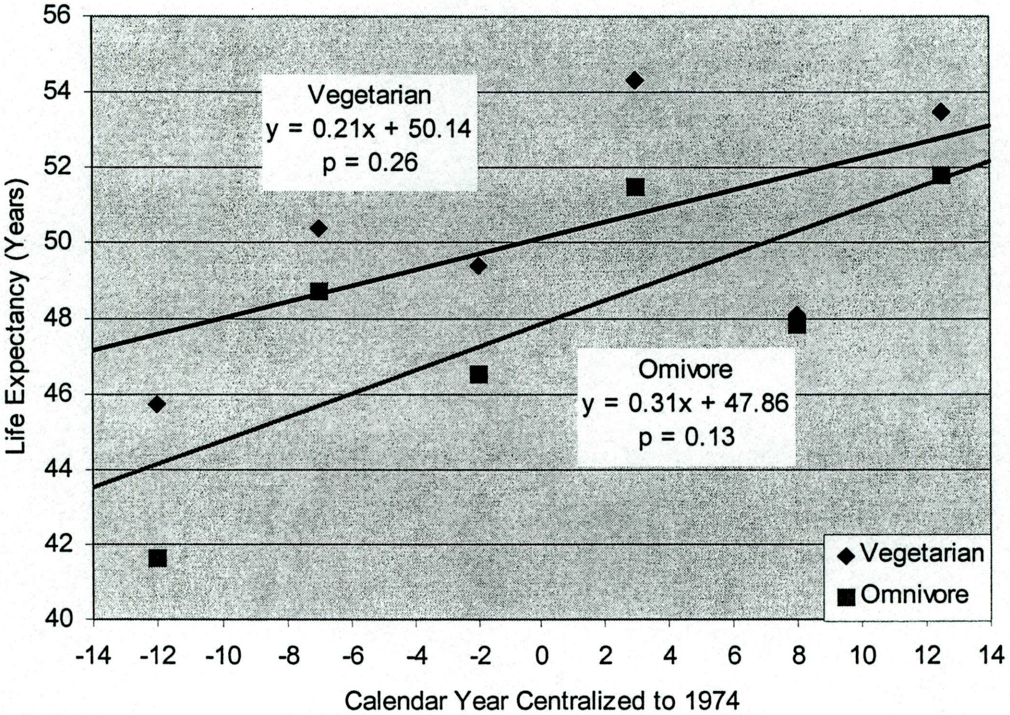

FIGURE 9. Comparison of change in life expectancy by calendar year and diet status in males with otherwise unfavorable lifestyle at age 30 in the Adventist Studies.

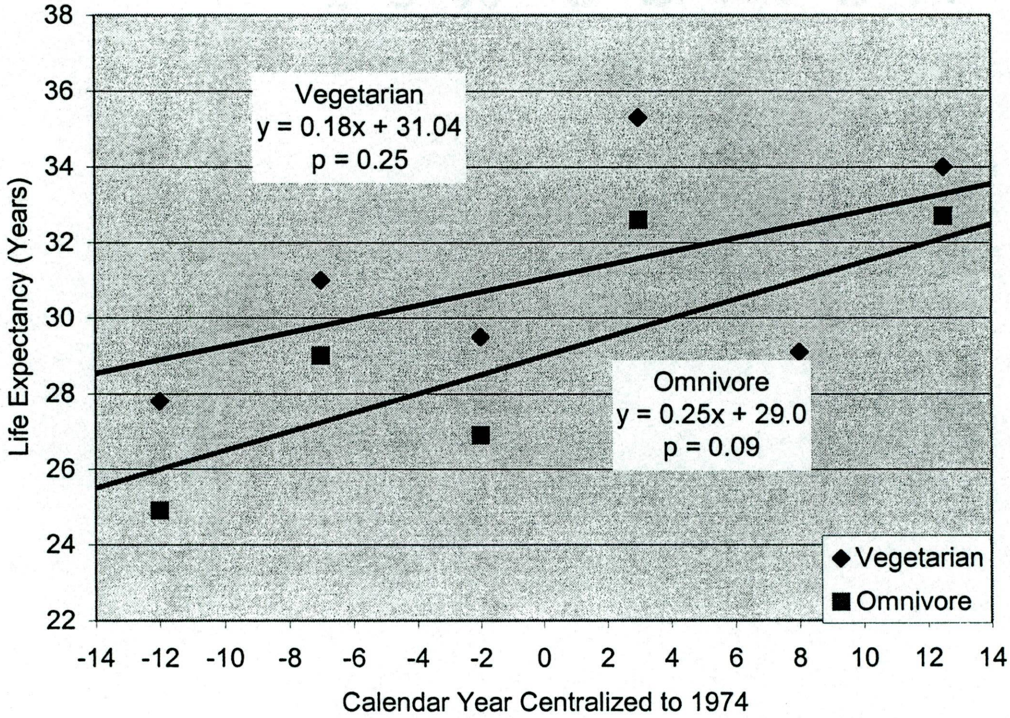

FIGURE 10. Comparison of change in life expectancy by calendar year and diet status in males with otherwise unfavorable lifestyle at age 50 in the Adventist studies.

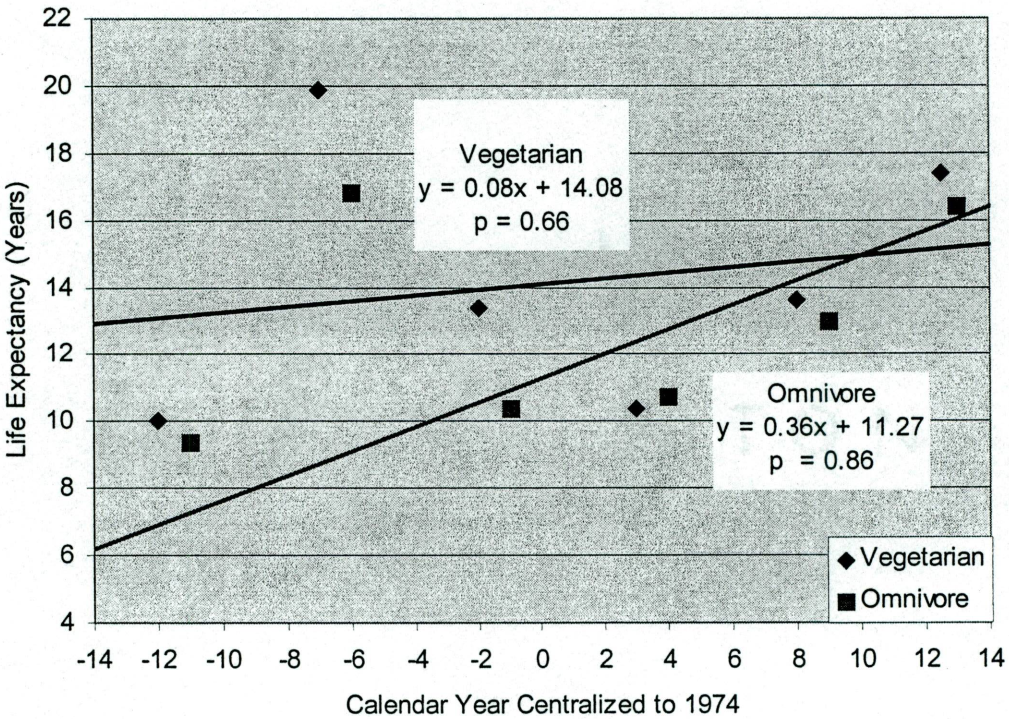

FIGURE 11. Comparison of change in life expectancy by calendar year and diet status in males with otherwise unfavorable lifestyle at age 70 in the Adventist Studies.

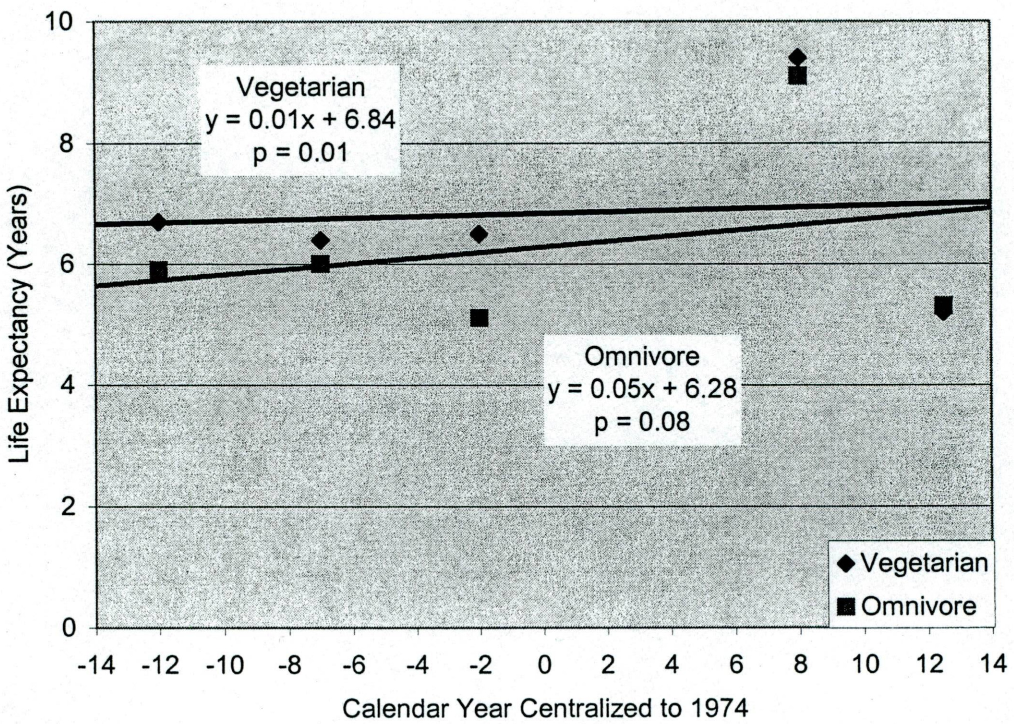

FIGURE 12. Comparison of change in life expectancy by calendar year and diet status in males with otherwise unfavorable lifestyle at age 80 in the Adventist Studies.

APPENDIX B

Additional Tables and Figures (Publishable Paper II)

TABLE 1. Univariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist studies for never-smoking females who eventually died from heart disease

Age		Calendar Year† 60-69	70-79	80-88	60-88
	Vegetarians	56.3	59.2	64.3	59.1
	Omnivores	55.1	57.6	63.4	57.6
30+	Difference	1.2	1.6	0.9	1.5
	95% CI	(-0.6, 2.9)	(0.2, 3.0)	(-1.6, 3.3)	(0.4, 2.4)
	p-values	0.19	0.03	0.49	<0.01
	Vegetarians	36.9	39.3	44.4	39.3
	Omnivores	35.3	37.8	43.7	37.9
50+	Difference	1.6	1.5	0.7	1.4
	95% CI	(-0.1, 3.3)	(0.1, 2.9)	(-1.7, 3.2)	(0.5, 2.4)
	p-values	0.06	0.04	0.55	<0.01
	Vegetarians	15.6	19.2	20.8	18.0
	Omnivores	13.3	16.4	19.4	16.1
70+	Difference	2.4	2.9	1.4	1.9
	95% CI	(0.1, 4.6)	(0.5, 5.3)	(-1.6, 4.3)	(0.5, 3.3)
	p-values	0.04	0.02	0.36	<0.01
	Vegetarians	8.4	13.6	13.5	11.3
	Omnivores	6.2	10.2	12.5	9.5
80+	Difference	2.2	3.4	1.0	1.8
	95% CI	(0.2, 4.3)	(1.1, 5.7)	(-2.0, 4.1)	(0.4, 3.2)
	p-values	0.03	<0.01	0.98	0.01

* Model includes diet status and product terms between diet and attained age.
† Separate analyses were performed for each calendar year period.

TABLE 2. Univariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist studies for never-smoking males who eventually died from heart disease

Age		Calendar Year†			
		60-69	**70-79**	**80-88**	**60-88**
	Vegetarians	53.4	56.4	58.7	55.5
	Omnivores	49.5	53.7	57.5	53.4
30+	**Difference**	3.8	2.7	1.2	2.1
	95% CI	(1.3, 6.5)	(0.2, 5.2)	(-1.7, 4.1)	(0.6, 3.6)
	p-values	<0.01	0.03	0.74	<0.01
	Vegetarians	33.6	36.5	38.7	35.7
	Omnivores	29.8	33.9	37.7	33.7
50+	**Difference**	3.8	2.6	1.0	2.0
	95% CI	(1.3, 6.4)	(0.1, 5.2)	(-1.9, 3.9)	(0.5, 3.5)
	p-values	<0.01	0.03	0.49	<0.01
	Vegetarians	15.6	19.2	20.8	18.0
	Omnivores	13.3	16.4	19.4	16.1
70+	**Difference**	2.4	2.9	1.4	1.9
	95% CI	(0.1, 4.6)	(0.5, 5.3)	(-1.6, 4.3)	(0.5, 3.3)
	p-values	0.04	0.02	0.36	<0.01
	Vegetarians	8.4	13.6	13.5	11.3
	Omnivores	6.2	10.2	12.5	9.5
80+	**Difference**	2.2	3.4	1.0	1.8
	95% CI	(0.2, 4.3)	(1.1, 5.7)	(-2.0, 4.1)	(0.4, 3.2)
	p-values	0.03	<0.01	0.98	0.01

* Model includes diet status and product terms between diet and attained age.

† Separate analyses were performed for each calendar year period.

TABLE 3. Univariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist studies for never-smoking females who eventually died from cancer

Age		Calendar Year† 60-69	70-79	80-88	60-88
	Vegetarians	44.8	46.0	48.0	46.8
	Omnivores	44.4	44.1	48.5	45.8
30+	Difference	0.4	1.9	-0.5	1.0
	95% CI	(-3.4, 4.1)	(-1.5, 5.3)	(-4.5, 3.4)	(-1.1, 2.9)
	p-values	0.85	0.28	0.79	0.37
	Vegetarians	26.3	28.0	29.6	28.4
	Omnivores	26.6	26.0	31.4	27.9
50+	Difference	-0.3	2.0	-1.8	0.5
	95% CI	(-3.6, 3.0)	(-0.8, 4.8)	(-1.0, 5.3)	(-1.3, 2.2)
	p-values	0.85	0.17	0.32	0.59
	Vegetarians	12.3	13.3	15.2	14.2
	Omnivores	13.0	12.6	17.9	14.5
70+	Difference	-0.7	0.7	-2.7	-0.3
	95% CI	(-3.6, 2.0)	(-1.9, 3.4)	(-6.1, 0.8)	(-1.9, 1.2)
	p-values	0.97	0.59	0.13	0.67
	Vegetarians	7.4	8.7	9.9	9.3
	Omnivores	8.0	7.1	14.2	9.9
80+	Difference	-0.6	1.6	-4.3	-0.6
	95% CI	(-3.7, 2.5)	(-1.4, 4.7)	(-8.4, -0.3)	(-2.2, 1.0)
	p-values	0.69	0.98	0.04	0.46

* Model includes diet status and product terms between diet and attained age.

† Separate analyses were performed for each calendar year period.

TABLE 4. Univariate* comparison of life expectancy by diet status for different calendar years and ages in the Adventist studies for non-smoking males who eventually died from cancer

Age		Calendar Year†			
		60-69	70-79	80-88	60-88
	Vegetarians	48.9	48.5	51.8	49.2
	Omnivores	46.1	48.5	47.8	47.3
30+	Difference	2.8	0.0	4.0	1.9
	95% CI	(-1.7, 7.2)	(-4.2, 4.2)	(-0.3, 8.3)	(-0.4, 4.2)
	p-values	0.20	0.99	0.07	0.11
	Vegetarians	29.3	29.9	32.4	19.9
	Omnivores	26.4	29.5	29.8	28.3
50+	Difference	2.9	0.4	2.7	1.6
	95% CI	(-1.4, 7.3)	(-3.4, 4.2)	(-1.2, 6.5)	(-0.5, 3.7)
	p-values	0.19	0.83	0.18	0.13
	Vegetarians	13.6	14.2	15.6	13.8
	Omnivores	10.4	14.9	12.4	12.7
70+	Difference	3.2	-0.7	3.2	1.1
	95% CI	(-0.4, 6.9)	(-4.5, 3.1)	(-0.4, 6.8)	(-0.8, 3.1)
	p-values	0.08	0.70	0.08	0.26
	Vegetarians	8.4	9.3	10.9	8.7
	Omnivores	6.6	8.4	7.2	7.8
80+	Difference	1.8	0.9	3.7	0.9
	95% CI	(-1.5, 5.0)	(-2.9, 4.85)	(0.2, 7.6)	(-01.1, 2.9)
	p-values	0.29	0.63	0.7	0.36

* Model includes diet status and product terms between diet and attained age.

† Separate analyses were performed for each calendar year period.

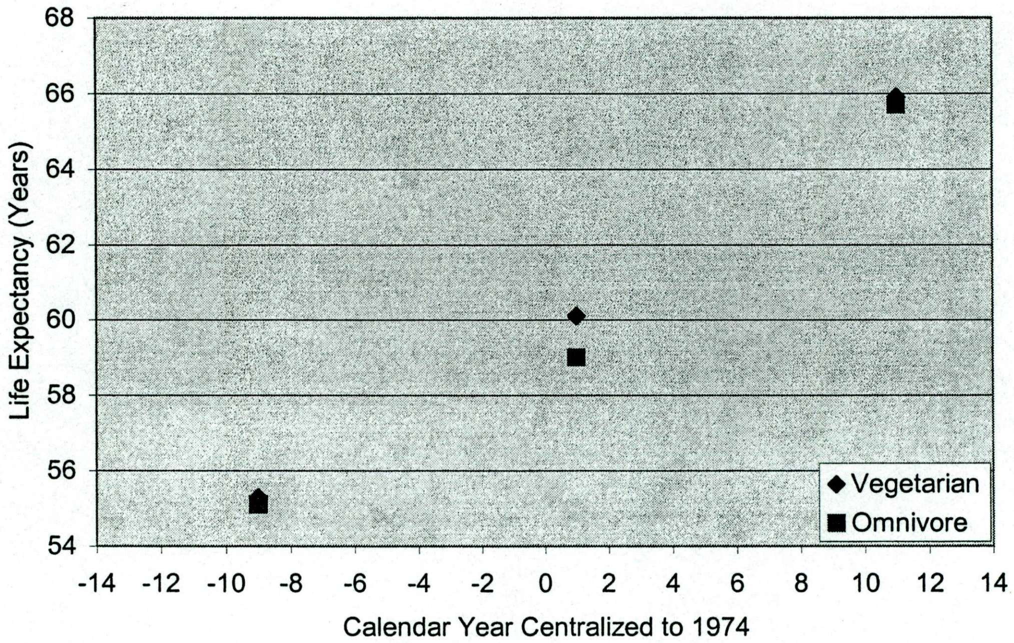

FIGURE 1. Comparison of change in life expectancy at age 30 by calendar year and diet status in females with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

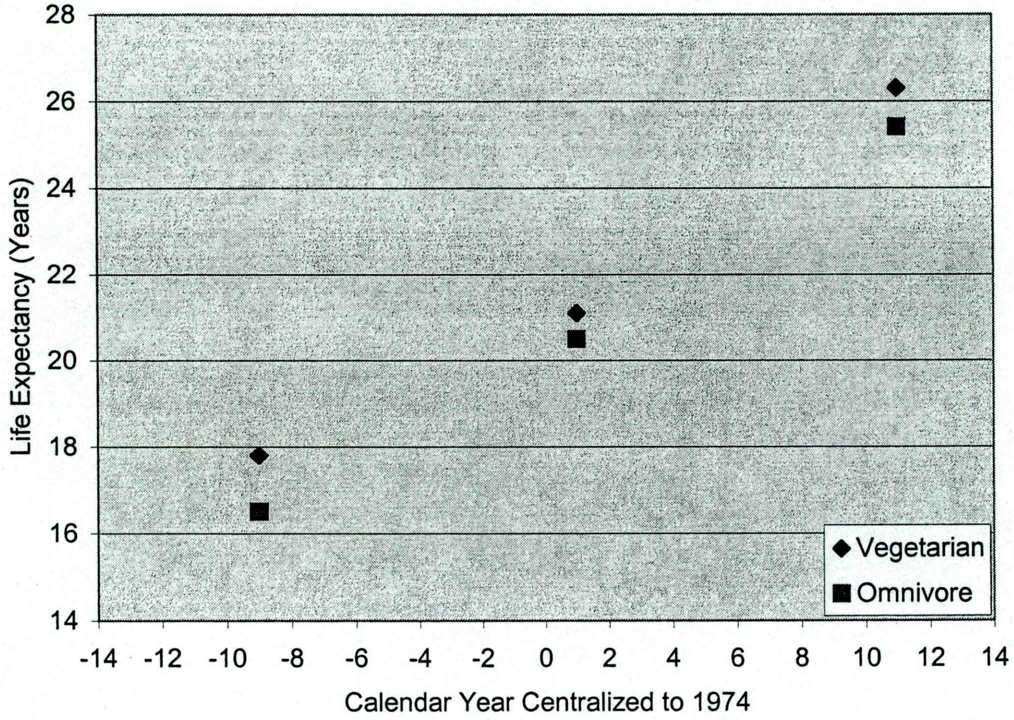

FIGURE 2. Comparison of change in life expectancy at age 70 by calendar year and diet status in females with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

