

The Effect of Biological Age on Survivorship in Midwestern Mennonites

Phillip E. Melton¹, R. Duggirala², MH Crawford¹

¹ Department of Anthropology, University of Kansas, Lawrence
² Department of Genetics, Southwest Foundation for Biomedical Research, San Antonio, TX

Introduction:

According to United States Census Bureau estimates, the elderly (over 65) population of the U.S. will double in size from 35 million to 70 million by 2030 (Figure 1, US Census Bureau 2005). Therefore, understanding the biological processes through which health differences accumulate during the aging process is an important area of gerontological research (Karasiik et al. 2004). Biological age is an estimate of the functional status in reference to chronological age and is defined as the variation in total biological, morphological, and behavioral characteristics observed after reproductive age (Crawford, 2000). In this sense, there are some individuals who appear older and persons who appear to be younger than their chronological age implies. This variation can be viewed as a complex phenotype related to genetic and environmental interactions related to senescence as chronological age increases (Uttley and Crawford 2000). The difference between actual chronological age and predicted biological age may help individuals at risk for chronic degenerative diseases associated with aging. This study examined the effects of biological age on survivorship in two Mennonite communities from the American Midwest in order to determine what biological risk factors that may be affecting these populations.

Objectives:

1. To determine the effect of biological age on all cause mortality in two Mennonite communities from Goessel, Kansas and Henderson, Nebraska.
2. To establish if underlying biological risk factors for all cause mortality were comparable between these two communities, stratified by age and sex.
3. To establish if these results are comparable to previous mortality research within these two communities.

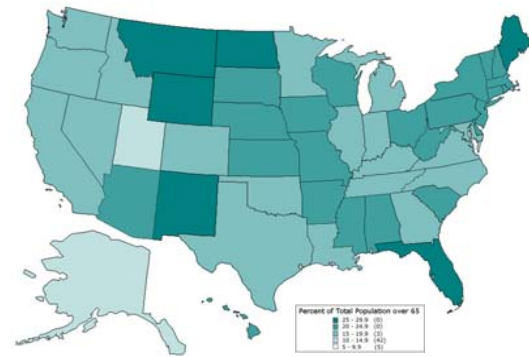


Figure 1: Estimated US Population over 65 in 2030 (US Census Bureau 2005)

Alexanderwhol Mennonite Population Background:

The Mennonites of Kansas and Nebraska (Figure 2) provide an excellent opportunity to investigate the relationship between mortality and biological aging in a homogenous population. Non-Amish Mennonites are an Anabaptist religious denomination that arose in Central Europe during the 1500s. Persecution, migration, and subsequent fissioning of the three major Anabaptist groups (Amish, Hutterite, Mennonite) led to a unique history that had an effect on the genetic variation in these populations (Rogers & Rogers, 2000). The Alexanderwhol Mennonite community immigrated from Russia to the United States in 1874. Shortly after arrival, this Mennonite population split into two groups with one group settling in south central Nebraska (Henderson) while the other group settled in central Kansas (Goessel) (Crawford et al. 1989).

This study investigated the relationship between biological age and mortality in 670 individuals from these two communities in order to determine what biological risk factors may be impacting this community.

Materials and Methods:

Biological Age: Biological age for this research was calculated using forward stepwise multivariate regression and obtained from residuals of actual and predicted age as previously described by Duggirala et al. (2002). Two different data sets were used to obtain these results. The first of these included 33 predictor variables and included data obtained for both Goessel and Henderson communities (G/H). A second data set included 41 predictor variables and included only information from the Goessel community (Duggirala et al., 2002). All of the variables used in determining biological age had previously been determined to be associated with chronological age and sex (Crawford, 2000, Uttley and Crawford 2000).

Mortality Data: Mortality data were collected from three sources for the Goessel, KS community. These included the Kansas Vital Records Office, the Social Security Death Index (SSDI), and the Goessel Mennonite Church Membership Directory. Mortality data for the Henderson Mennonite community was obtained from the SSDI. All data was obtained using queries consisting of first name, surname, and date of birth. Queries involving SSDI also used place of birth to avoid potential conflicts. All data were collected in 2001 and 2002 (Melton et al. 2006).

Risk Factors: A total of 26 biological risk factors were examined for their potential relationship to mortality in these two communities. These data were collected during the original 1980-1981 study period and were measured using automated blood chemistry techniques by Roche laboratories (Wichita, KS).

