Centenarians' Children Have Favorable Health Outcome in China
-- effects of genetic inherence and its interactions with environment on healthy aging

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Abstracts:

We present a comparative analysis of the health outcome and health risk factors between 417 centenarians' children who are also elderly themselves and their peers with compatible gender, age and other socioeconomic characteristics living in the same longevity areas or in different ordinary areas. We test the two null hypotheses: $\mathbf{H_1}$: The children of centenarians are healthier than their peers due to genetic heritability; $\mathbf{H_2}$: The interactions between the genetic propensity and social, behavior, and community environmental factors also play important roles in determine health outcome at old ages. The preliminary results indicate that, controlling for age, gender, ethnicity, childhood conditions, adulthood SES, family/social support and health practice, the children of centenarians have significantly better health outcome measured by IADL, depression symptom, cognitive ability, number of chronic diseases, self-rated health and self-rated life satisfaction. More findings concerning the genetic-environment interaction are forthcoming given the data collection was just completed recently.

INTRODUCTION

Background and significance

The population of China, which consists of about one-fifth of the world's total population, is aging rapidly due to rapid declines in both fertility and mortality. Under the medium mortality assumption, the total number of elderly aged 65+ in China is estimated to increase dramatically from 101 million in 2007 (7.7% of the total population) to 352 million in 2050 (24.1%); there were about 13 million Chinese oldest-old aged 80+ in 2005, but this number will climb extraordinarily to more than 100 million in 2050 (Zeng and George, 2008). The average annual rate of increase of oldest-old in 2000-2050 is about 4.4 percent in China, twice that of the U.S. and other industrialized countries (U.N. 2007). CLHLS data show that the prevalence of Activities of Daily Living (ADL) disability increases dramatically with age, from <5% at ages 65-69 to 20% at ages 80-84 and 40% at ages 90-94; the oldest-old also consume services and medical care at a much higher rate than younger elderly (Torrey,1992). However, China and many other developing countries where populations are aging rapidly are much behind in economic and social welfare development, and face the serious challenges of "becoming aging before rich," with little preparation for the aging society.

Population aging accompanied with rapid growth of the oldest-old is unavoidable. A fundamental question is whether it will be accompanied by a compression or an expansion or a dynamic equilibrium of the period of disability and morbidity among the elderly persons (Fries 1980; Gruenberg 1977; Manton 1982). Is it possible to realize morbidity compression, or at least dynamic equilibrium, among the elderly while the human lifespan is increasing and the number of elderly (especially oldest-old) is rapidly growing? Why do some people survive to advanced ages with good health while others suffer severe disability and diseases? The answers to these questions will determine quality of life not only for the elderly but for all members of the society. So far, however, there are few answers to these important questions.

Recent research has shown that, in addition to direct genetic transmission, the interactions between genetic and environmental factors also play a crucial role; environmental factors may regulate gene expression via DNA methylation and histone modification, which then influences health and longevity of the elderly (IOM, 2006; Tsankova et al., 2007). Research shows that the effect of genes becomes increasingly significant with advancing age (Perls et al., 2002). Drawing on 1,100

males from the National Longitudinal Study of Adolescent Health, Guo et al. (2008) demonstrated that the genetic effects of DRD2 and MAOA genes on delinquency and violence are conditional and interact with family processes, school processes, and friendship networks. Based on intensive literature reviews and investigations/discussions including several workshops, the Committee of Institute of medicine of U.S. Academy Sciences concluded in their recent widely-cited report: "Few diseases or conditions are caused purely by genetic factors; most are the result of interactions between genetic and environmental factors. Therefore, to expand our knowledge of how to improve the health of individuals and populations, **it becomes imperative to conduct research that explores the effects of interactions among social, behavioral, and genetic factors on health** (IOM, 2006: 15). However, research on this crucially important topic are very much underdeveloped, and especially very little is known about the effects of interactions of genetic factors with social and behavioral factors on healthy at old ages in developing countries, because the relevant issues are very complex and there are few good, large sources of data with needed genetic information available. Clearly, there is an urgent public health need to investigate factors that underlie successful aging among the elderly, which will increase rapidly over the next fifty years with high costs of medical care and substantial burden of disability.