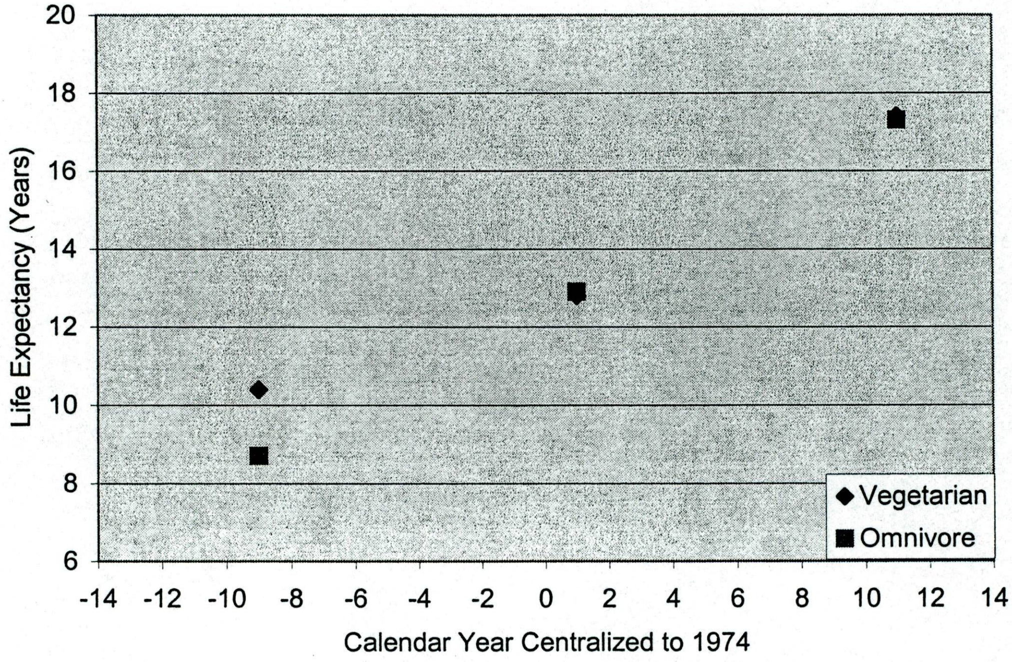

FIGURE 3. Comparison of life expectancy at age 80 by calendar year and diet status in females with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

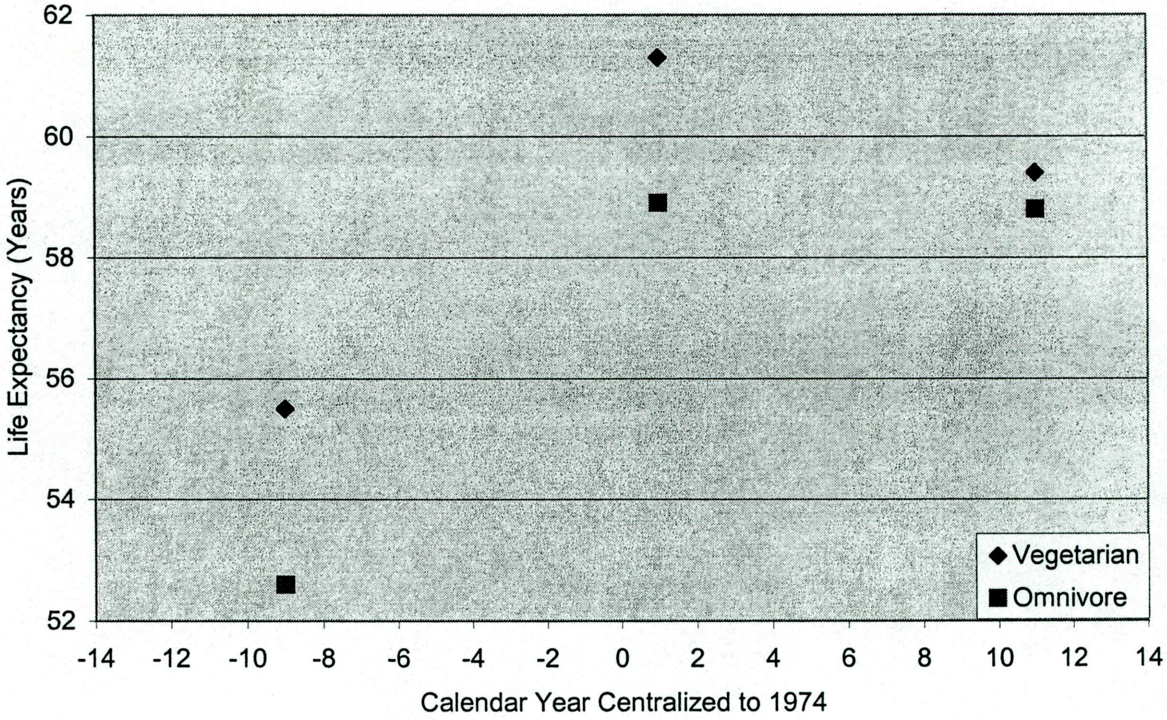

FIGURE 4. Comparison of change in life expectancy by age 30 by calendar year and diet status in males with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

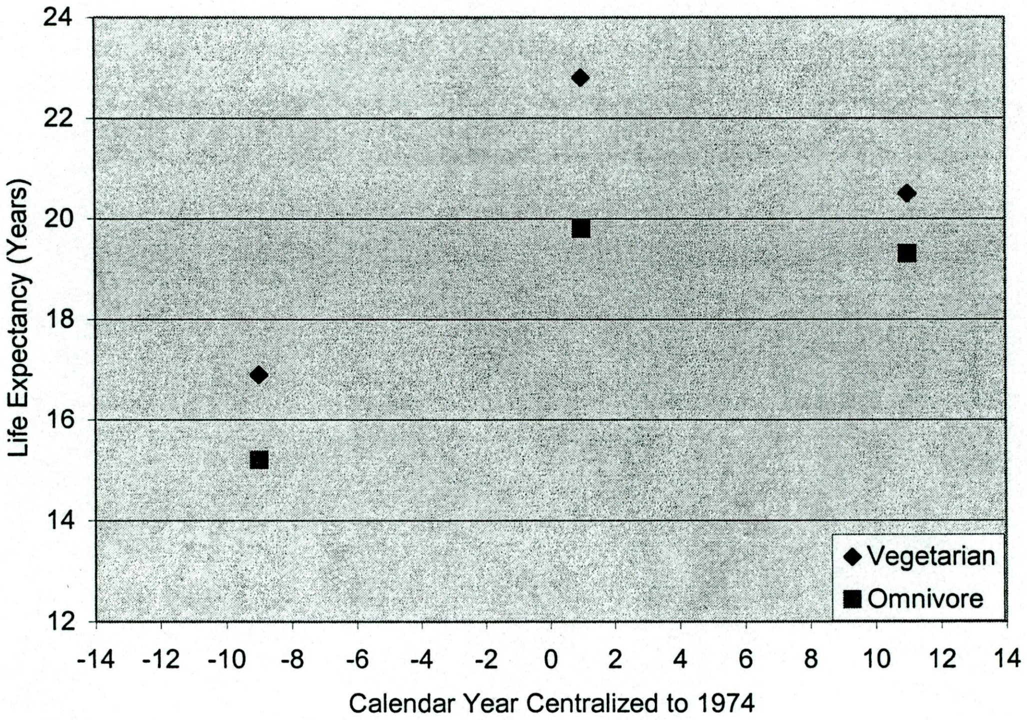

FIGURE 5. Comparison of change in life expectancy at age 70 by calendar year and diet status in males with otherwise favorable lifestyles who died from heart disease in the Adventist Studies.

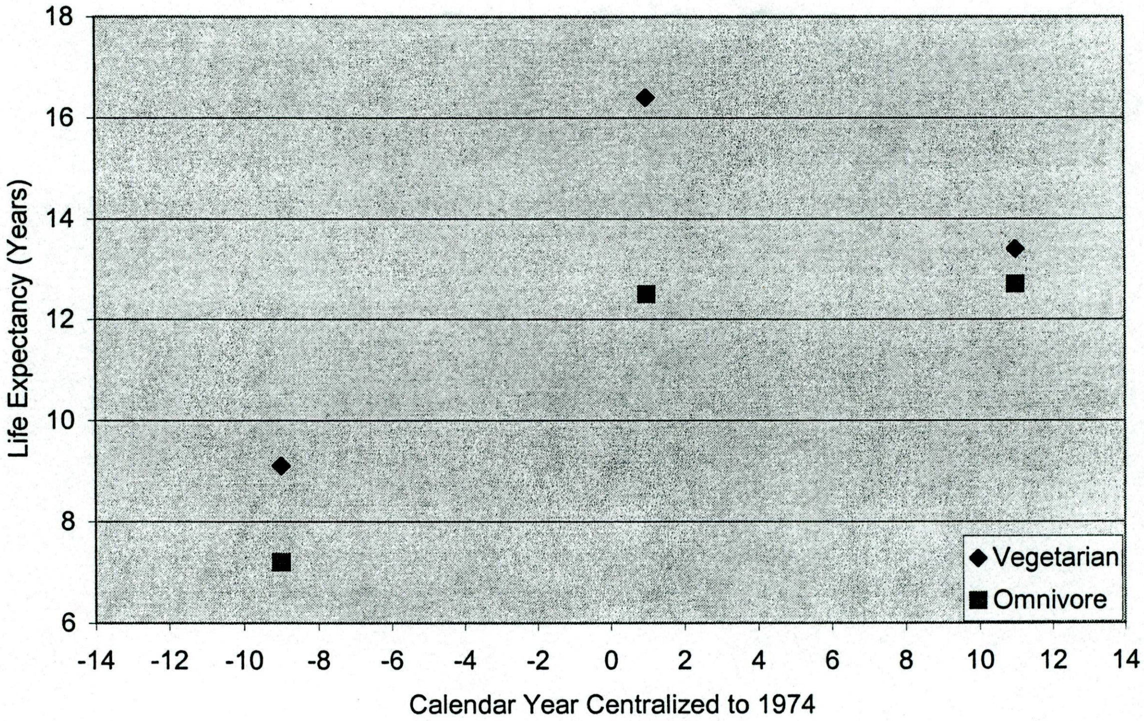

FIGURE 6. Comparison of life expectancy at age 80 by calendar year and diet status in males with otherwise favorable lifestyles who died of heart disease in the Adventist Studies.

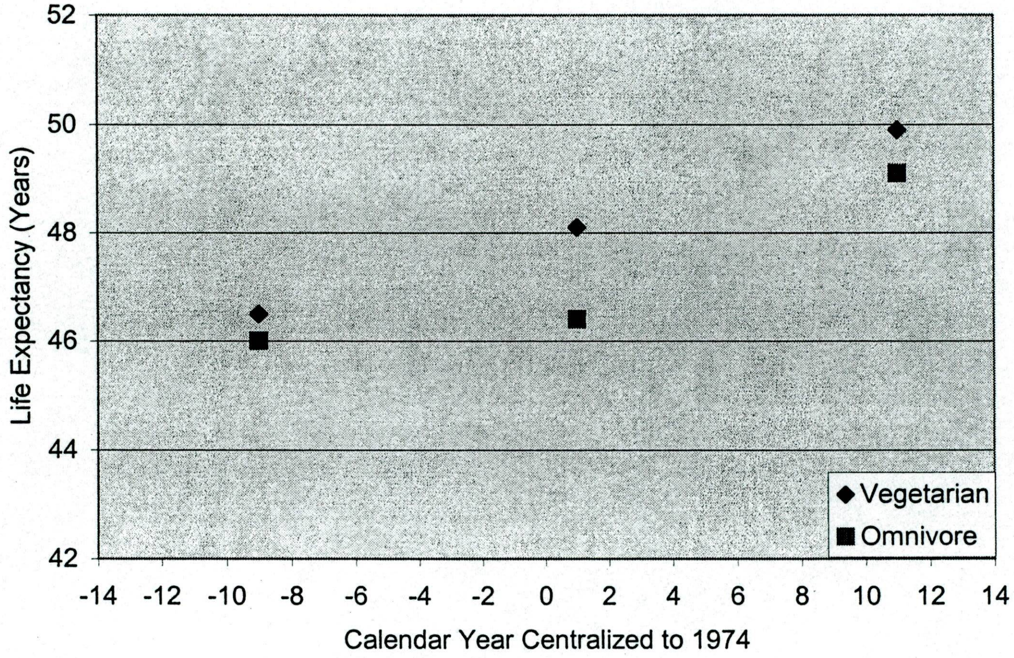

FIGURE 7. Comparison of change in life expectancy at age 30 by calendar year and diet status in females with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

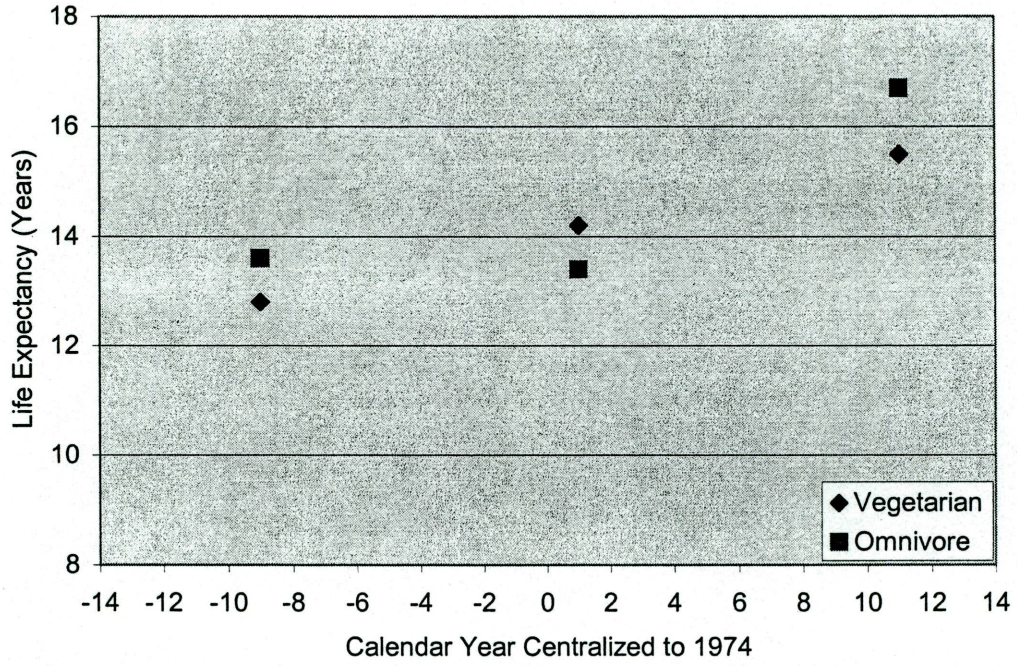

FIGURE 8. Comparison of change in life expectancy at age 70 by calendar year and diet status in females with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

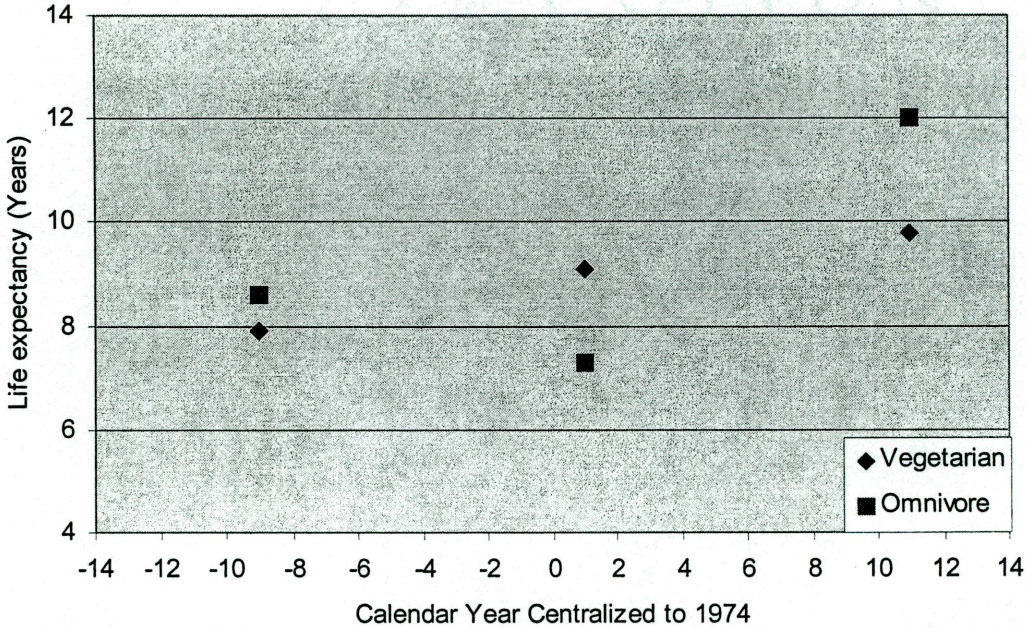

FIGURE 9. Comparison of change in life expectancy at age 80 by calendar year and diet status in females with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

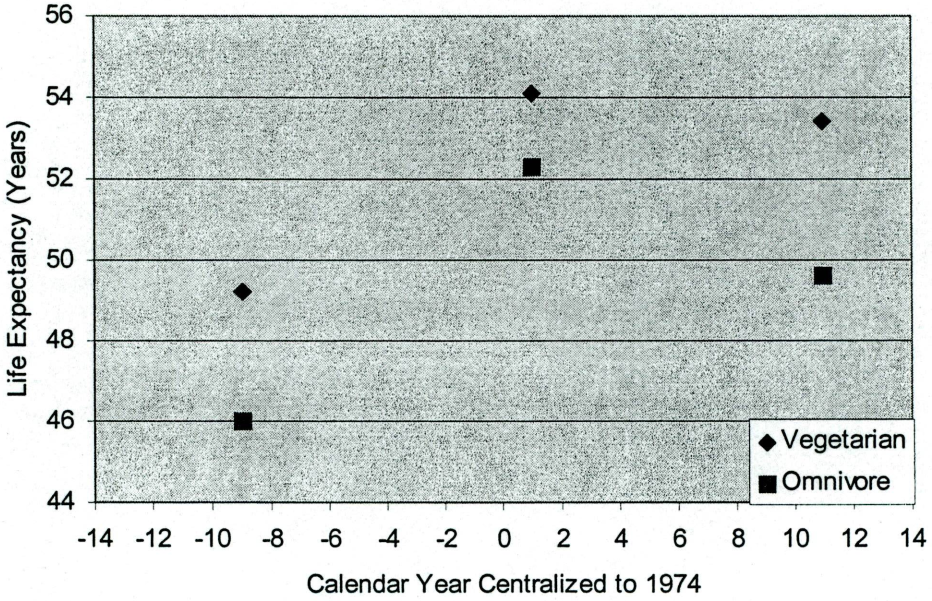

FIGURE 10 . Comparison of change in life expectancy at age 30 by calendar year and diet status in males with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