Analysis of Variance (ANOVA): In order to determine if significant statistical differences occurred between survivors and deceased individuals a series of ANOVAs for continuous variables with unequal means were used and calculated using the Minitab 12.1 (1998) statistical package.

Cox Proportional Hazard Models (Cox, 1972): This analysis was used to calculate risk factors for all-cause mortality. A series of stepwise multivariate models were developed using the equation:

$$h(t) = h_0 \exp\left(\sum_k \beta_k x_k\right)$$

where $h(t)$ is risk of mortality at time t , β_k are the sets of unknown parameters to be estimated, and X_k are the covariates (K) measured at baseline. Data from the mortality sources were used to determine the censoring of observations. The length of the study was from the onset of the Mennonite Study in January, 1980 until June, 2002 and measured in months (270). Parameters in this model were estimated using a forward and backward stepwise model using the PHREG procedure in SAS 9.1 (SAS Software, 2003). Relative risks (RR) are presented in terms of estimated hazard ratios. Covariates used in this model included biological age and blood chemistry markers.

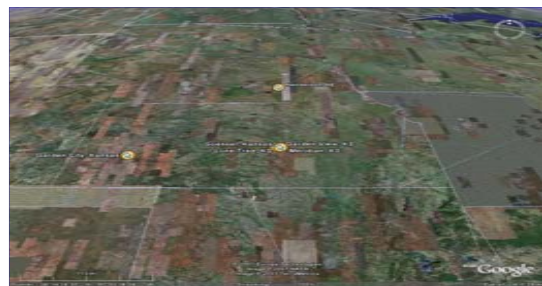


Figure 2: Geographic location of Mennonite Communities in Kansas and Nebraska

Results: Mortality Data by age group

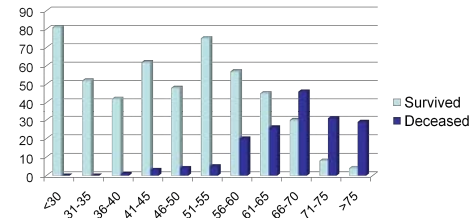


Figure 3: Of the original 670 individuals in the two Mennonite cohorts a total of 156 (23%) were deceased by the end of the study period. A total of 441 individuals were from Henderson where 108 (24%) were deceased and total of 229 individuals from Goessel where 48 individuals (21%) were deceased. This latter mortality data differs significantly from a previously published mortality frequency of 40% for the same community. However, this likely due to the smaller sample size used to construct biological age for Goessel community that included younger participants (Duggirala et al. 2002).

Results: Biological Risk Factors ANOVA

Variable	Deceased	Survivor
Biological Age*	59.09 ± 8.944	49.340 ± 10.11
Uric Acid**	5.405 ± 1.326	4.991 ± 1.338
Glucose*	105.86 ± 26.99	97.62 ± 18.05
Blood Urea Nitrogen (BUN)*	19.245 ± 5.332	16.488 ± 3.990
Cholesterol**	216.60 ± 43.71	206.76 ± 36.61
Total Protein**	6.7094 ± 0.358	6.8079 ± 0.4150
Albumin*	4.1006 ± 0.227	4.2358 ± 0.2677
SGOT**	18.063 ± 6.079	16.551 ± 5.400
Alkaline Phosphatase*	87.04 ± 27.35	74.63 ± 26.31
BUN/Creatinine Ratio*	15.911 ± 4.579	14.584 ± 3.563
Hemoglobin*	15.406 ± 1.495	15.025 ± 1.602

Table 1: Statistically significant results for ANOVA between survivor and deceased individuals in both Goessel and Henderson Mennonite communities. A total of six variables (Biological Age, Glucose, B.U.N., Albumin, Alkaline Phosphate, B.U.N./Creatinine Ratio, and Hemoglobin) were found to be highly statistically significant ($p < 0.0001$). The remaining four variables were statistically significant at $p < 0.001$.

A statistical difference demonstrated by survivors and deceased individuals in B.U.N. B.U.N./Creatinine ratio, uric acid, albumin indicates a relationship between kidney disease and mortality in these populations. This is comparable with other research on mortality in these groups that also indicated these biological variables as risk factors (Uttley and Crawford 2000, Arya et al 2000, Melton et al. 2006).