A focus on extreme cases is often a good way to gain research leverage at reasonable expense, and thus investigation on exceptionally successful aging people including centenarians and their families especially their offspring is an efficient way to learn how to reach goal of healthy aging. This is particularly relevant in developing countries mainly because the centenarians in developing countries are more robust as compared to their Western counterparts -- they are highly selected by severe life conditions and high mortality in the past. The proportion of centenarians in developing countries is much lower than in developed countries. For example, there were about five centenarians per million in China in the 1990s, compared with 50 per million in Western Europe (Jeune, 1995). According to recent period data, the probability of surviving from age 52.5 (mean age of our middle-age controls) to age 100 was 0.38% and 1.05% for Chinese men and women, respectively, which was slightly less than one-fifth of that in the U.S. The chance of surviving to age 100 was much lower for the cohorts born 100 years ago than what is implied by the recent life table, since mortality level in old China was much higher than that today. Clearly, oldest-old in developing countries are much more selected than their counterparts in the West because they are the survivors of the brutal mortality regimes of the past when famine and starvation operated on birth cohorts of many millions. Thus, research on the centenarians and their children is particularly useful for identifying the healthy longevity related genetic inherence and its interactions with behavior, lifestyle, family and community environment factors.

A brief literature review

-- mostly done and to be summarized a bit later

Hypothesis to be tested

In this study, we will compare the health outcome and health risk factors between centenarians' children who are also elderly and their peers with same sex and similar age and other socioeconomic characteristics to test the follow two null hypotheses:

$\mathbf{H_1}$: The children of centenarians are on average healthier than the ordinary people with same age, gender and similar socioeconomic characteristics, due to genetic heritability;

$\mathbf{H_2}$: The interactions between the genetic propensity (measured by whether the subjects is a biological child of a centenarians or none of his or her first-degree relatives ever survived to age 85 or higher in this study) and self-behavior, life style, personality, social/family connection and support, and community conditions, etc., also play important and significant roles in determine health outcome at old ages.

DATA SOURCE AND METHOD

The current analysis of this study is based on recently collected survey interviews data from the respondents living in eight designated "longevity areas" in China that is part of the Chinese Longitudinal Healthy Longevity Survey (CLHLS). The survey interviews, village-based health exam with blood/urine sample collection by medical personnel in the longevity areas was carried out from February to June 2009, supported by our R01 competitive supplement grant awarded by the NIH on February 1, 2009 and the Chinese matching funds. These eight selected longevity areas are among the eleven "Chinese Longevity Areas (CLA)" professionally evaluated and formally designated by the Chinese Society of Gerontology (CSG). The CSG criteria for designating a CLA, which are publicly released and widely disseminated in China include density of centenarians and nonagenarians, life expectancy, and a series of within-area consistency checks including general health status and environmental quality. The locations of the longevity areas in China are diverse, and include locales in Jiangsu, Hubei, Hunan, Sichuan, Henan, Shangdong, Hainan, Guandong, Guanxi provinces. The sample size of our eight-longevity areas data collection project, which is a sub-project of ongoing CLHLS. is 4,167 participants, including 684, 737, 801, 800, 1,029 centenarians, nonagenarians, octogenarians, young-old aged 65-79 and middle-age adults aged 40-64.

Among the 4,167 participants, 417 individuals who are biological children of the interviewed centenarians (each centenarians has only one child included in this study) and their 560 compatible not-related neighboring peers are the subjects of this study. The criteria to choose peers living in the same sampled county or city district as comparative group of centenarians' children based on the available information in our CLHLS 2008-09 dataset are:

(1) Both parents died before age 85, and none of his or her siblings survived to age 85 or higher.
(2) Number of male and female peers in one area should be roughly close as much as possible to the # of male and female children of the centenarians (regardless of centenarians' sex).
(3) All peers and children of centenarians are between ages 60 and 80.

The age-gender distributions of the sample data used in this paper are shown in Table 1.

We employ the multivariate regression models to explore the differentials of health outcome between centenarians' children and their neighboring peers, controlling for the potential confounding factors.

Dependent variables (health outcome) considered are:
Physical health: ADL, IADL, # of self-reported major chronic diseases;
Mental health: cognitive function measured by MMSE, depressive symptoms;
Subjective well-being: self-rated life satisfaction and health;

Note: A bit later, we will also compare the major biomarkers of health between centenarians' children and their neighboring peers. We are not able to do it before Sept. 21, because we just received the biomarkers lab tests results about 10 days ago.

Independent variables considered:
Whether the respondent is a centenarian's child or a neighboring peer who have no any first-degree relatives survived to age 85 and over.