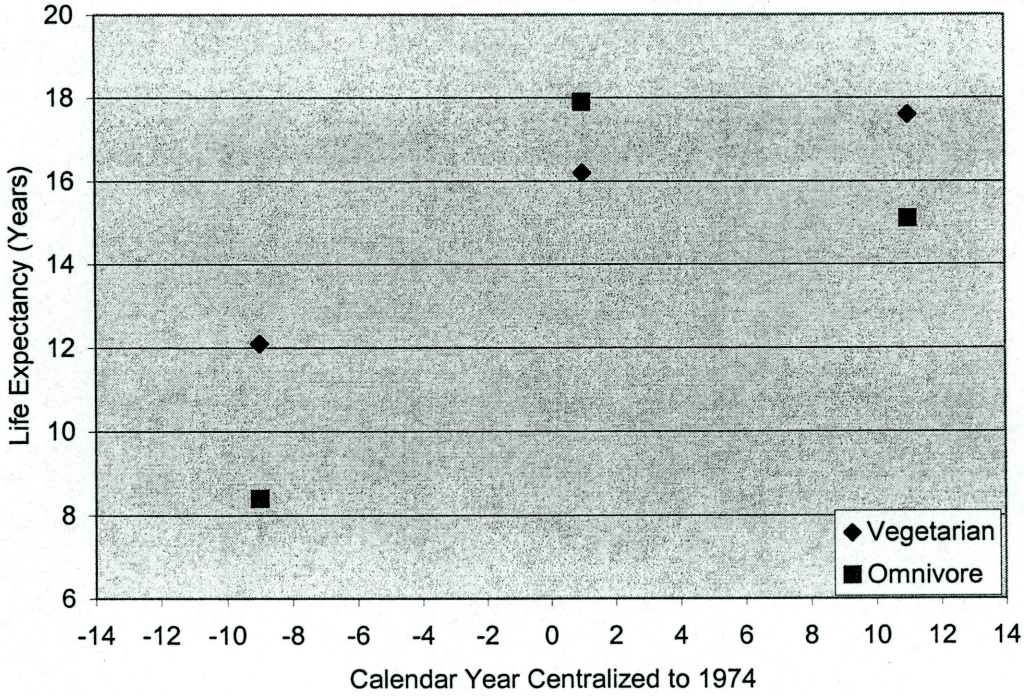

FIGURE 11. Comparison of change in life expectancy at age 70 by calendar year and diet status in males with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

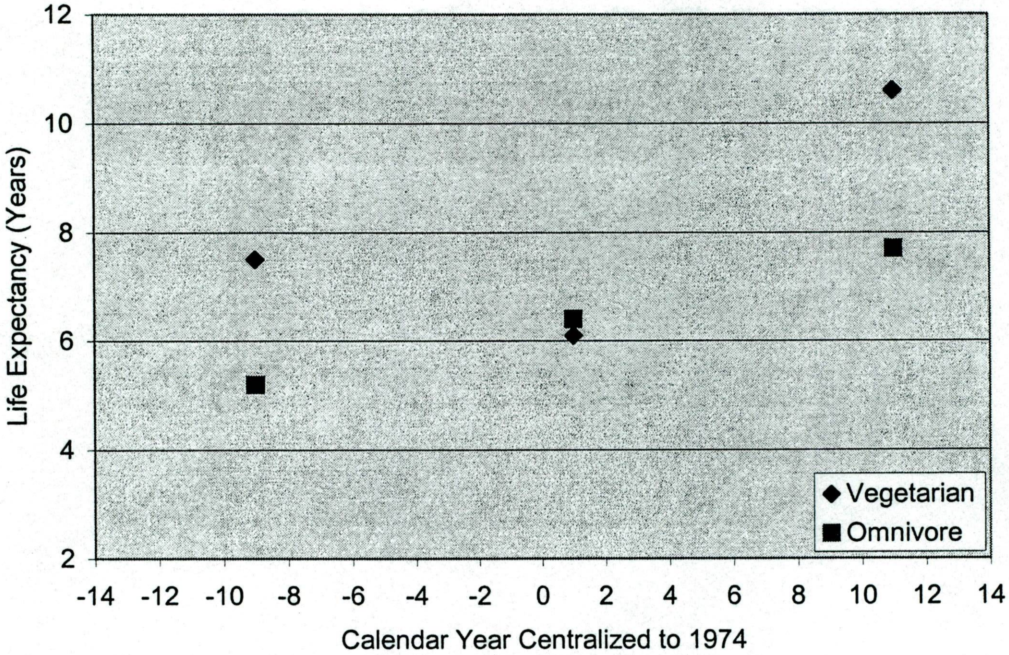

FIGURE 12. Comparison of change in life expectancy at age 80 by calendar year and diet status in males with otherwise favorable lifestyles who died from cancer in the Adventist Studies.

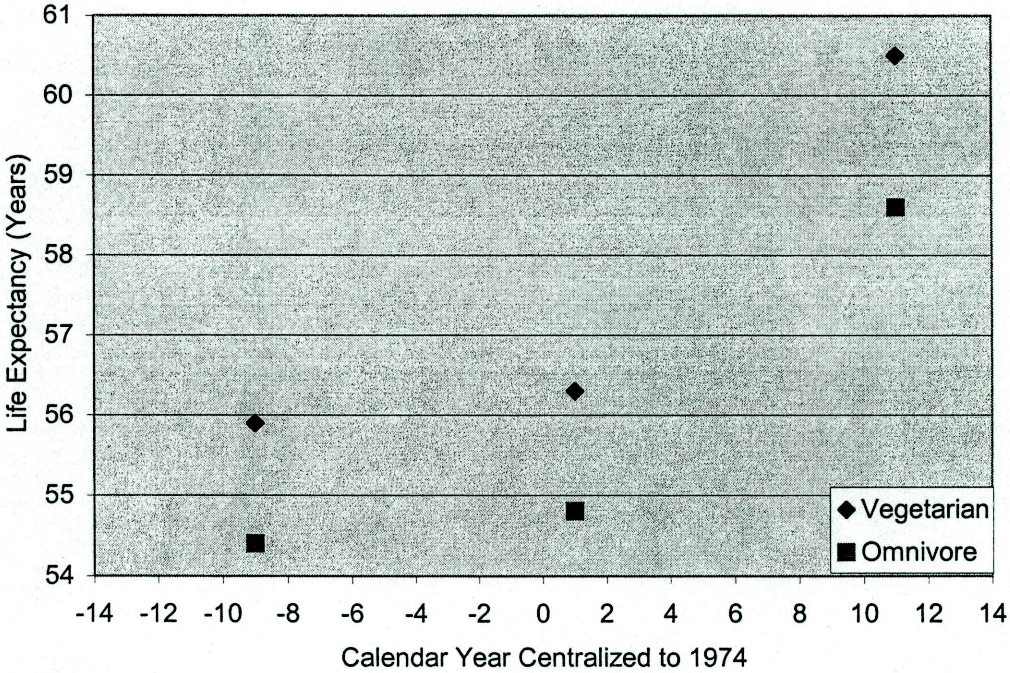

FIGURE 13. Comparison of change in life expectancy at age 30 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

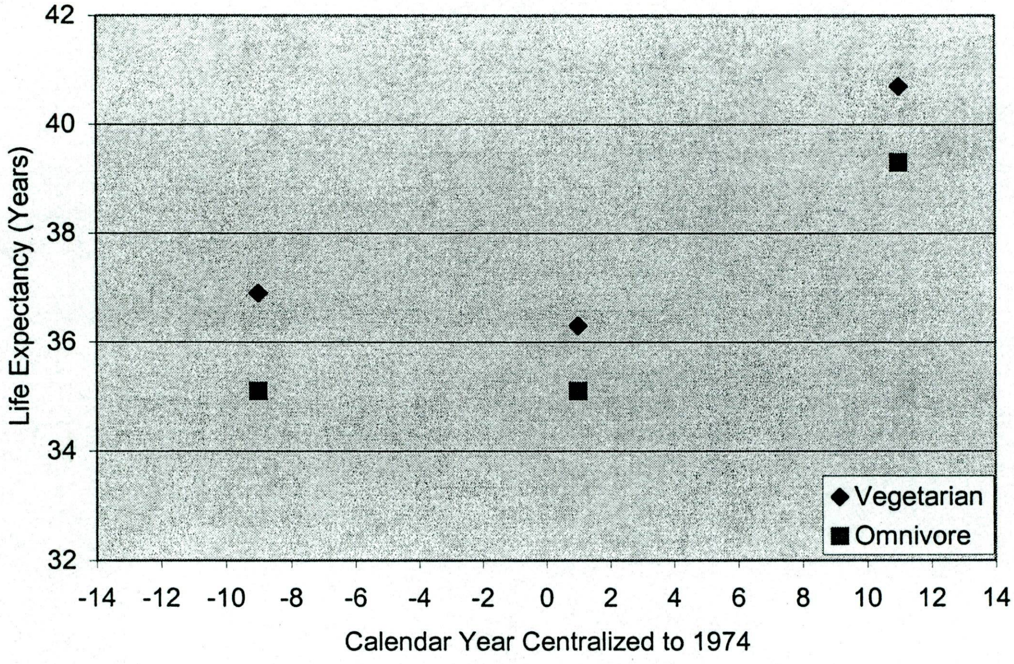

FIGURE 14. Comparison of change in life expectancy at age 50 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

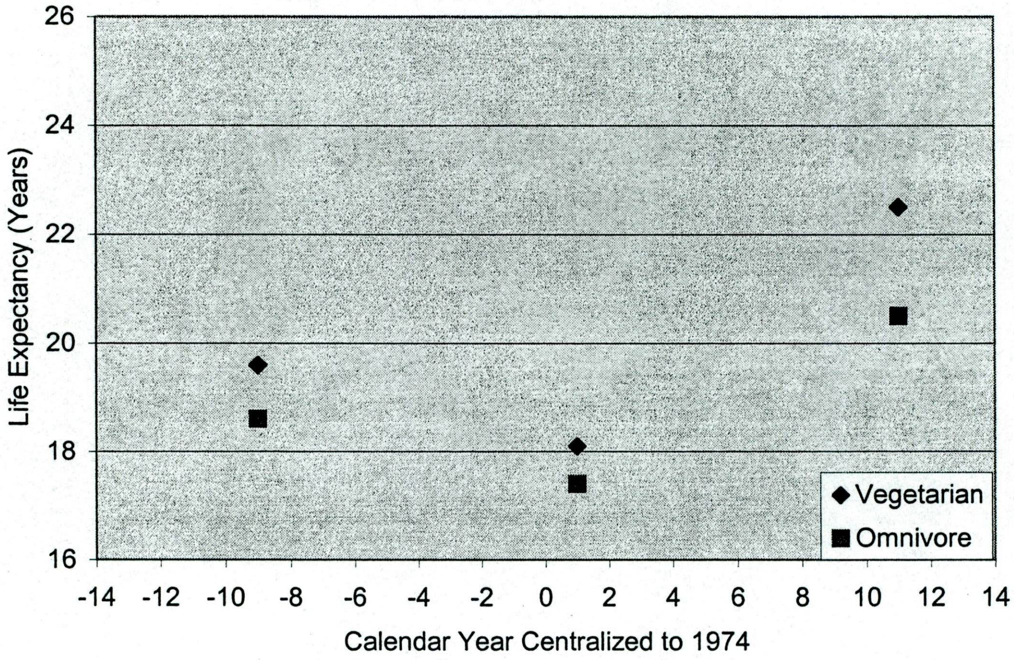

FIGURE 15. Comparison of change in life expectancy at age 70 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

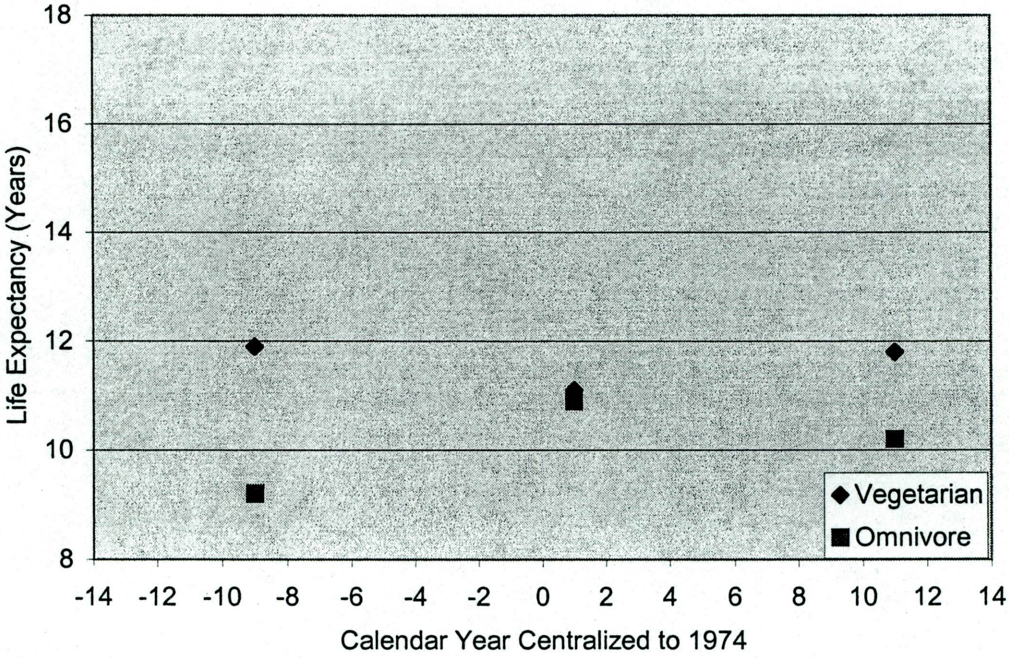

FIGURE 16. Comparison of change in life expectancy at age 80 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

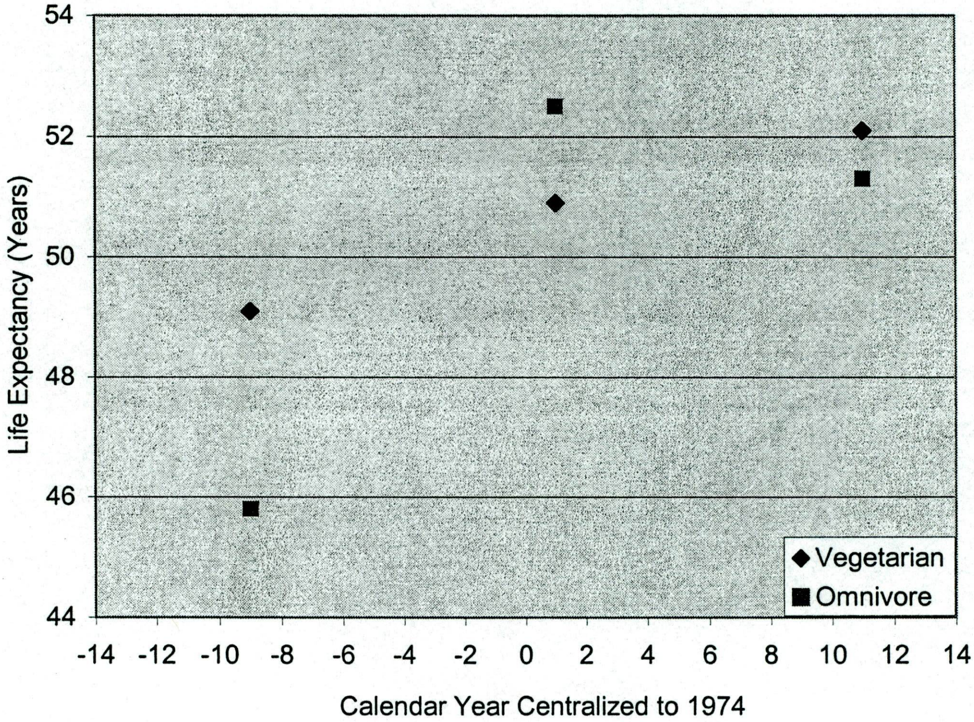

FIGURE 17. Comparison of life expectancy at age 30 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

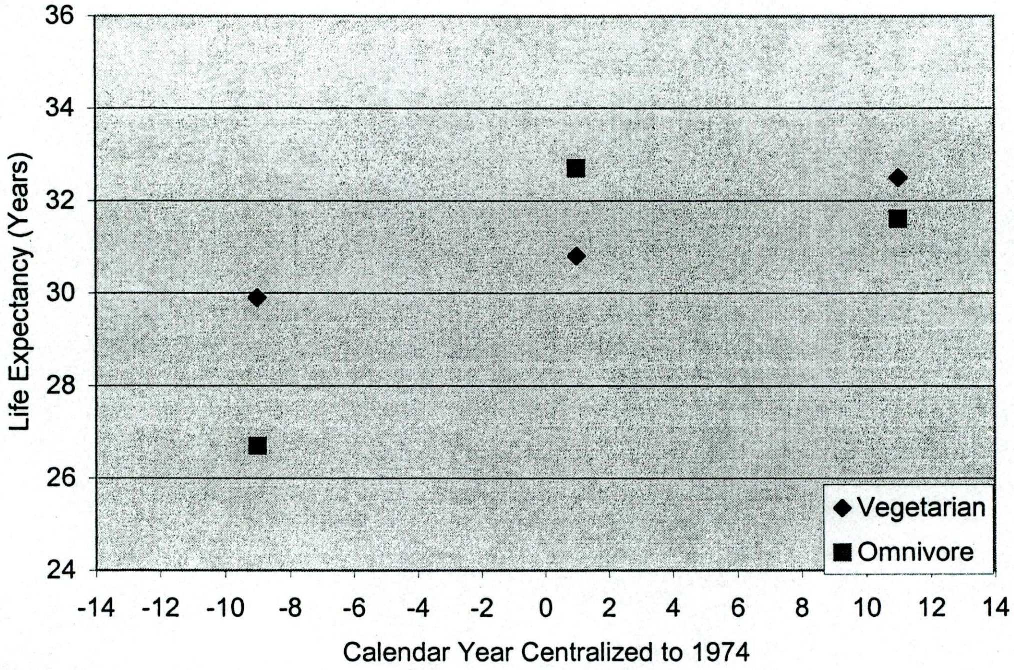

FIGURE 18. Comparison of life expectancy at age 50 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

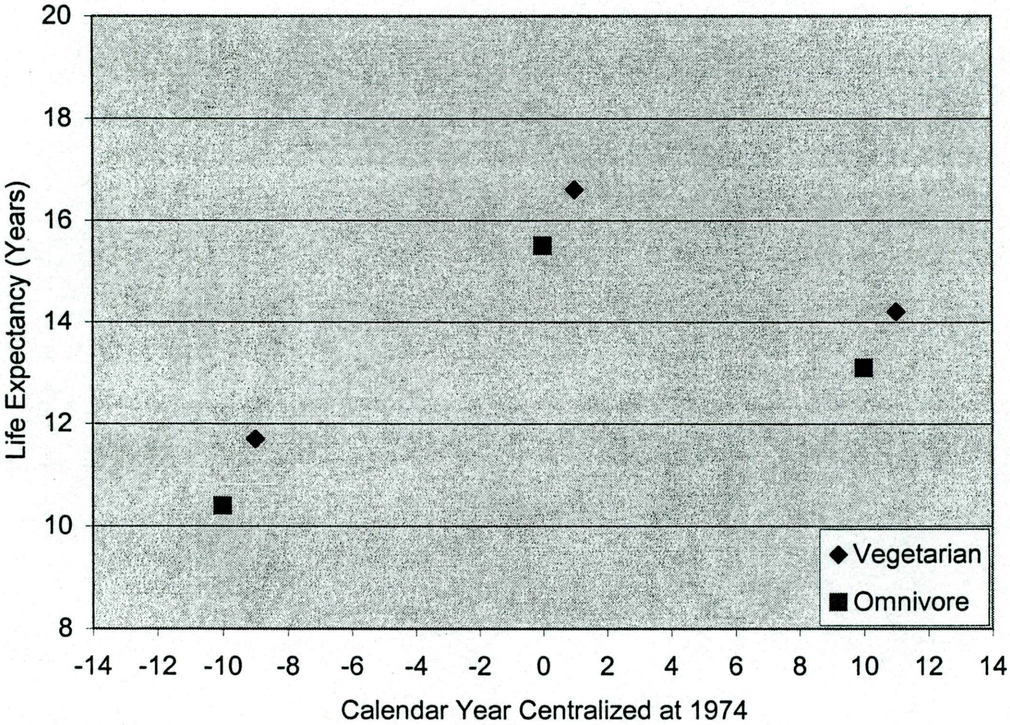

FIGURE 19. Comparison of life expectancy at age 70 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

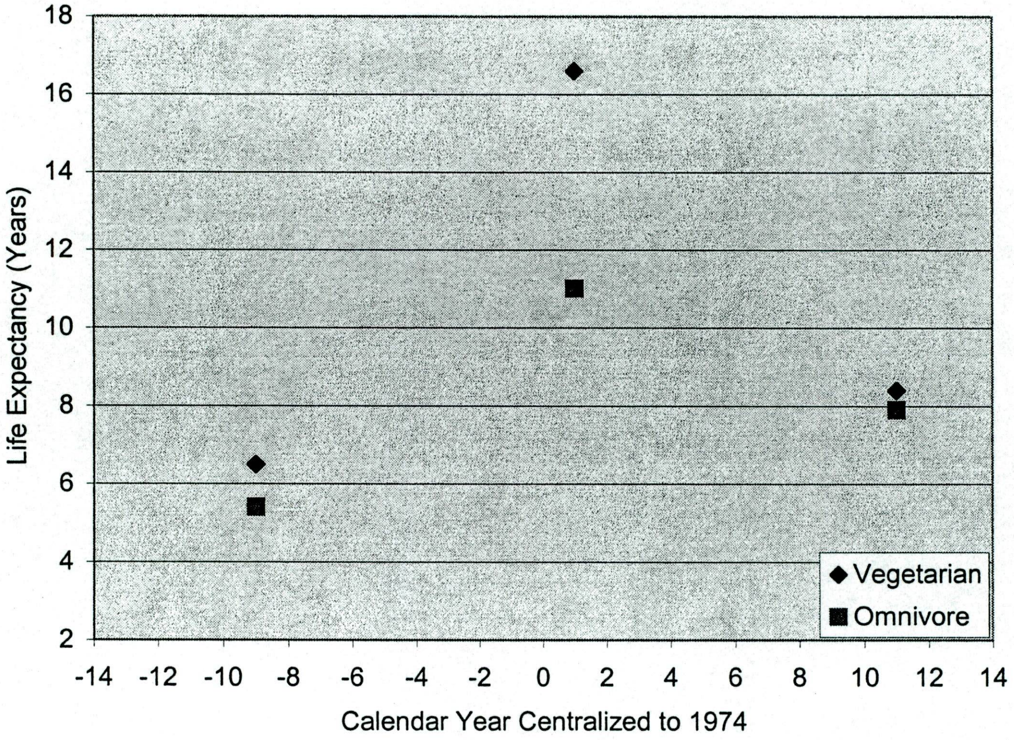

FIGURE 20. Comparison of life expectancy at age 80 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from heart disease in the Adventist Studies.