Results: Cholesterol and Age

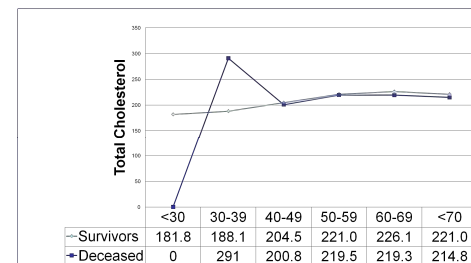


Figure 3: With the exception of a single individual who died in his 30s all other 10 year age cohorts' survivors demonstrate higher total cholesterol than deceased individuals.

Results: Cox Proportional Hazard Analysis

Covariate	Parameter (β)	Risk	95% CI Hazard Ratio	p-value
Goessel/Henderson Biological Age				
Biological Age	0.09799	1.103	1.059-1.149	<.0001
Hgb	0.16844	1.183	1.029-1.361	0.0182
Alkaline Phosphatase	0.00655	1.007	1.001-1.012	0.0204
SGOT	0.07339	1.076	1.031-1.123	0.0008
SGPT	-0.03007	0.970	0.951-0.990	0.0029
Goessel/Henderson Males				
Biological Age	0.12782	1.136	1.070-1.206	<.0001
Cholesterol	-0.01334	0.987	0.977-0.996	0.0076
SGOT	0.06764	1.070	1.008-1.136	0.0265
SGPT	-0.03762	0.963	0.937-0.989	0.0062
T-4	0.15265	1.165	1.012-1.340	0.0329
Goessel/Henderson Females				
Biological Age	0.06296	1.065	1.002-1.132	0.0425
Blood Urea Nitrogen	0.11240	1.119	1.005-1.246	0.0407
SGOT	0.09401	1.099	1.019-1.184	0.0143
Alkaline Phosphatase	0.01370	1.014	1.004-1.023	0.0036
Goessel Biological Age				
Biological Age	0.13656	1.146	1.091-1.204	<.0001
Total Cholesterol	-0.01759	0.983	0.972-0.993	0.0008
SGOT	0.12293	1.131	1.031-1.240	0.0090
GGT	-0.02013	0.980	0.966-0.995	0.0077
LDH	-0.01267	0.987	0.977-0.997	0.0140
Alkaline Phosphatase	0.02141	1.022	1.006-1.038	0.0069
Goessel Females				
Biological Age	0.25437	1.290	1.137-1.463	<.0001
Uric Acid	0.85064	2.341	1.251-4.382	0.0078
Cholesterol	-0.05016	0.951	0.922-0.981	0.0016
Triglycerides	0.01800	1.018	1.006-1.030	0.0031
SGOT	0.62635	1.871	1.332-2.627	0.0003
SGPT	-0.18989	0.827	0.714-0.959	0.0116
LDH	-0.04649	0.955	0.926-0.984	0.0030
Goessel Males				
Biological Age	0.14529	1.156	1.064-1.256	0.0006
Triglycerides	-0.02062	0.980	0.960-1.000	0.0457
Alkaline Phosphatase	0.05781	1.060	1.024-1.097	0.0010
HDL	-0.08190	0.921	0.852-0.996	0.0398

Table 2: In order to establish the relationship between biological age and all-cause mortality patterns in these communities a series of Cox-hazard models were conducted. All models demonstrated that increased biological age was associated with mortality. However, unlike a previous study of mortality in this community (Melton et al. 2006), biological age did not demonstrate a high relative risk, indicating that it may be a more efficient covariate in epidemiological studies than chronological age. The biological risk factor covariate that is found in all but one of the Cox models is serum glutamic-oxaloacetic transaminase (SGOT, AST), which is an enzyme present in the liver and heart. This enzyme is elevated when there is insult to either of these two organs and may be an important marker for understanding cardiovascular diseases in these populations.

The covariate with the highest relative risk was uric acid (2.23) in Goessel females and may be related to the presence of renal disease in this population (Melton et al. 2006)

Key Points:

1. Biological age is more efficient than chronological age in elucidating potential biological risk factors associated with mortality patterns in these communities.
2. Based on these Cox hazard models (Table 2) significant differences between biological risk factors in males and females are apparent with some overlap indicating a shared biological history.
3. Analogous to a previous mortality study on the Goessel Mennonite community (Melton et al. 2006), increased levels of total cholesterol appear to lower the risk of mortality in these communities (Figure 4).

Acknowledgements:

This research was sponsored by grants from the National Institute of Aging (#AG01646). We would like to thank all individuals who participated in this study.



For further information, references or for a PDF version of this poster: Contact: Phillip E. Melton via e-mail: pmelton@ku.edu