Controlling covariate: Age, sex, Han or minorities, education, occupation and other potential confounding factors (see Tables 3).

Interactions term:
(whether the respondent is a centenarians' child) x (the social/behavior risk factors)

RESULTS AND DISCUSSION

The preliminary results are shown in Table 3. The results indicate that, controlling for age, gender, ethnicity, childhood conditions measured by 7 variable, adulthood SES measured by 6 variables, family/social connections and support measured by 4 variables and health practice measured by 3 variables (See Table 3 for details), the children of centenarians have significantly better health outcome measured by IADL, depression symptom, cognitive ability, number of chronic diseases, presence or absence of any major chronic diseases, self-rated health and self-rated life satisfaction. The estimate for the ADL is not statistically significant, perhaps due to the fact that only 2.9% of the centenarians' children and 3.2% of the peers were ADL disabled in the samples.

The preliminary results clearly indicate that the genetic inheritance is significantly associated with health at ages 60-80 in China, and our first hypothesis is supported.

We will continue to perform the analysis to test the second hypothesis that the interactions between genetic propensity inherited from parents and self-behavior/life style/SES may also play significant roles in determine the health outcome at old ages.

We will also randomly select the already-interviewed subjects who have no any first-degree relatives survived to age 85 or higher and who are of same sex and similar ages and socioeconomic characteristics (as compared with the centenarians' children) from other 935 non-longevity areas (counties/cities) surveyed in the CLHLS 2008-09 wave. Comparative analysis among centenarians' children and their neighboring peers in the eight longevity areas and the compatible subjects in the other 935 non-longevity areas will provide insights about effects of interactions between genetic, social, behavior and community environmental factors on health at old ages.

-- to be completed a bit later

Table 1. Sample distribution by age and gender of children of centenarians (CC) and their neighboring peers

	Men			Women			Two sex combined		
Age	CC	Peer	Total	CC	Peer	Total	CC	Peer	Total
60-64	82	57	139	29	49	78	111	106	217
65-69	87	73	160	26	61	87	113	134	247
70-74	88	63	151	20	62	82	108	125	233
75-80	62	98	160	23	97	120	85	195	280
Total	319	291	610	98	269	367	417	560	977

Table 2. Sample distributions by the study variables and the covariates

	Centenarian children	Peers
Samples: Number of centenarians' children and the comparable peers	417	560
Health outcomes		
% ADL disabled	2	3
% IADL disabled	17	33
% having depressive symptoms	26	40
Average score of Cognitive test [a]	0.90	0.85
% receiving full-points on Cognitive test	25	12
Average number of major chronic diseases	0.70	0.96
% with at least one chronic disease	48	60
% poor self-rated health	37	54
% poor self-reported quality of life	39	48
Demographics		
Mean age of the elderly respondents	69.02	70.97
% of male elderly respondents	76	52
% of Non-Han ethnicities among the elderly respondents	6	8
Childhood SES conditions		
% elderly respondents born in an urban area	6	9
% elderly respondents' father's occupation is white-collar	4	2
% elderly respondent's both parents alive when he/she was age 10	92	84
% elderly respondents got adequate medication when ill in childhood	30	28
% elderly respondents frequently went to bed hungry in childhood	77	78
% first-born	23	44
Mean of the arm length [b]	51.79	50.65
SES conditions in Adulthood		
% currently living in an urban area	27	29
% primary lifetime job is white collar	13	5
% family household economic condition is good	16	11
% financially independent	71	48
% had 1+ years of schooling	78	57
% medical expenses primarily covered by public funds or insurance	10	9
Family/social connection and support		
% currently married	85	71
Average number of living children	3.48	3.75
% with close proximity to children	92	92
Mean of the Social and Leisure Activity Index [c]	2.58	2.43

Health practice		
% smoked in the past five years	46	33
% consumed alcohol in the past five years	39	29
% regularly exercised in the past five years	32	32

[a] Score of Cognitive test =" No. of Correct answers/25", where 25 is the total questions of cognitive test.

[b] Arm length is measured by the length from processus styloideus ulnae to acromion.

[c] Social and Leisure Activity Index is defined as a summation of seven dichotomized variables of gardening, personal outdoor activities (excluding exercise), raising poultry or pets, reading, playing cards/mah-jong, listening to the radio/watching TV, and participating in some organized social activities (excluding religious participation).