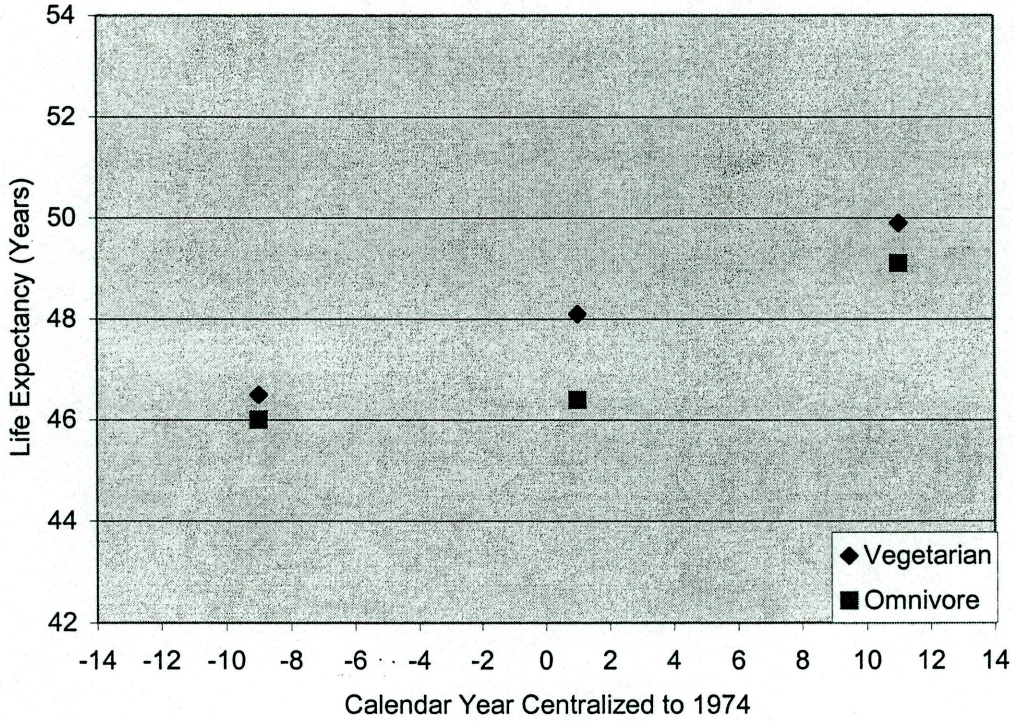

FIGURE 21. Comparison of change in life expectancy at age 30 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

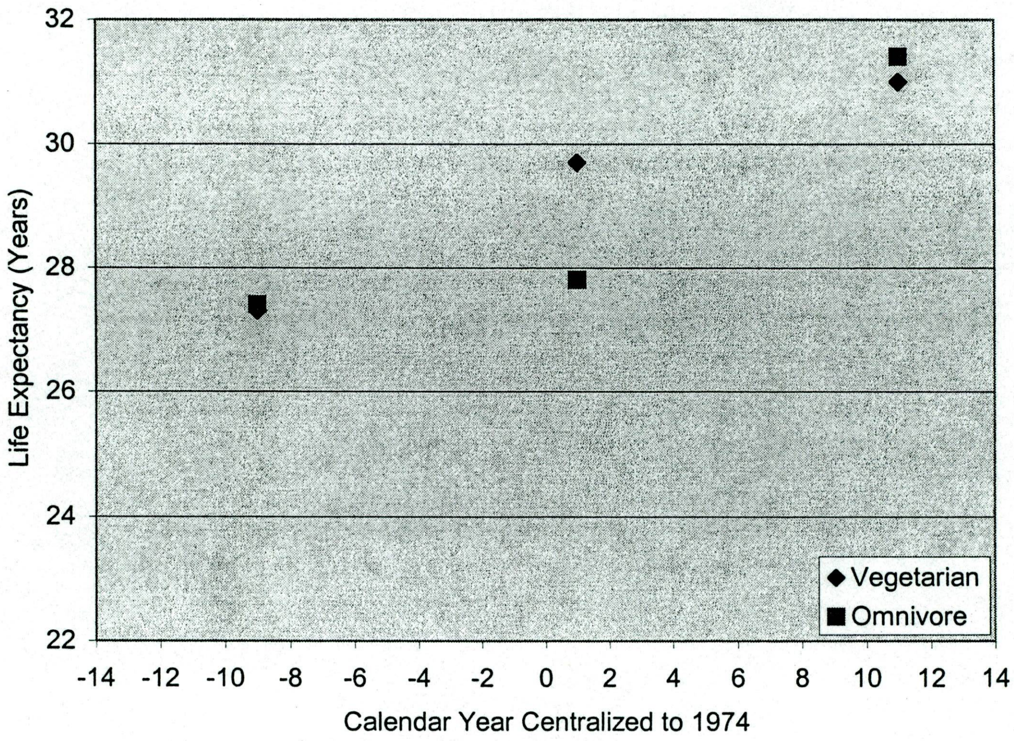

FIGURE 22. Comparison of change in life expectancy at age 50 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

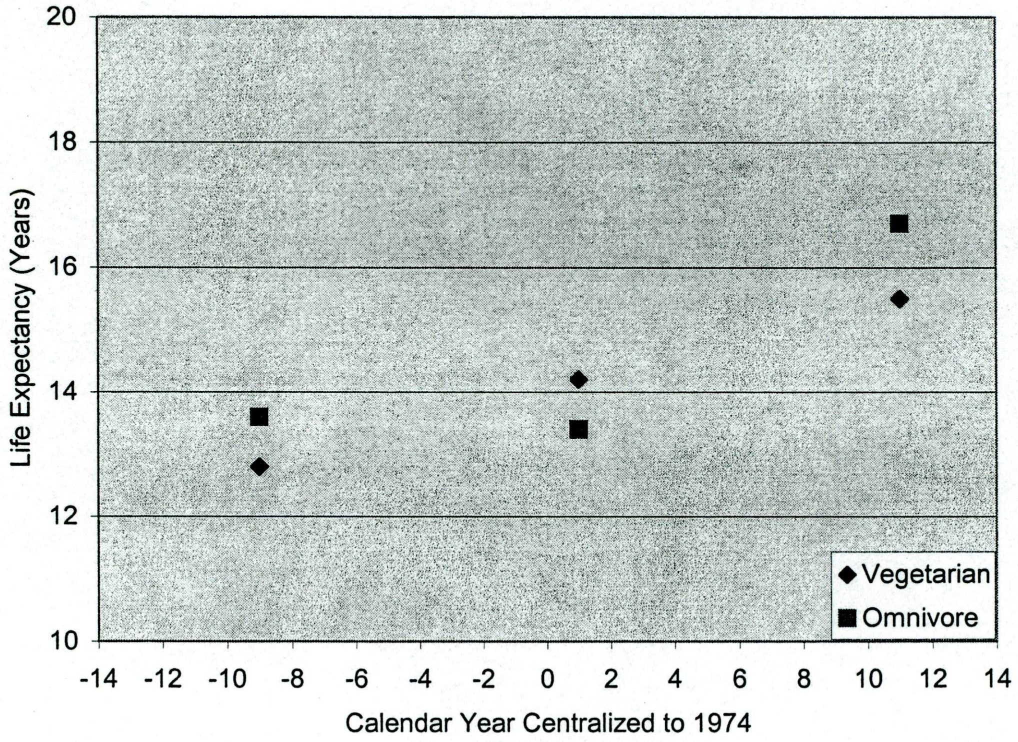

FIGURE 23. Comparison of change in life expectancy at age 70 by calendar year and diet status in females with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

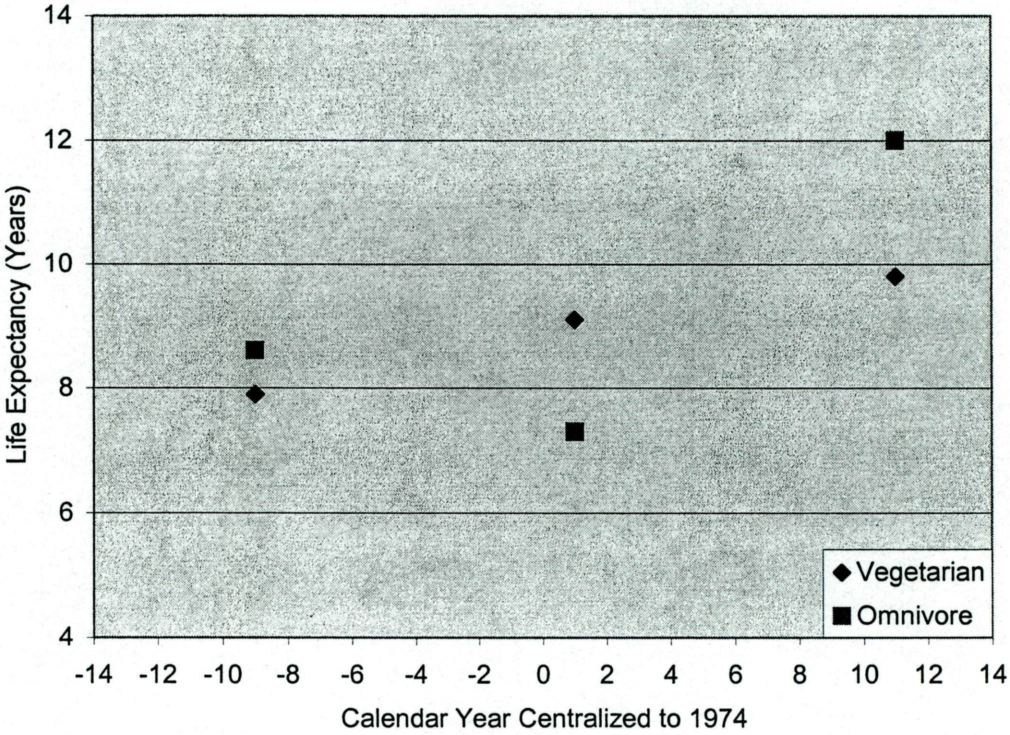

FIGURE 24. Comparison of change in life expectancy at age 80 in females with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

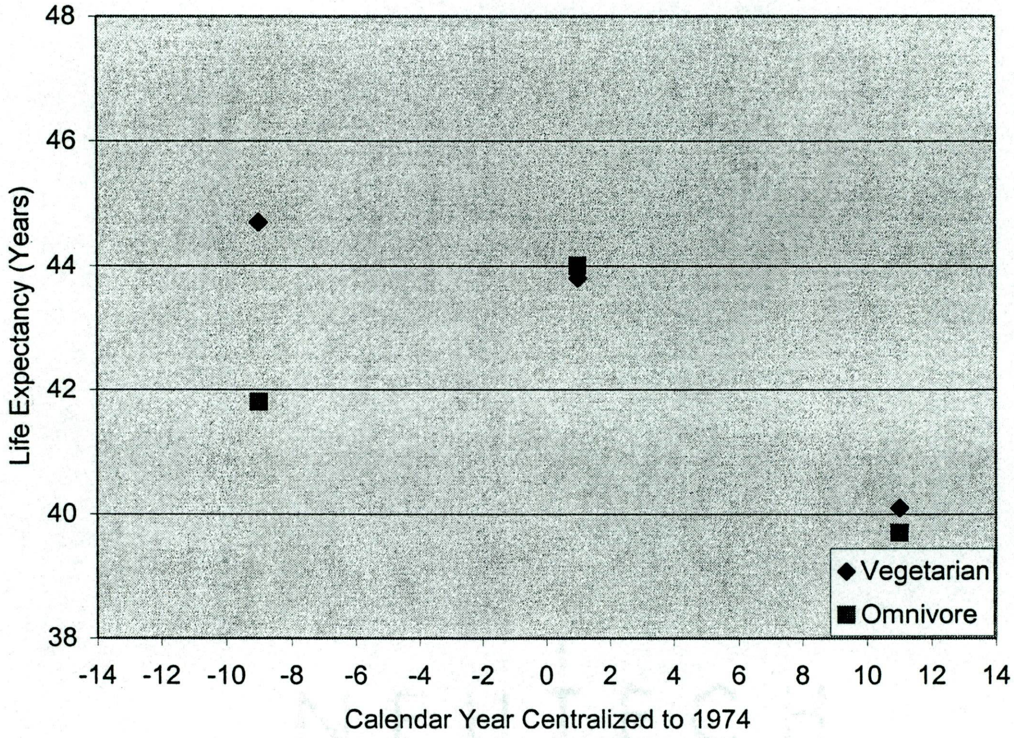

FIGURE 25. Comparison of change in life expectancy at age 30 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

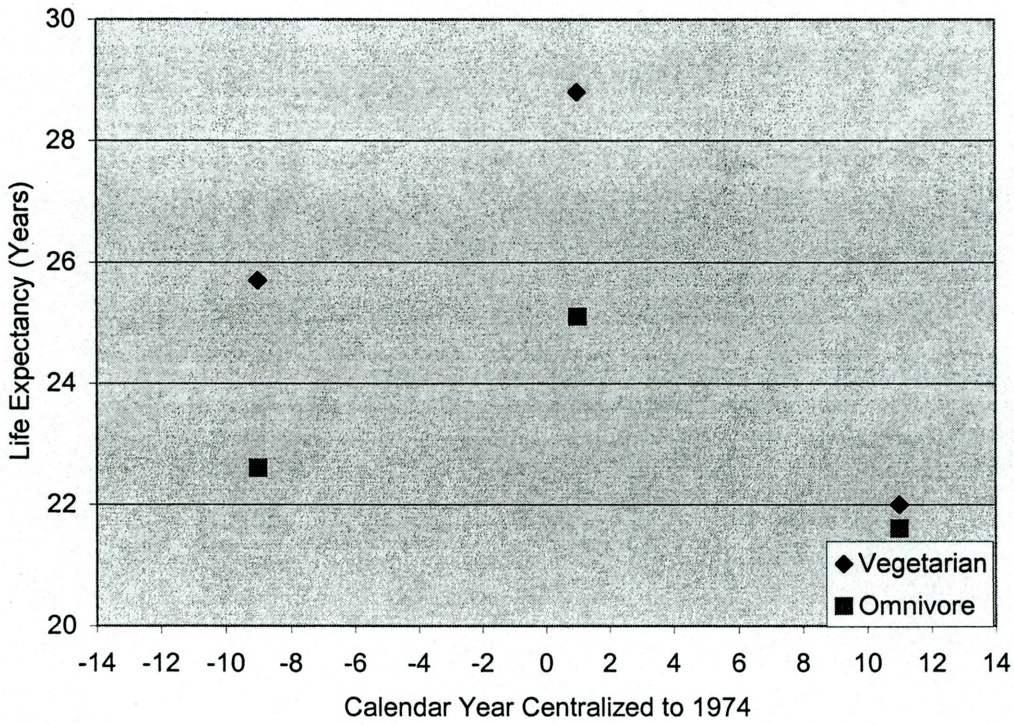

FIGURE 26. Comparison of change in life expectancy at age 50 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

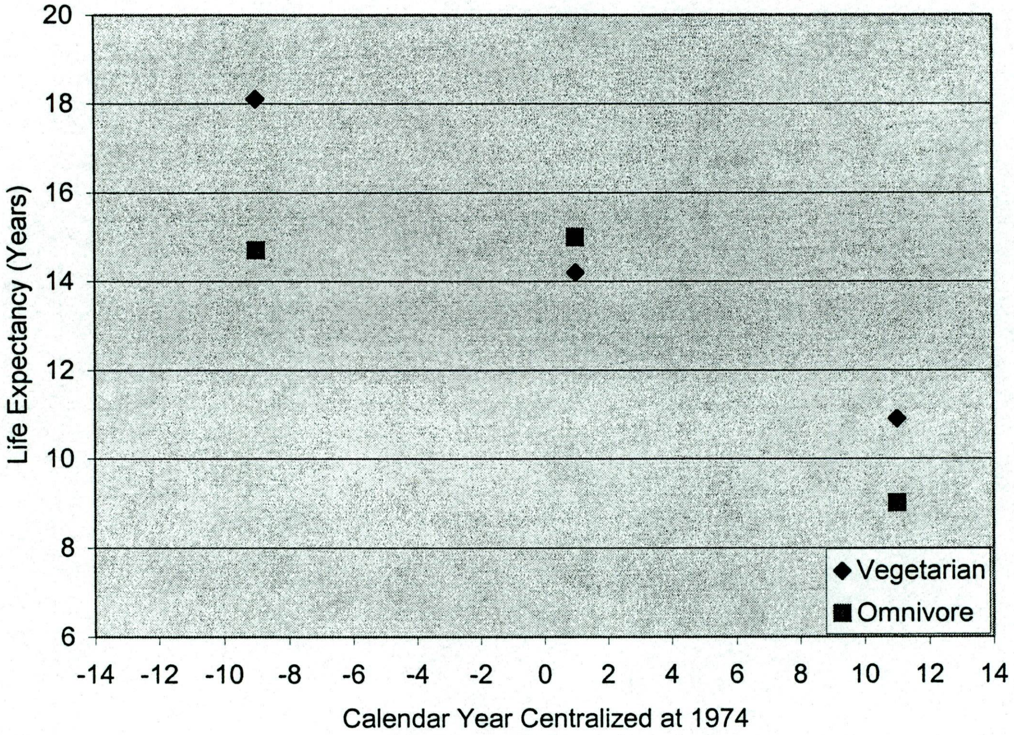

FIGURE 27. Comparison of change in life expectancy at age 70 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

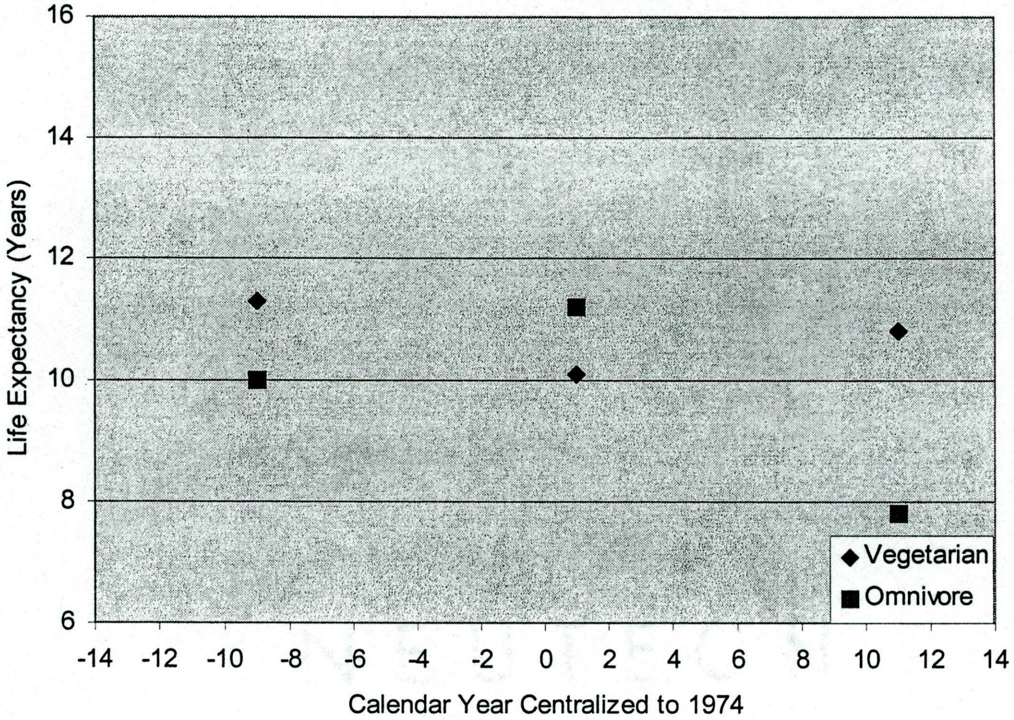

FIGURE 28. Comparison of change in life expectancy at age 80 by calendar year and diet status in males with otherwise unfavorable lifestyles who died from cancer in the Adventist Studies.