Table 3. Estimates of the coefficients of the multivariate models (the figures in parentheses after the coefficient estimates are standard errors)

	ADL disabled		IADL disabled		Depressive symptoms		Cognitively ability	
Centenarians' children (Peers)	0.42	(0.49)	-0.47	(0.19) *	-0.33	(0.16) *	0.51	(0.21) *
Demographics								
Age	0.19	(0.05) ***	0.13	(0.02) ***	0.02	(0.01)	-0.03	(0.02) +
Male (female)	-0.60	(0.55)	-0.14	(0.23)	-0.06	(0.19)	-0.05	(0.27)
Non-Han ethnicity (Han)	---		-0.46	(0.37)	0.30	(0.27)	-1.02	(0.48) *
Childhood SES conditions								
Born in urban (rural) area	-0.28	(1.12)	-0.08	(0.39)	0.07	(0.30)	0.25	(0.36)
Father's occupation was white-collar (no)	0.62	(1.29)	0.10	(0.61)	0.16	(0.48)	-0.18	(0.50)
Both parents alive when the respondent was age 10 (no)	0.09	(0.63)	0.25	(0.25)	-0.17	(0.20)	-0.23	(0.30)
Got adequate medication when ill in childhood (no)	-1.68	(0.81) *	-0.88	(0.22) ***	-0.42	(0.17) *	0.67	(0.20) ***
Frequently went to bed hungry in childhood (no)	0.17	(0.59)	-0.11	(0.22)	-0.24	(0.18)	0.30	(0.23)
Born as the first birth (no)	-0.94	(0.48) +	0.06	(0.18)	-0.09	(0.15)	-0.17	(0.22)
Top 20% of the arm length (other 80%)	-0.75	(0.70)	-0.44	(0.23) +	0.13	(0.18)	0.09	(0.23)
Adulthood SES conditions								
Urban resident (rural)	0.66	(0.50)	-0.59	(0.22) **	-0.37	(0.18) *	-0.19	(0.24)
Primary lifetime job is white collar (no)	---		0.01	(0.40)	-0.52	(0.34)	0.73	(0.29) *
Family economic condition is good (no)	0.01	(0.71)	-0.65	(0.30) *	-0.28	(0.22)	0.25	(0.26)
Financially independent (no)	-0.65	(0.51)	-0.78	(0.19) ***	0.01	(0.16)	0.13	(0.23)
Has 1+ years of schooling (no)	0.13	(0.52)	-0.36	(0.20) +	-0.11	(0.17)	1.91	(0.36) ***
Medical expenditures covered by public funds or insurance (no)	1.13	(0.73)	0.87	(0.31) **	0.05	(0.27)	0.06	(0.32)
Family/social connection and support								
Currently married (no)	1.05	(0.54) +	0.23	(0.20)	-1.03	(0.17) ***	-0.11	(0.27)
Number of living children	-0.09	(0.14)	0.04	(0.06)	-0.01	(0.05)	-0.02	(0.08)
High proximity to children (low)	-1.15	(0.74)	-0.64	(0.33) +	-0.59	(0.26) *	-0.50	(0.34)
Social and leisure activity index	-0.64	(0.22) **	-0.22	(0.08) **	-0.09	(0.07)	0.18	(0.08) *
Health practice								
Smoked in the past five years (no)	-0.86	(0.64)	-0.15	(0.22)	-0.42	(0.18) *	-0.09	(0.22)
Consumed alcohol in the past five years (no)	0.12	(0.61)	-0.28	(0.22)	-0.27	(0.18)	0.16	(0.22)
Regularly exercised in the past five years (no)	0.31	(0.53)	0.48	(0.21) *	0.34	(0.17) *	0.46	(0.21) *
_cons	-15.0	(4.19) ***	-8.05	(1.34) ***	-0.53	(1.07)	-1.45	(1.48)
_cons (2)	---		---		1.07	(1.08)	---	
Log likelihood	-90		-428		-761		-369	
Pseudo R2	0.26		0.23		0.08		0.19	
# of observation	833		977		962		977	

Notes:

(1) + p<0.1, *p<0.05, **p<0.01, ***p<0.001.

(2) The category in the parentheses after each variable listed in the first column is the reference group.

(3) Dependent variable "depressive symptoms" uses Ordered Logistic Regression Method, where 0=neither "feel fearful or anxious" nor "feel lonely and isolated"; 1= either "feel fearful or anxious" or "feel lonely and isolated"; 2= both "feel fearful or anxious" and "feel lonely and isolated".