APPENDIX C

Changes in Life Expectancy in Seventh-day Adventists From 1960-1988

CHANGES IN LIFE EXPECTANCY IN SEVENTH-DAY ADVENTISTS FROM 1960-1988

NS Daher, KD Lindsted, Department of Epidemiology, Loma Linda University, Loma Linda, CA

PURPOSE:

To evaluate the changes in age-specific life expectancy and mortality rate from 1960 to 1988 for males and females in the Adventist Mortality Study (AMS) (n = 27,517) and the Adventist Health Study (AHS) (n = 34,192) combined. Differences in life expectancy by subgroups with different life styles are explored. The life styles considered are physical activity (high and low), and diet status (vegetarians and omnivores).

METHODS:

We used the abridged life table to calculate life expectancy for all-cause mortality for the ages 30-49 and every five- year interval up to 95+ years of age. In a univariate analysis, we modeled the life expectancies using multiple linear regression analysis. The model used is: $e_{t,x} = \alpha + \beta_1 x + \beta_2 year + \beta_3 x*(Y)$ where t indicates age, x is a binary variable for a given lifestyle factor coded 1 for high and zero otherwise, and Y is the calendar year from 1960 through 1988 centralized to 1974. The product term between the calendar year and the lifestyle factor is used to test for differences in the regression slopes. Differences in Y-intercepts were evaluated through standard statistical tests for significance.

Vegetarians were defined as anyone who ate meat less than once per week, based on the simple food questionnaire in the AMS administered in 1960, and the semi-quantitative food questionnaire administered in the AHS in 1976.

The analysis for the physical activity was limited to men. In the AMS, physical activity was determined through a single question: "How much exercise do you get (work or play)? Heavy, moderate, slight or none?" In the AHS, the physical activity index was calculated from the subjects' responses to questions about their participation in leisure time or occupational activities. The index was considered "high" for frequent participation three or more time per week for 15 minutes or more per session. The index was "moderate" for less frequent participation (less than three times per week for less than 15 minutes per session), or "none/low" for those who "rarely or never" participated in vigorous physical activity.

Physical activity was assessed differently in both cohorts. We first evaluated the comparability of the classification into two physical activity groups (high and low). We did this by combining the two populations and then comparing subjects with high levels of activity (moderate/high) in the combined population to subjects with high levels of physical activity in the AMS population. Similarly we compared subjects with low physical activity (none or low) in the combined cohort to subjects with low physical activity in the AMS population. The two different methods of assessing physical activity were comparable.

RESULTS:

For all age groups, the life expectancy increased linearly from 1960 to 1988. For males, the life expectancy was 26.04 years for subjects 50-54 years in 1960 versus 30.29 in the year 1988. For males 90-94 years of age the life expectancy was 3.29 years in

1960 versus 3.71 in the year 1988. Mortality rates decreased from 0.00823 in 1960 to 0.00294 in 1988 for males 50-54 year of age and from 0.030 in 1960 to 0.2391 in 1988 for males 90-94 years of age.

For females 50-54 years of age, the life expectancy increased from 26.65 in 1960 to 34.34 in the year 1988. For females 90-94 years of ages, it increased from 4.83 in 1960 to 4.95 in 1988. The mortality rates for females 50-54 years of age decreased from 0.00675 in 1960 to 0.00276 in 1988 and from 0.16941 in 1960 to 0.16220 in 1988 for females 90-94 years of age.

Figures 1-4 show that a linear model fits the data well. The slope of increase in life expectancy is substantially greater for women than for men, particularly among vegetarians (Figures 2 and 3).

The slope of increase in life expectancy is substantially greater for females than for males for all ages up to 80 years of age ($p<.01$, Figure 1).

The slope of increase in life expectancy is substantially greater for female than for male vegetarians (Table 2). The average life expectancy is higher in vegetarians when compared to omnivores ranging from 6 to 1 year in males and from 4 to 1 year in females (Table 3). Among vegetarians, females had significantly higher slopes than males ($p<.05$). On the other hand this difference is not statistically significant ($p>.05$). The average life expectancy is higher in females when compared to males, ranging from 2 to 1 year in vegetarians and from 3 to 1 year in omnivores.

Among males, the slope of increase in life expectancy of subjects up to 70 years of age with moderate to high levels of exercise is significantly higher than for males with no to low levels of exercise. The y-intercepts are also higher in males with moderate to high levels of exercise (Table 5).

CONCLUSION:

Even in the oldest old, there is an increase in life expectancy and decrease in mortality rate from 1960 to 1988. The slope of increase in life expectancy is significantly greater for women than for men, particularly for vegetarians. For males, there is no significant difference in regression slopes between vegetarians and omnivores. For females, the slopes are significantly different fro age groups 60 through 89, and for these ages, the slopes diverge with calendar time.

For physical activity, there are no significant differences in average life expectancies for any age category, but life expectancies increase faster in subjects with a high level of physical activity up to 70 years of age. Perhaps the effect of physical activity is sort-lived, and subjects above 70 years of age may not be able to sustain enough physical activity to improve their life expectancy.

TABLE 1. Comparison of regression lines of life expectancy as a function of calendar year (1960-1988, centralized for 1974) between males and females in the combined cohort (AMS & AHS, age 30 through 95+)

Age Intervals	y-Intercepts			p-values for Differences between y-Intercepts	Slopes of Regression Lines			p-values for Interactions between Gender and Calendar Year
	Females	Males	Difference Between y-Intercepts		Females	Males	Difference Between Slopes	
30-49	49.6	47.1	2.5	0.789	0.26	0.17	0.09	0.008
50-54	30.6	28.4	2.2	0.693	0.20	0.11	0.09	0.001
55-59	26.1	24.0	2.1	0.654	0.18	0.09	0.09	0.002
60-64	21.9	19.9	2.0	0.604	0.17	0.07	0.10	<0.0001
65-69	17.9	16.1	1.8	0.571	0.16	0.06	0.10	<0.0001
70-74	14.0	12.6	1.4	0.607	0.15	0.07	0.08	0.001
75-79	10.7	9.7	1.0	0.598	0.14	0.06	0.08	<0.0001
80-84	7.8	7.2	0.6	0.675	0.11	0.06	0.05	0.004
85-89	5.5	5.1	0.4	0.673	0.07	0.06	0.02	0.246
90-94	4.2	3.6	0.6	0.386	0.04	0.04	0.00	0.854
95+	3.8	2.3	1.5	0.006	0.07	0.05	0.03	0.500

TABLE 2. Comparison of regression lines of life expectancy as a function of calendar year (1960 - 1988, centralized for 1974) between males and females in the combined cohort (AMS & AHS, age 30 through 90+) separately by diet status

Gender	Age Intervals	y-Intercepts			p-values for Differences between y-Intercepts	Slopes of Regression Lines			p-values for Interactions between Diet Status and Calendar Year
		Females	Males	Difference Between y-Intercept		Females	Males	Difference Between Slopes	
Vegetarians	30-49	51.4	49.6	1.8	0.898	0.27	0.14	0.13	0.001
	50-59	32.1	30.4	1.7	0.842	0.24	0.10	0.14	0.000
	60-69	23.2	21.5	1.6	0.789	0.21	0.09	0.12	0.001
	70-79	15.0	13.7	1.3	0.735	0.18	0.10	0.08	0.018
	80-89	8.4	7.7	0.7	0.749	0.15	0.08	0.07	0.121
	90+	5.8	4.6	1.2	0.408	0.11	0.01	0.10	0.044
Omnivores	30-49	47.0	43.9	3.1	0.803	0.25	0.22	0.03	0.426
	50-59	28.3	25.5	2.8	0.707	0.16	0.15	0.02	0.618
	60-69	20.1	17.4	2.6	0.614	0.13	0.08	0.05	0.071
	70-79	12.8	11.0	1.8	0.577	0.11	0.06	0.05	0.853
	80-89	7.5	6.5	1.0	0.605	0.07	0.05	0.02	0.120
	90+	5.0	3.4	1.6	0.187	0.07	0.09	-0.02	0.120

TABLE 3. Comparison of gender-specific regression lines of life expectancy as a function of calendar year (1960-1988, centralized for 1974) between vegetarians and omnivores in the combined cohort (AMS & AHS, age 30 through 90+)

		y-Intercepts				Slopes of Regression Lines			
Gender	Age Intervals	Vegetarians	Omnivores	Difference Between y-Intercepts	p-values for Differences between y-Intercepts	Vegetarians	Omnivores	Difference Between Slopes	p-values for Interactions between Diet Status and Calendar Year
Males	30-49	49.6	43.9	5.7	< 0.001	0.14	0.22	-0.09	0.060
	50-59	30.4	25.5	4.9	< 0.001	0.10	0.15	-0.05	0.227
	60-69	21.5	17.4	4.1	< 0.001	0.09	0.08	0.01	0.830
	70-79	13.7	11.0	2.7	< 0.001	0.10	0.06	0.04	0.229
	80-89	7.7	6.5	1.2	< 0.001	0.08	0.05	0.03	0.218
	90+	4.6	3.4	1.2	< 0.001	0.01	0.09	-0.08	0.072
Females	30-49	51.4	47.0	4.4	< 0.001	0.27	0.25	0.02	0.665
	50-59	32.1	28.3	3.8	< 0.001	0.24	0.16	0.08	0.064
	60-69	23.2	20.1	3.1	< 0.001	0.21	0.13	0.08	0.011
	70-79	15.0	12.8	2.2	< 0.001	0.18	0.11	0.07	0.022
	80-89	8.4	7.5	0.9	< 0.001	0.15	0.07	0.08	0.001
	90+	5.8	5.0	0.8	0.011	0.11	0.07	0.04	0.397

TABLE 4. Comparison of regression lines of life expectancy as a function of calendar year (1960-1988, centralized for 1974) between males with no to low levels of exercise and males with moderate to high levels of exercise in the combined cohort (AMS & AHS, age 30 through 90+)

		y-Intercepts				Slopes of Regression Lines			
Gender	Age Intervals	No/Low Exercise	Moderate / High Exercise	Difference Between y-Intercepts	p-values for Difference between y-intercepts	No/Low Exercise	Moderate / High Exercise	Difference Between Slopes	p-values for Interaction between Exercise Status and Calendar Year
Males	30-49	45.4	47.0	-1.6	0.896	0.08	0.24	-0.16	0.006
	50-59	26.9	28.2	-1.2	0.869	0.01	0.18	-0.16	0.004
	60-69	19.0	19.6	-0.6	0.905	0.01	0.12	-0.11	0.031
	70-79	12.5	12.3	0.2	0.957	0.07	0.09	-0.02	0.656
	80-89	7.5	7.1	0.4	0.836	0.07	0.09	-0.02	0.572
	90+	3.9	4.3	-0.4	0.711	0.08	0.04	0.04	0.422

TABLE 5. Comparison of Regression Lines of Life Expectancy as a Function of Calendar Year (1960 - 1988, Centralized for 1974) in the Combined Cohort (AMS & AHS, age 30 through 90+)

	Differences e_i	Difference in Secular Change in e_i
Females vs. Males	2.5 to 1.5	0.09 to 0.02
Vegetarian		
Females vs. Males	1.5 to 1.6	0.12 to 0.03
Omnivores		
Females vs. Males	3.0 to 1.3	0.02 to 0.01
Females		
Vegetarian vs. Omnivores	3.7 to 0.5	0.12 to 0.09
Males		
Vegetarian vs. Omnivores	5.2 to 0.1	-0.05 to -0.03
Males		
No/Low vs. Moderate/ High Exercise	-1.6 to -0.4	-0.16 to -0.03

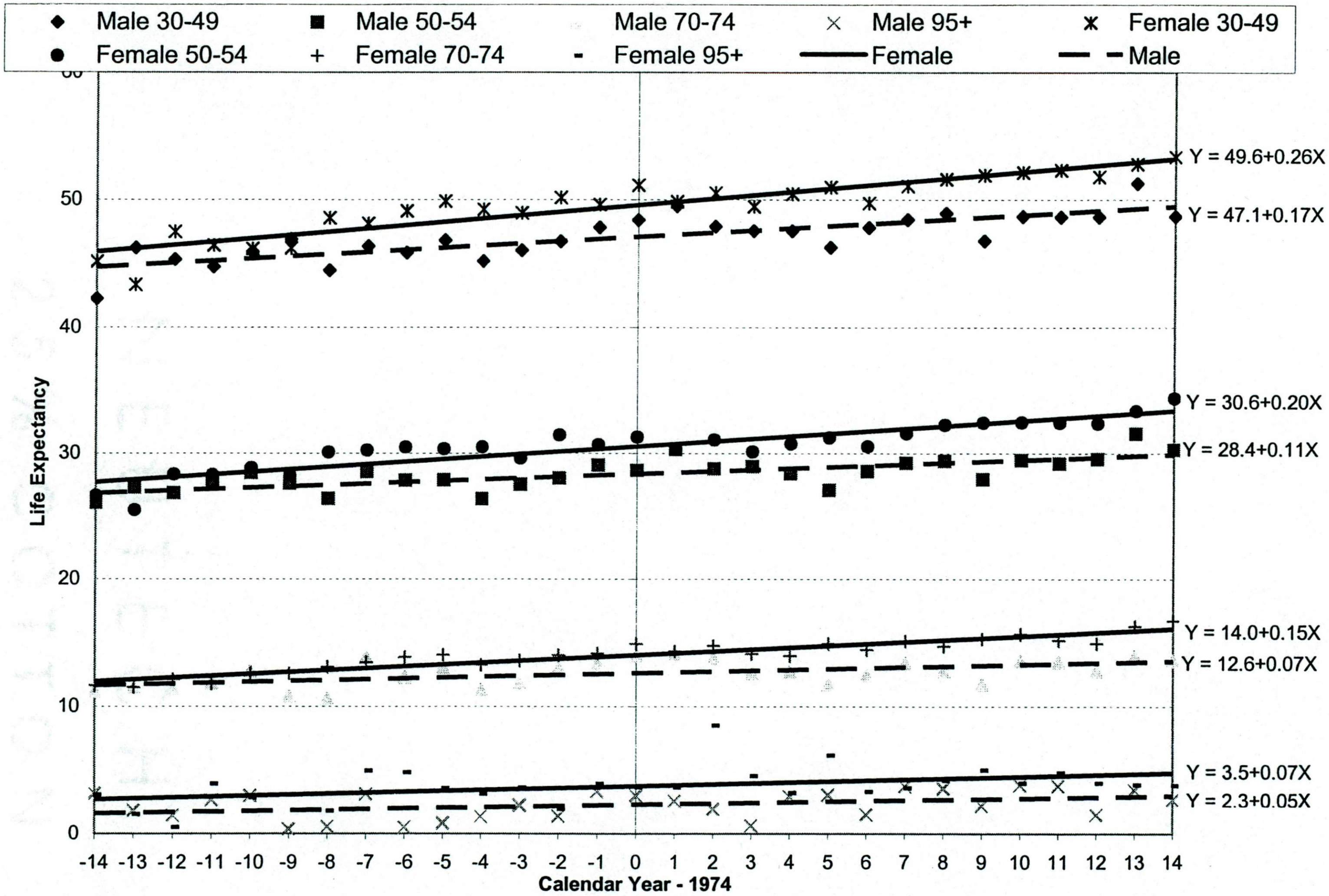

FIGURE 1. Comparison of regression lines of life expectancy by calendar year between males and females (1960-1988, centralized for 1974) for the combined AMS and AHS subjects (age 30 through 95+).

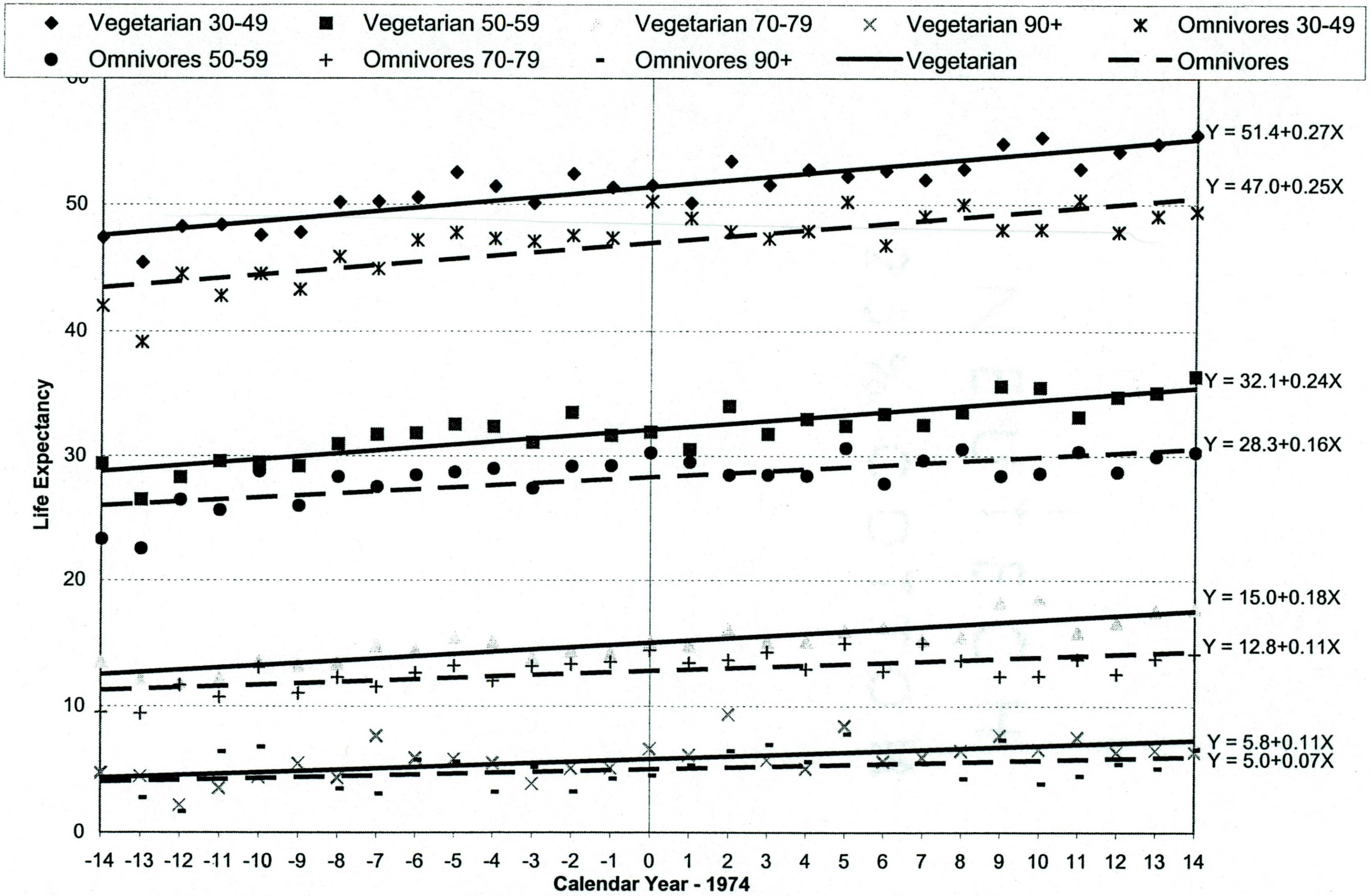

FIGURE 2. Comparison of regression lines of life expectancy by calendar year between vegeratians and omnivores (1960-1988, centralized for 1974) for the combined AMS and AHS females (age 30 through 90+).

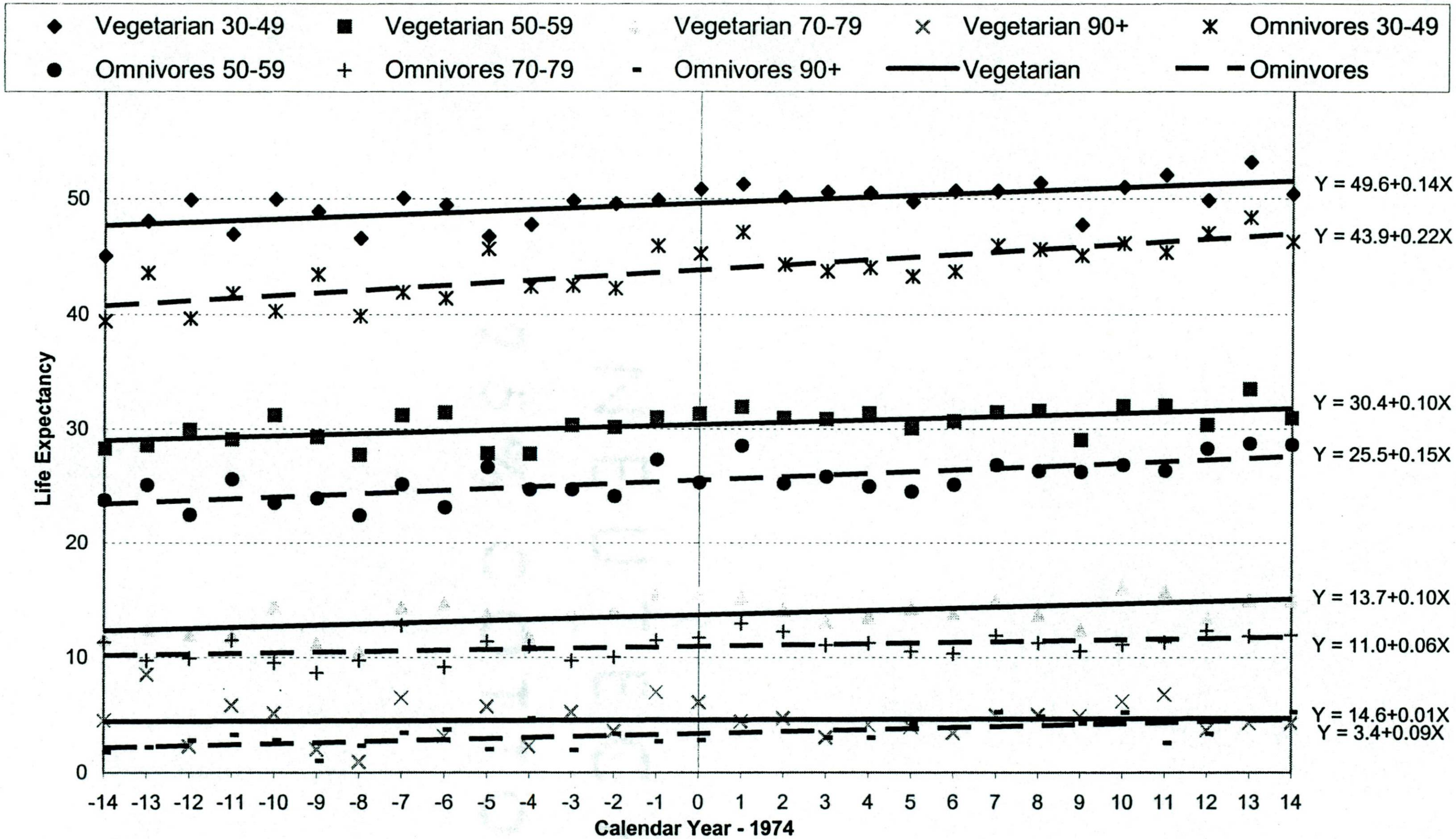

FIGURE 3. Comparison of regression lines of life expectancy by calendar year between vegetarians and omnivores (1960-1988, centralized for 1974) for the combined AMS and AHS males (age 30 through 90+).

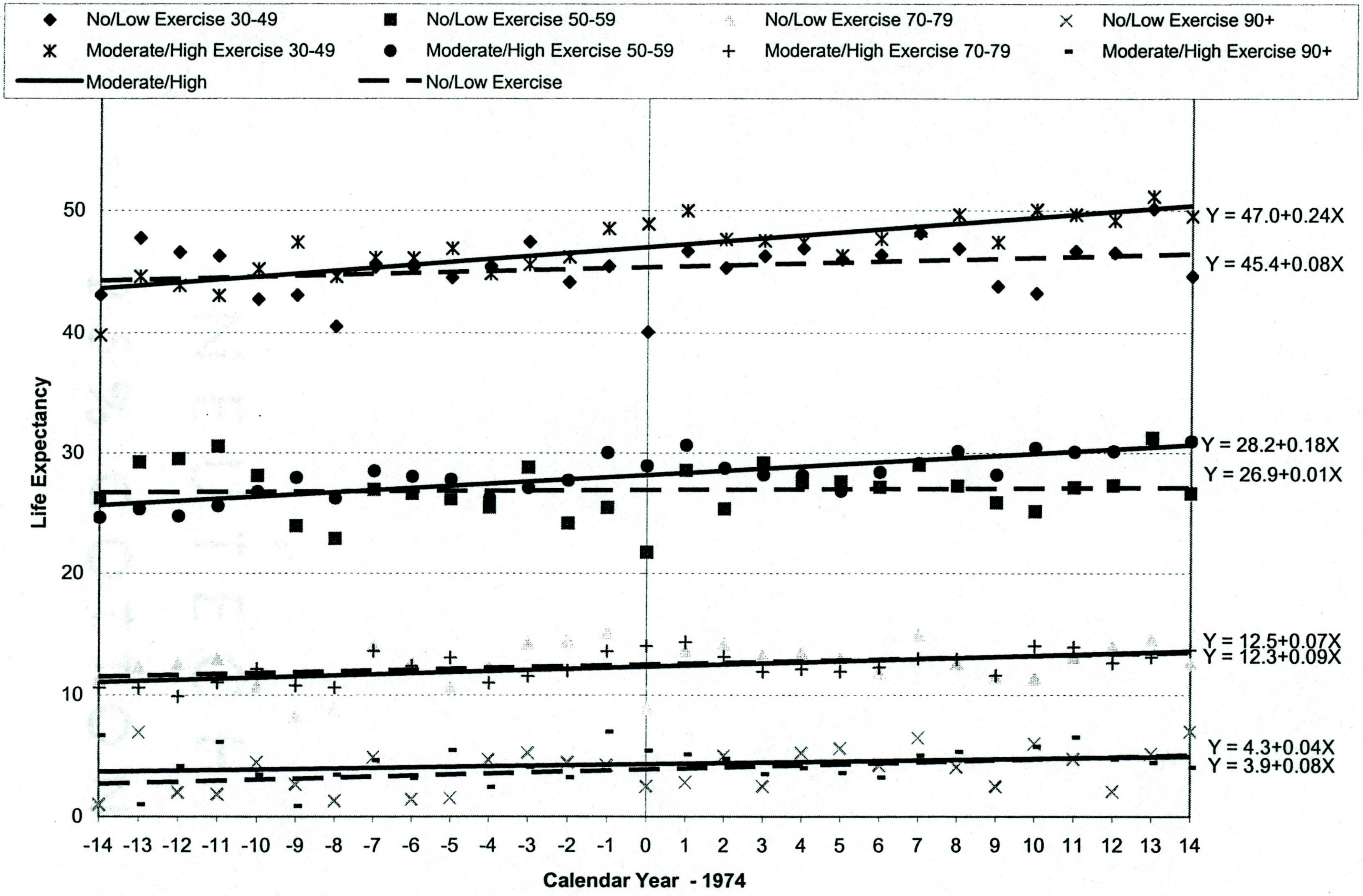

FIGURE 4. Comparison of regression lines of life expectancy by calendar year (1960-1988, centralized for 1974) between males with no to low levels of exercise and males with moderate to high levels of exercise (age 30 through 90+).

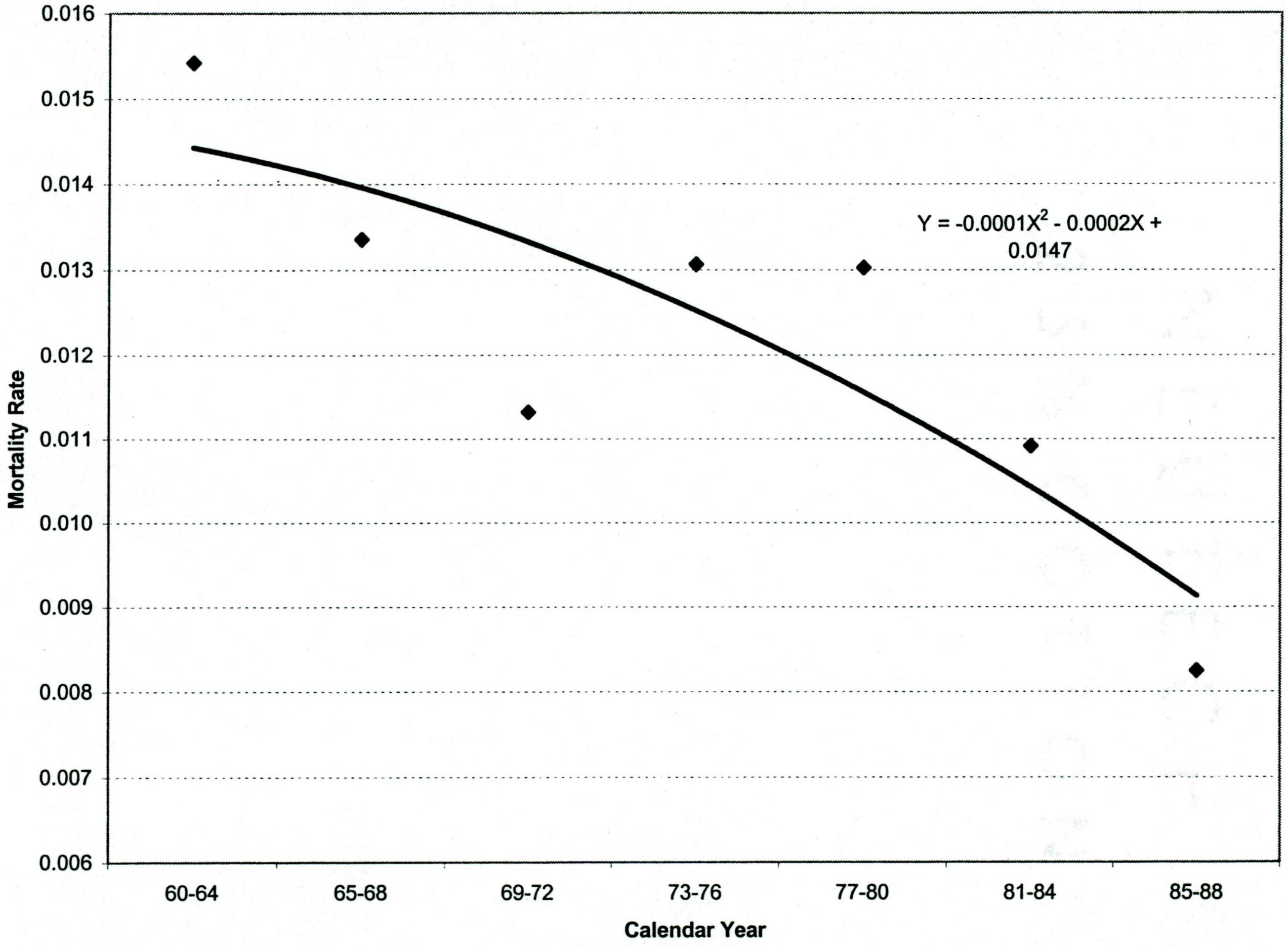

FIGURE 5. All cause mortality rates for females 60-69 years of age by calendar year in the combined cohort (AMS & AHS, 1960 - 1988).

APPENDIX D

Changes in Life Expectancy of Subjects who Died From Cardiovascular Heart Disease and All-Sites Cancer in Seventh-day Adventists

CHANGES IN LIFE EXPECTANCY OF SUBJECTS WHO DIED FROM CARDIOVASCULAR HEART DISEASE AND ALL-SITES CANCER IN SEVENTH-DAY ADVENTISTS

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PURPOSE:

To evaluate age-specific life expectancy and death rate of subjects who died from Cardiovascular Heart Disease (CHD) from 1960 to 1988 for males and females in the Adventist Mortality Study (AMS) (n = 27,517) and the Adventist Health Study (AHS) (n = 34,192) combined. Differences in life expectancy of subjects who died from CHD and all-sites cancer by subgroups with different life styles are explored. The life styles considered are physical activity (high and low), and diet status (vegetarians and omnivores).

METHODS:

We used the abridged life table to calculate life expectancy of subjects who died from CHD and all-sites cancer for the ages 30-49 and every ten-year interval up to 90 years of age from 1960 to 1988. In a univariate analysis, we modeled the life expectancies using multiple linear regression analysis. The model used is: $e_{t,x} = \alpha + \beta_1 x + \beta_2 \text{year} + \beta_3 x^*(Y)$ where t indicates age, x is a binary variable for a given lifestyle factor coded 1 for high and zero otherwise, and Y is the calendar year from 1960 through 1988 centralized to 1974. The product term between the calendar year and the lifestyle factor is used to test for differences in the regression slopes. Differences in Y-intercepts were evaluated through standard statistical tests for significance. Vegetarians were defined as anyone who ate meat less than once per week, based on the simple food questionnaire in the AMS administered in 1960, and the semi- quantitative food questionnaire administered in the AHS in 1976.

The analysis for the physical activity is limited to men. In the AMS, physical activity was determined through a single question: "How much exercise do you get (work or play)? Heavy, moderate, slight or none?" In the AHS, the physical activity index was calculated from the subjects' responses to questions about their participation in leisure time or occupational activities. The index was considered "high" for frequent participation three or more time per week for 15 minutes or more per session. The index was "moderate" for less frequent participation (less than three times per week for less than 15 minutes per session), or "none/low" for those who "rarely or never" participated in vigorous physical activity.

Physical activity was assessed differently in both cohorts. We first evaluated the comparability of the classification into two physical activity groups (high and low). We did this by combining the two populations and then comparing subjects with high levels of activity (moderate/high) in the combined population to subjects with high levels of physical activity in the AMS population. Similarly we compared subjects with low physical activity (none or low) in the combined cohort to subjects with low physical activity in the AMS population. The two different methods of assessing physical activity were comparable.

RESULTS:

For all age groups, the life expectancy of subjects who died from CHD increased linearly from 1960 to 1988 (Table 1). For males, the life expectancy was 15.77 years for subjects 60-69 years in 1960 versus 19.73 in the year 1988. For males 80-89 years of age the life expectancy was 6.04 years in 1960 versus 6.31 in the year 1988. The death rate from CHD decreased from 0.03288 in 1960 to 0.01491 in 1988 for males 60-69 years of age and from 0.14483 in 1960 to 0.132 in 1988 for males 80-89 years of age. For females 60-69 years of age, the life expectancy of subjects who died from CHD increased from 16.79 in 1960 to 27.03 in the year 1988. For females 80-89 years of age, it increased from 5.46 in 1960 to 11.3 in 1988. The death rate from CHD for females 60-69 years of age decreased from 0.025 in 1960 to 0.00688 in 1988 and decreased from 0.16667 in 1960 to 0.05471 in 1988 for females 80-89 years of age.

The slope of increase in life expectancy is substantially greater for females than for males for all ages up to 90 years of age ($p<.01$, Figure 1). The average life expectancy is higher for females than for males, which is indicated by the y-intercepts ($p>.05$, Table 1). This difference may be attributed to their diet.

Vegetarian males had a higher slope increase in life expectancy than male omnivores for ages 60 through 80 (Figure 3). Female vegetarians had a higher slope increase than female omnivores for all ages except for subjects 80 through 89 years of age (Figure 2). This difference is statistically significant for female subjects up to 70 years of age (Table 2). The slope of increase in life expectancy is substantially greater for female than for male vegetarians. The average life expectancy is higher in vegetarians when compared to omnivores ranging from 5 to 1 year in males and from 4 to 1 year in females (Table 2).

Among males, the slope of increase in life expectancy of subjects up 30-49 years of age with moderate to high levels of exercise is significantly higher than for males with no to low levels of exercise (Figure 6). The y-intercepts are also higher in males with moderate to high levels of exercise. Subjects above 50 years of age may not be able to sustain enough physical activity to improve their life expectancy (Table 4).

For all age groups, the life expectancy of subjects who died from all-sites cancer increased linearly from 1960 to 1988. The slope of increase in life expectancy is greater for women than for males for all ages up to 90+ years of age ($p>.05$, Table 1). The average life expectancy is higher for females than for males, which is indicated by the y-intercepts ($p>.05$, Table 1).

The slope of increase in life expectancy is higher for male than for female vegetarians (Figures 4 & 5). The average life expectancy is higher in vegetarians when compared to omnivores ranging from 4 to 1 year in males and from 3 to 1 year in females (Table 3).

Male vegetarians had a lower slope of increase in life expectancy than omnivores for all ages up to 90 years and over. Female vegetarians had a lower slope of increase in life expectancy than omnivores for all ages up to 80 years of age (Table 3). Omnivores are catching up with omnivores in terms of cancer; possibly they started to modify their diet once they got diagnosed. This difference does not prevail for females 80 and over. Subjects then may die of old age.

Among males, the slope of increase in life expectancy of subjects 30-69 years of age with moderate to high levels of exercise is higher than for males with no to low levels of exercise (Figure 7). The y-intercepts are lower in males with moderate to high levels of exercise. Subjects above 70 years of age may not be able to sustain enough physical activity to improve their life expectancy (Table 4).

CONCLUSION:

Even in the oldest old, there is an increase in life expectancy of subjects who died from CHD and decrease in death rate from 1960 to 1988. The slope of increase in life expectancy of subjects who died from CHD is significantly greater for women than for men for all ages up to 89 years. On the other hand, the slope of increase in life expectancy of subjects who died from all-sites cancer is greater for women than for men, yet not significant.

For females, the slope of increase in life expectancy of subjects who died from CHD is significantly greater for vegetarians than for omnivores for all ages up to 69 years, and for these ages, the slopes diverge with calendar time. For males, there is no difference in regression slopes between vegetarians and omnivores. There are no significant differences in average life expectancies for both causes of death for any age category.

The slope of increase in life expectancy of males 30-49 years of age who died from CHD with moderate to high levels of exercise is significantly higher than for males with no to low levels of exercise. The slope of increase in life expectancy of males up to 69 years of age who died from all-sites cancer with moderate to high levels of exercise is significantly higher than for males with no to low levels of exercise. Subjects above 70 years of age may not be able to sustain enough physical activity to improve their life expectancy.