Table 3. Estimates of the coefficients of the multivariate models (the figures in parentheses after the coefficient estimates are standard errors) -- continued

	number of chronic diseases		Presence/absence of chronic disease		poor self-rated health		poor self-rated life satisfaction	
Centenarians' children (Peers)	-0.21	(0.07) **	-0.42	(0.15) **	-0.80	(0.15) ***	-0.49	(0.15) **
Demographics								
Age	0.01	(0.01) +	0.02	(0.01)	0.01	(0.01)	0.01	(0.01)
Male (female)	-0.03	(0.09)	-0.03	(0.19)	0.10	(0.19)	0.37	(0.19) +
Non-Han ethnicity (Han)	-0.43	(0.13) ***	-0.88	(0.28) ***	-0.93	(0.30) **	0.14	(0.28)
Childhood SES conditions								
Born in urban (rural) area	-0.04	(0.13)	0.11	(0.29)	-0.09	(0.29)	-0.42	(0.30)
Father's occupation was white-collar (no)	-0.15	(0.20)	-0.12	(0.42)	0.46	(0.44)	-0.04	(0.48)
Both parents alive when the respondent was age 10 (no)	-0.05	(0.10)	-0.23	(0.21)	0.01	(0.21)	0.01	(0.21)
Got adequate medication when ill in childhood (no)	-0.03	(0.07)	-0.05	(0.16)	-0.46	(0.16) **	-0.08	(0.16)
Frequently went to bed hungry in childhood (no)	0.09	(0.08)	0.29	(0.17) +	0.17	(0.17)	-0.11	(0.18)
Born as the first birth (no)	0.00	(0.07)	-0.10	(0.15)	-0.18	(0.15)	-0.03	(0.15)
Top 20% of the arm length (other 80%)	-0.07	(0.08)	-0.20	(0.17)	-0.04	(0.17)	-0.02	(0.18)
Adulthood SES conditions								
Urban resident (rural)	0.04	(0.08)	0.07	(0.17)	0.04	(0.17)	-0.40	(0.17) *
Primary lifetime job is white collar (no)	0.11	(0.13)	0.12	(0.27)	0.11	(0.28)	-0.03	(0.29)
Family economic condition is good (no)	-0.03	(0.10)	0.06	(0.21)	-0.92	(0.22) ***	-1.65	(0.26) ***
Financially independent (no)	-0.09	(0.07)	-0.25	(0.15)	0.05	(0.16)	0.39	(0.16) *
Has 1+ years of schooling (no)	0.12	(0.08)	0.13	(0.17)	0.23	(0.17)	-0.16	(0.17)
Medical expenditures covered by public funds or insurance (no)	0.22	(0.12) +	0.22	(0.26)	0.14	(0.26)	0.01	(0.27)
Family/social connection and support								
Currently married (no)	-0.08	(0.08)	-0.14	(0.17)	0.05	(0.17)	0.15	(0.17)
Number of living children	0.01	(0.02)	0.04	(0.05)	0.04	(0.05)	-0.04	(0.05)
High proximity to children (low)	-0.09	(0.13)	-0.36	(0.27)	-0.34	(0.27)	-0.49	(0.27) +
Social and leisure activity index	-0.02	(0.03)	0.00	(0.06)	-0.18	(0.06) **	-0.11	(0.06) +
Health practice								
Smoked in the past five years (no)	-0.01	(0.08)	0.01	(0.17)	0.00	(0.17)	0.13	(0.17)
Consumed alcohol in the past five years (no)	-0.17	(0.08) *	-0.23	(0.16)	-0.17	(0.17)	-0.52	(0.17) **
Regularly exercised in the past five years (no)	0.20	(0.08) **	0.46	(0.16) **	0.10	(0.16)	0.56	(0.17) ***
_cons	0.30	(0.49)	-0.80	(1.04)	0.34	(1.05)	0.14	(1.06)
Log likelihood	---		-640		-630		-618	
Pseudo R2	0.05		0.05		0.07		0.08	
# of obs	977		977		977		977	

Notes:

(1) + p<0.1, *p<0.05, **p<0.01, ***p<0.001.

(2) The category in the parentheses after each variable listed in the first column is the reference group.

(3) The analysis with dependent variable "# of chronic diseases" uses OLS Regression Method, while others use Logistic Regression Method.