TABLE 1. Comparison of regression lines of life expectancy for specific causes of death as a function of calendar year (1960-1988, centralized for 1974) between males and females in the combined cohort (AMS & AHS, age 30 through 90+)

Cause of Death	Age Intervals	y-Intercepts: Females	y-Intercepts: Males	Difference Between y-Intercepts	p-values for Differences between y-Intercepts	Slopes of Regression Lines: Females	Slopes of Regression Lines: Males	Difference Between Slopes	p-values for Interactions between Gender and Calendar Year
Cardio-vascular Heart Disease	30-49	51.2	48.0	3.2	0.814	0.24	0.11	0.14	0.043
	50-59	31.3	28.4	2.9	0.725	0.24	0.08	0.16	0.019
	60-69	21.9	19.0	2.9	0.603	0.25	0.06	0.19	0.002
	70-79	13.5	11.5	2.1	0.552	0.20	0.04	0.17	0.001
	80-89	7.6	6.3	1.3	0.507	0.15	0.03	0.13	0.005
	90+	4.2	2.7	1.5	0.165	0.13	0.04	0.09	0.085
All-Sites Cancer	30-49	49.7	48.9	0.8	0.959	0.25	0.16	0.09	0.523
	50-59	30.3	29.5	0.8	0.931	0.22	0.11	0.11	0.375
	60-69	21.6	20.5	1.1	0.862	0.17	0.11	0.06	0.614
	70-79	14.1	12.8	1.3	0.746	0.13	0.04	0.09	0.336
	80-89	8.2	6.9	1.3	0.593	0.13	0.06	0.07	0.376
	90+	4.8	2.7	2.0	0.119	0.07	0.06	0.01	0.594

TABLE 2. Comparison of gender-specific regression lines of life expectancy of subjects who died from cardiovascular heart disease as a function of calendar year (1960 - 1988, centralized for 1974) between vegetarians and omnivores in the combined cohort (AMS & AHS, age 30 through 90+)

		y-Intercepts				Slopes of Regression Lines			
Gender	Age Intervals	Vegetarians	Omnivores	Difference Between y-Intercepts	p-values for Differences between y-Intercepts	Vegetarians	Omnivores	Difference Between Slopes	p-values for Interactions between Diet Status and Calendar Year
Males	30-49	50.6	45.4	5.1	0.698	0.09	0.16	-0.07	0.573
	50-59	30.6	26.3	4.3	0.587	0.09	0.11	-0.01	0.717
	60-69	20.8	17.1	3.7	0.478	0.11	0.07	0.04	0.779
	70-79	12.5	10.2	2.3	0.471	0.09	0.02	0.08	0.311
	80-89	6.4	5.7	0.7	0.702	0.03	0.05	-0.03	0.608
	90+	2.1	2.2	-0.1	0.865	-0.01	0.02	-0.03	0.075
Females	30-49	52.8	49.1	3.7	0.791	0.29	0.15	0.14	0.015
	50-59	32.8	29.3	3.5	0.685	0.29	0.13	0.16	0.008
	60-69	23.3	20.1	3.2	0.598	0.29	0.17	0.11	0.023
	70-79	14.6	12.2	2.4	0.525	0.19	0.16	0.03	0.540
	80-89	7.8	6.9	0.9	0.655	0.14	0.15	-0.01	0.813
	90+	3.9	3.4	0.5	0.634	0.17	0.05	0.12	0.074

TABLE 3. Comparison of gender-specific regression lines of life expectancy of subjects who died from all site-cancer as a function of calendar year (1960 - 1988, centralized for 1974) between vegetarians and omnivores in the combined cohort (AMS & AHS, age 30 through 90+)

Gender	Age Intervals	y-Intercepts				Slopes of Regression Lines			
		Vegetarians	Omnivores	Difference Between y-Intercepts	p-values for Differences between y-Intercepts	Vegetarians	Omnivores	Difference Between Slopes	p-values for Interactions between Diet Status and Calendar Year
Males	30-49	51.0	47.0	4.0	0.767	0.26	0.34	-0.08	0.603
	50-59	31.4	27.8	3.5	0.659	0.20	0.24	-0.04	0.806
	60-69	22.3	18.8	3.5	0.543	0.14	0.24	-0.09	0.529
	70-79	14.7	11.2	3.6	0.342	0.08	0.19	-0.11	0.365
	80-89	7.7	6.1	1.7	0.417	0.04	0.18	-0.14	0.119
	90+	2.8	2.2	0.6	0.630	0.05	0.16	-0.11	0.210
Females	30-49	50.4	47.5	3.0	0.826	0.11	0.22	-0.11	0.439
	50-59	31.1	28.2	2.8	0.721	0.11	0.17	-0.06	0.653
	60-69	22.4	19.8	2.6	0.659	0.07	0.14	-0.07	0.498
	70-79	14.5	12.7	1.8	0.639	0.02	0.11	-0.09	0.319
	80-89	7.8	7.5	0.4	0.866	0.08	0.03	0.05	0.415
	90+	4.0	3.3	0.7	0.568	0.07	-0.05	0.12	0.087

TABLE 4. Comparison of regression lines of life expectancy for specific causes of death as a function of calendar year (1960 - 1988, centralized for 1974) between males with no to low levels of exercise and males with moderate to high levels of exercise in the combined cohort (AMS & AHS, age 30 through 90+)

		y-Intercepts				Slopes of Regression Lines			
Cause of Death	Age Intervals	No/Low Exercise	Moderate /High Exercise	Difference Between y-Intercepts	p-values for Differences between y-Intercepts	No/Low Exercise	Moderate /High Exercise	Difference Between Slopes	p-values for Interactions between Exercise Status and Calendar Year
Cardiovascular Heart Disease	30-49	41.8	47.6	-5.8	0.346	0.44	0.18	0.26	0.027
	50-59	22.2	28.0	-5.8	0.404	0.39	0.16	0.23	0.059
	60-69	14.2	18.6	-4.4	0.343	0.30	0.12	0.18	0.065
	70-79	8.4	10.8	-2.4	0.372	0.18	0.07	0.11	0.207
	80-89	6.0	5.8	0.2	0.907	0.09	0.03	0.06	0.356
	90+	2.3	1.9	0.4	0.619	0.19	0.02	0.17	0.463
All-Sites Cancer	30-49	49.5	48.4	1.1	0.936	0.15	0.20	-0.05	0.791
	50-59	29.9	29.1	0.8	0.921	0.09	0.14	-0.06	0.756
	60-69	20.8	20.1	0.7	0.906	0.06	0.15	-0.09	0.573
	70-79	12.8	12.7	0.2	0.965	0.05	0.03	0.02	0.870
	80-89	7.7	6.4	1.3	0.556	0.08	0.05	0.04	0.665
	90+	2.3	2.3	0.0	0.996	0.06	0.08	-0.02	0.786

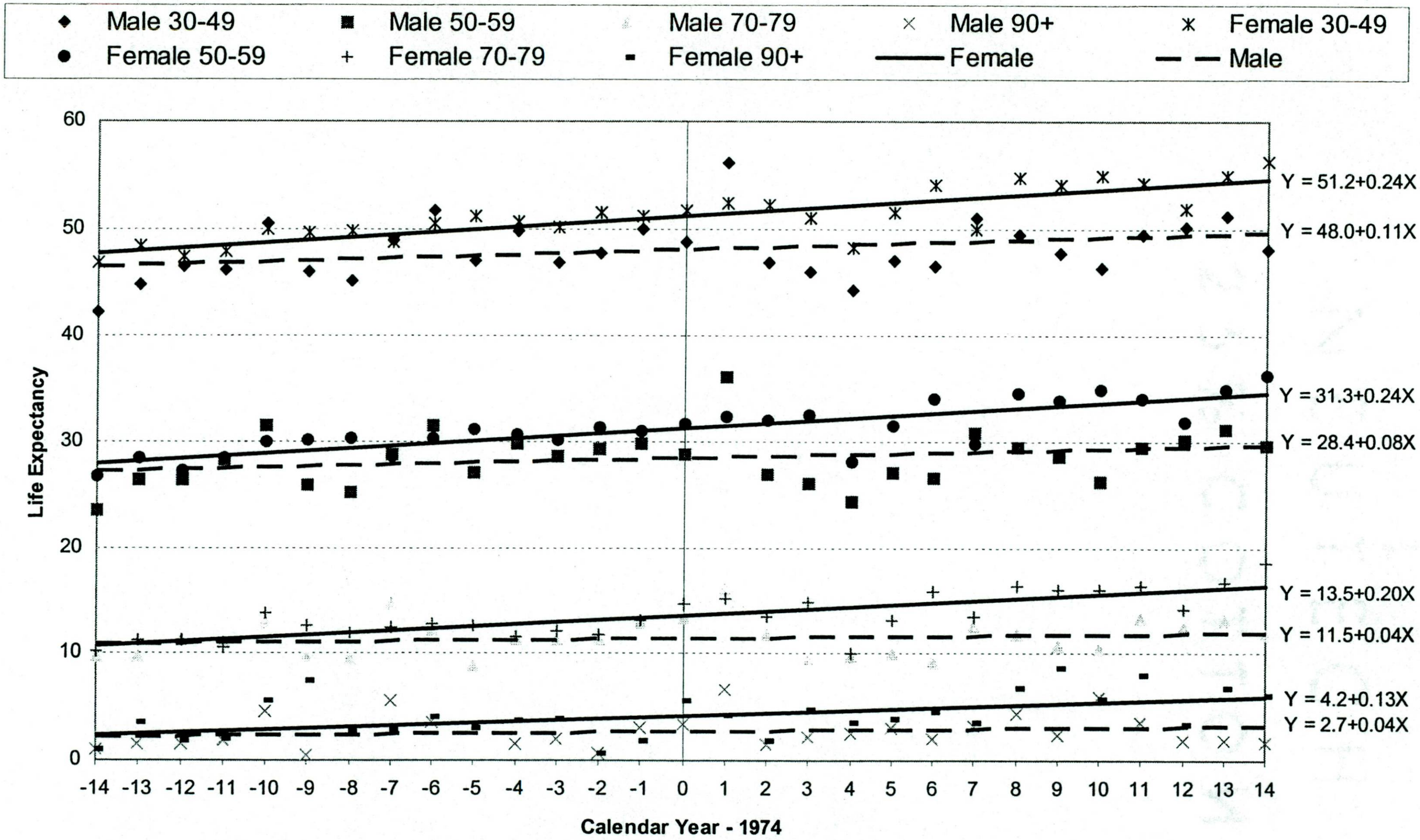

FIGURE 1. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for subjects who died from cardiovascular heart disease separately for males and females.

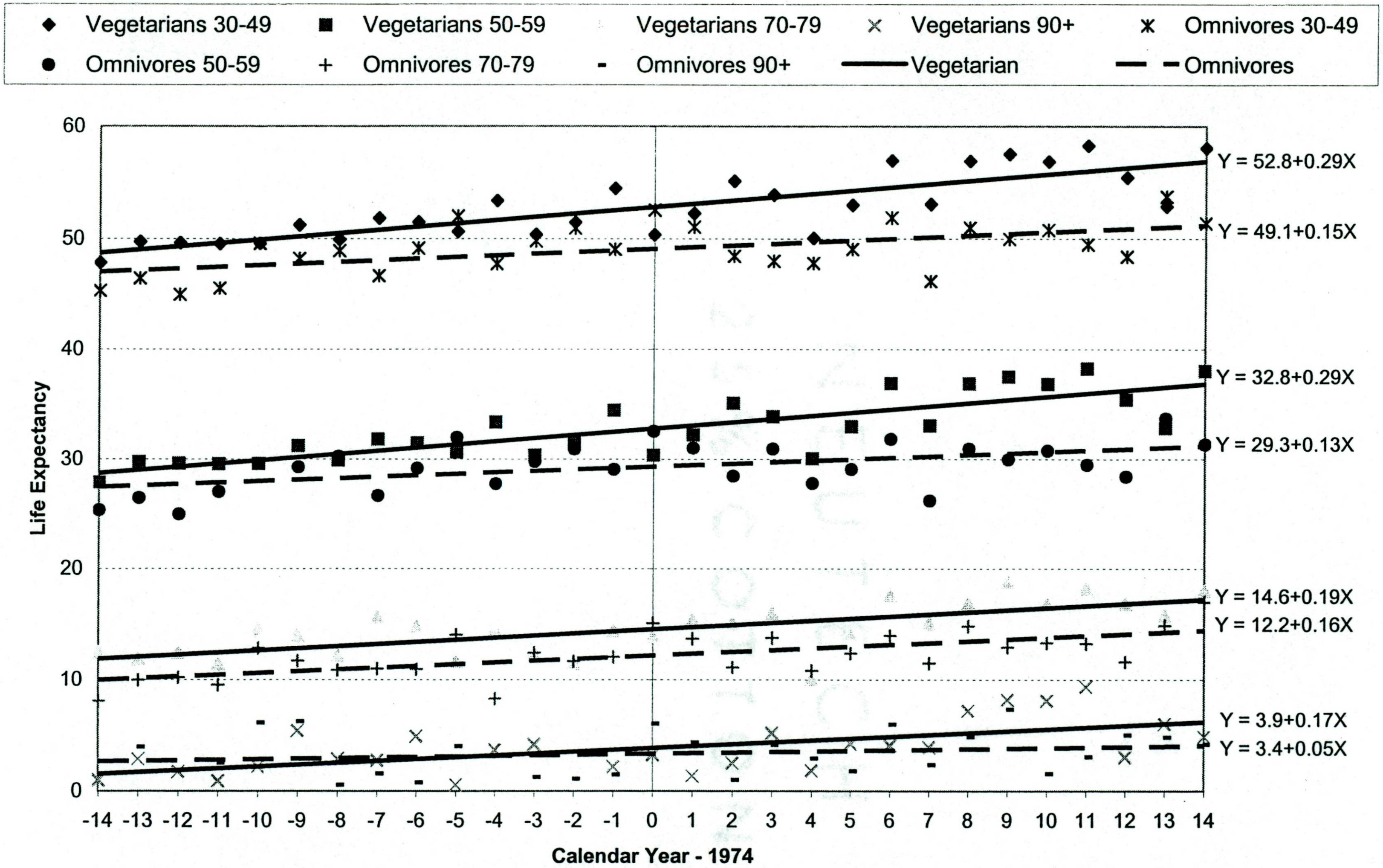

FIGURE 2. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for females who died from cardiovascular heart disease separately for vegetarians and omnivores.

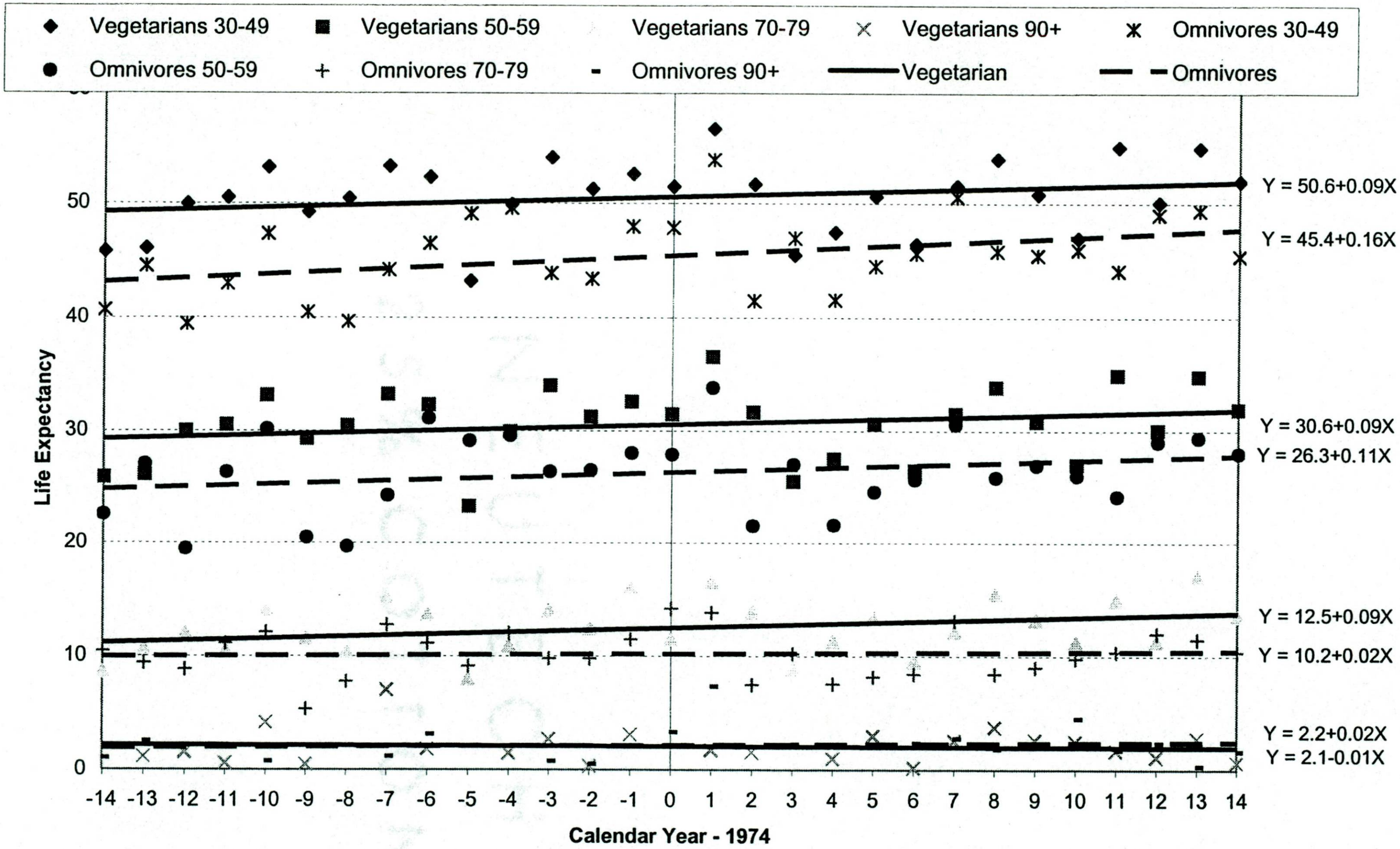

FIGURE 3. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for males who died from cardiovascular heart disease separately for vegetarians and omnivores.

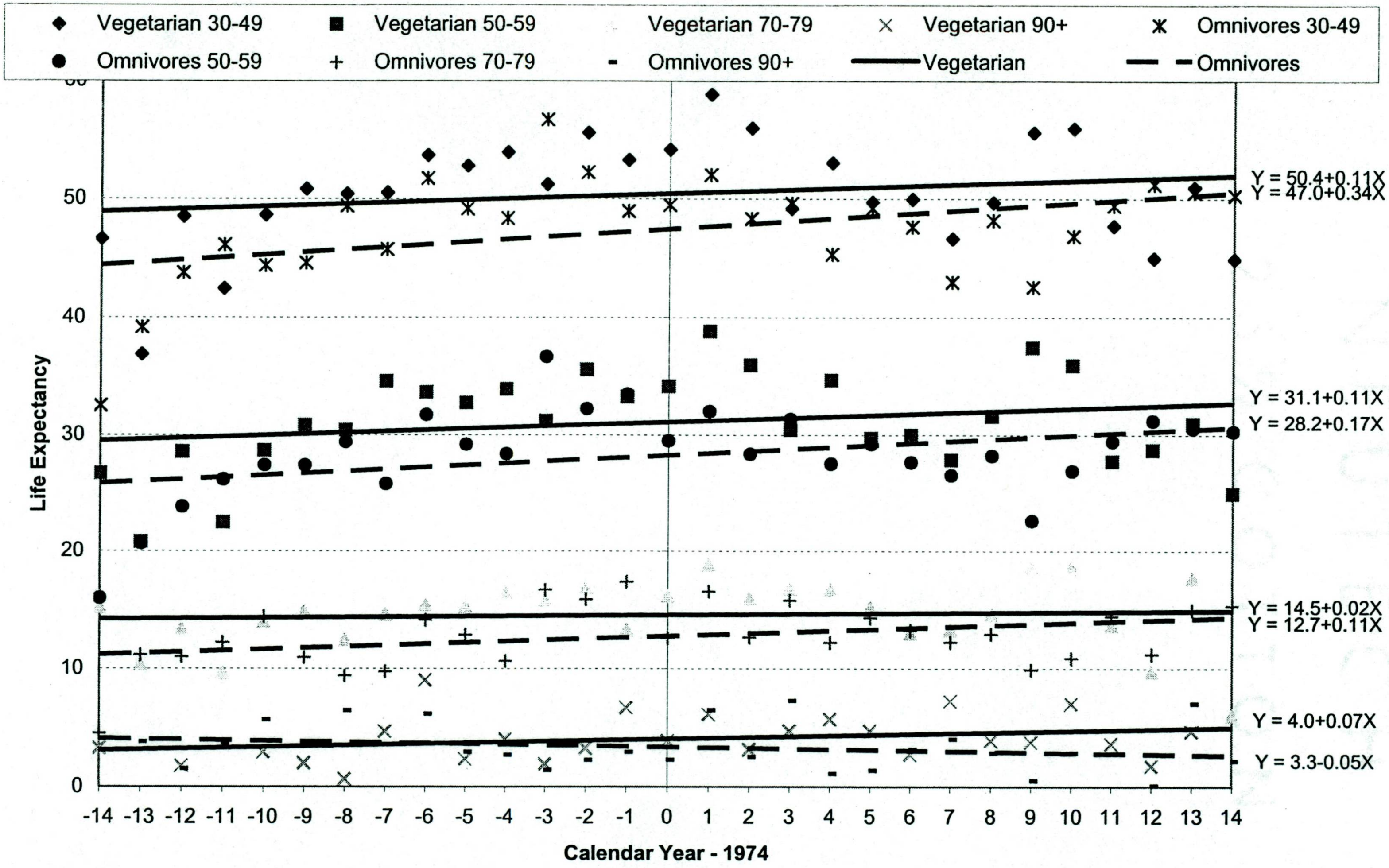

FIGURE 4. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for females who died from all-sites cancer separately from vegetarians and omnivores.

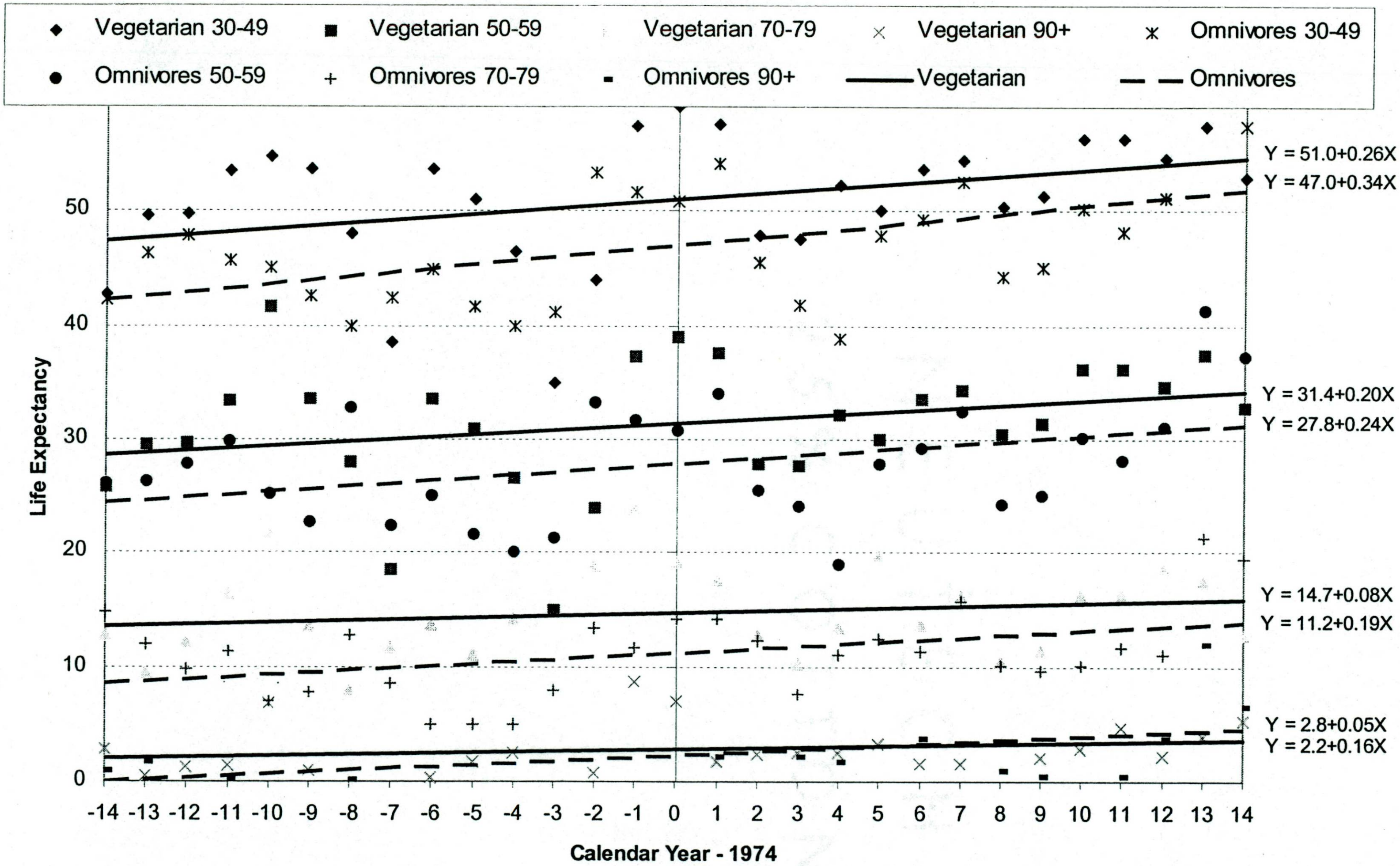

FIGURE 5. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for males who died from all-sites cancer separately for vegetarians and omnivores.

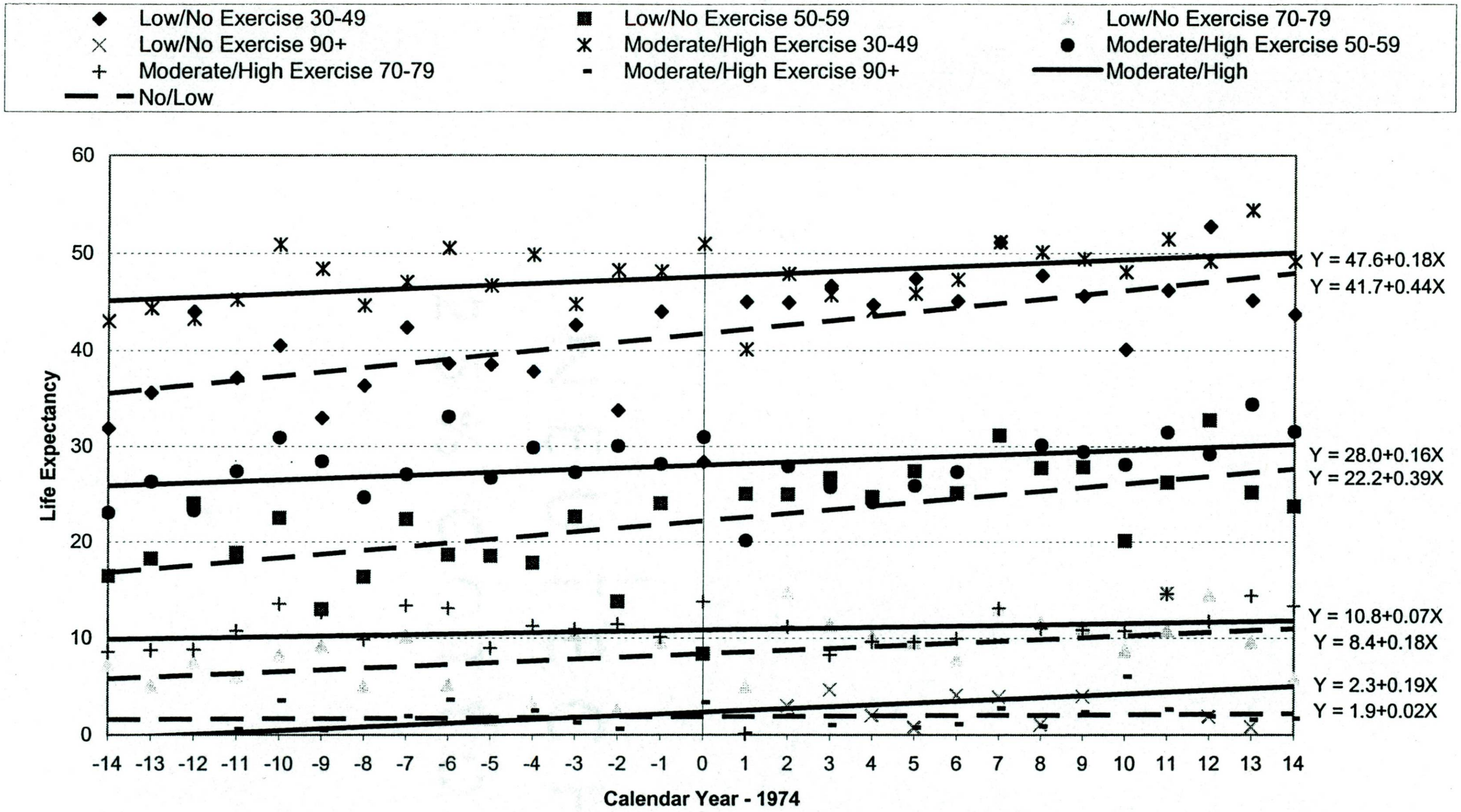

FIGURE 6. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for males who died from cardiovascular heart disease separately for males with no to low levels of exercise and males with moderate to high levels of exercise.

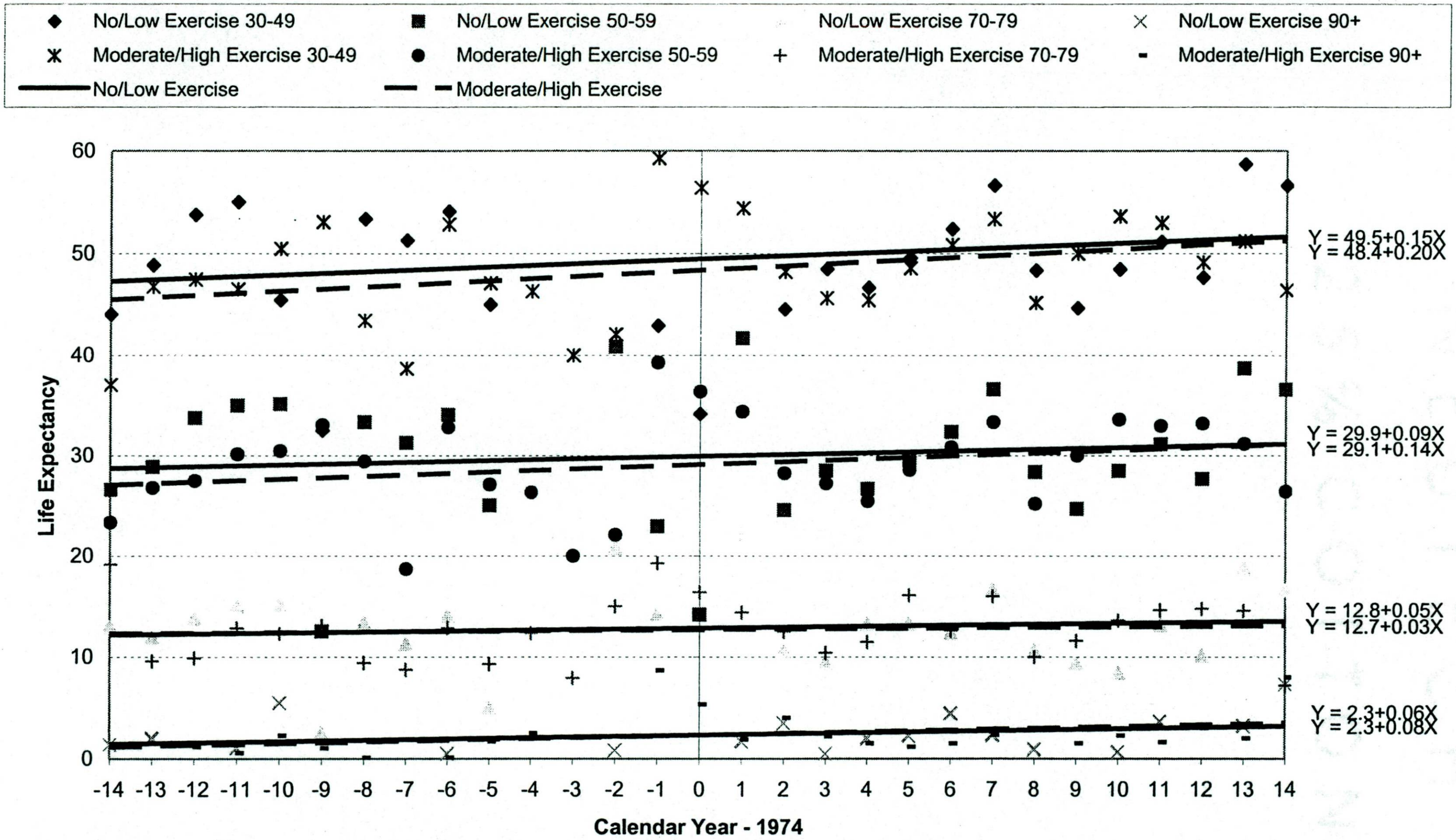

FIGURE 7. Age-specific life expectancy regressed on calendar year (1960-1988, centralized for 1974) for males who died from all-sites cancer separately for males with no to low levels of exercise and males with moderate to high levels of exercise.

APPENDIX E

Preliminary Tables and Figures From the Adventist Studies

TABLE 1. Comparison of distribution of selected variables in the AMS[1] and AHS[2] cohorts

	AMS (1960 – 1985)		**AHS** (1976 – 1988)	
	Frequency	Percent (%)	Frequency	Percent (%)
Number enrolled	27517		34192	
Number of deaths	9659	35.1	6186	18.1
Gender				
Male	9824	35.7	13857	40.5
Female	17693	64.3	20341	59.5
Education				
8^{th} or less	6113	23.0	3233	9.5
Some high school	5922	22.3	4329	12.7
High school grad	3330	12.5	4574	13.5
Some college	6975	26.3	12723	37.4
College & above	4226	15.9	9131	26.9
# Missing	951		208	
Exercise*				
None / light	176	1.9	2905	21.4
Low	1794	18.9	1489	11.0
Moderate	5902	62.1	3053	22.4
High	1629	17.2	6157	45.2
# Missing	323		253	
Smoking History				
Yes	195	2.0	1229	3.7
Yes not now	3280	34.1	7146	21.5
Never	6133	63.8	24940	74.9
# Missing	17909		883	
Dietary Status				
Omnivore	13998	53.5	16405	50.9
Vegetarian	12145	46.5	15815	49.1
# Missing	1374		1978	
Cancer reported at baseline				
	1355	5.1	1817	5.7
Coronary Heart Disease				
	2537	9.4	1931	6.0

[1] AMS = Adventist Mortality Study.
[2] AHS = Adventist Health Study.
* Exercise level was measured for males only in AMS, and for the comparison of this table only the males in AHS are included.

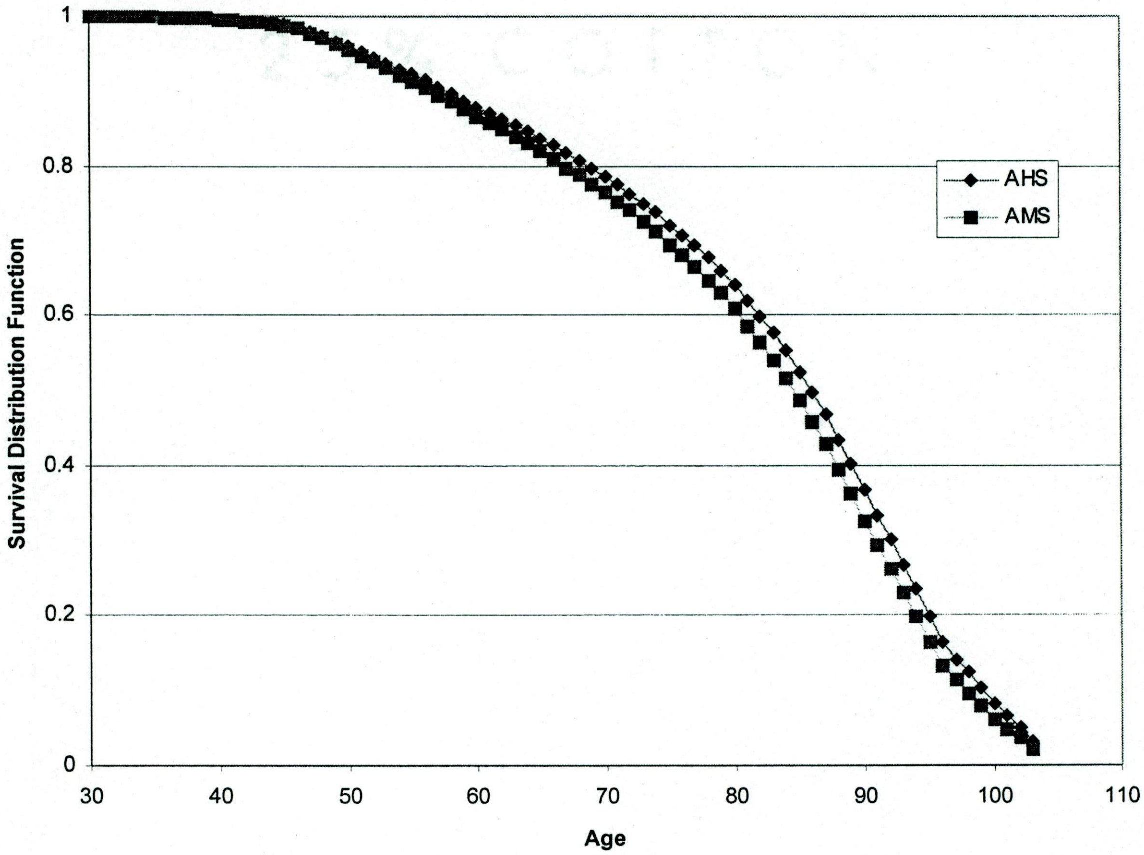

FIGURE 1. Survival curves comparing AMS* (1960-1976) and AHS* (1977-1988) females only computed using the MDLTAP* software without controlling for potential confounders except for competing risks.

* AMS = Adventist Mortality Study.
* AHS = Adventist Health Study.
* MDLTAP: Multivariate Decrement Life table Analysis Program

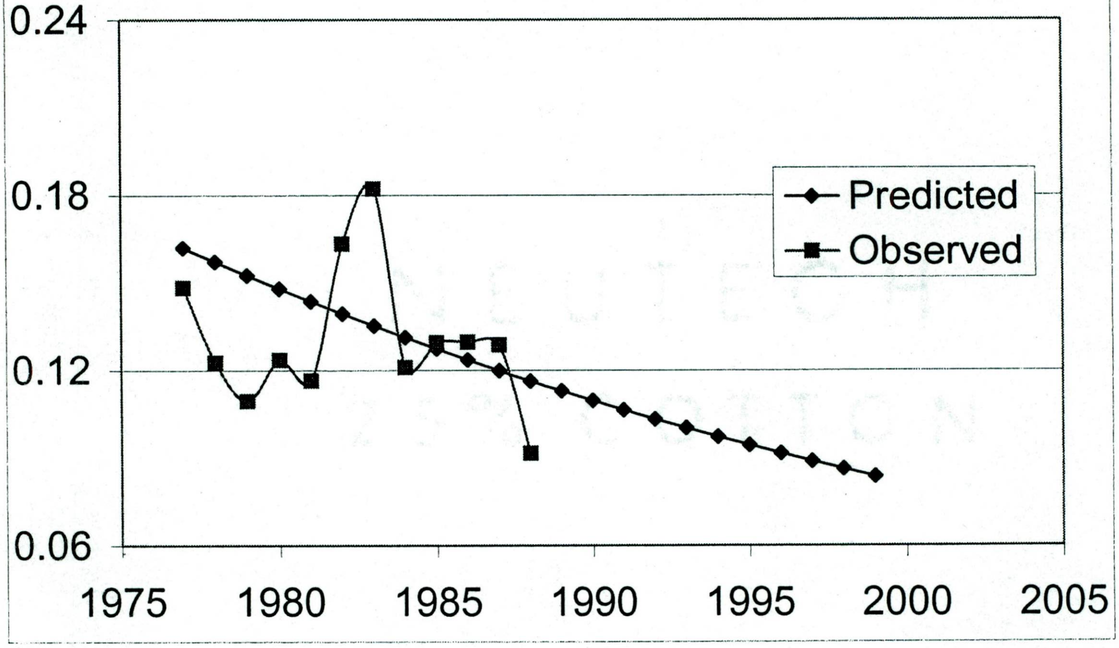

FIGURE 2. Observed Mortality Rates from 1977-1988 and Modeled Mortality Rates from 1977-1999 for the ages 75-79 in Women in the Adventist Health Study.