Author's response to reviews

Title: Chronic Diseases are Important Determinants of Self-reported Health among Older Adults

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Author's response to reviews: see over
Dear Editor and Reviewers,

We have documented below our responses to your questions and comments. We very much appreciate your helpful feedback. We hope that the revised paper meets with your approval.

**Dr. Terry Lum**  
**Comment:** The background and literature review section is very fragmented.

**Response:** We thank you for the feedback and have revised these sections accordingly (see pages 4-6).

**Comment:** How did the researchers know that a participant had a chronic disease?

**Response:** Chronic disease was self-reported. In the revised version of our paper, we clarified it this way:

“There are 14 illnesses or conditions reported: high blood pressure, diabetes, heart disease (does not include palpitations), stroke (cerebral haemorrhage), cancer or malignant tumour, bronchitis/emphysema/pneumonia/lung disease/asthma/other lower respiratory tract diseases, arthritis/rheumatism, gastric ulcer/stomach ailment, liver or gall bladder disease, hip fracture, cataract, kidney disease (including stones), gout and spinal/vertebrae spur. All the chronic diseases were self-reported in response to the question “Have you ever had this illness?”

**Comment:** It is unclear why the authors need to recode SRH into a dummy variable for poor health, instead of using it as an ordinal variable.

**Response:** Thank you very much for the suggestion. We are in agreement that keeping SRH as an ordinal variable would obtain more information and we reanalyzed using Stereotpye Ordinal Logit model, which is better than Ordinal Logit model because the Stereotpye Ordinal Logit is not constrained by the parallel regression assumption. The outcome measure SRH was originally measured on a 5-point scale: excellent, good, average, not so good, and poor. Since the percentage of “poor” in the sample is as low as 3.42%, we merged “not so good” and “poor” into one scale and we found the results of Stereotpye Ordinal Logit model are not dramatically different (See Table 2). In order to keep the results brief, we reported only the results of the binary dependent variable.

**Comment:** It is not clear why household size was used as an indicator for life stress.

**Response:** We cited two references on using household size as a life stress factor [16, 25].

**Comment:** Please specify how the combined effects on p.8 were tested.

**Response:** Certainly. We have added clarification at the end of the Statistical Analysis section as follows:
“Finally, after the estimation of life stress factors, health behaviour factors, genetic factors and adjusted disease status on poor health in Model 3, linear combination of coefficients is performed to assess the combined effect of individual factors. The linear combination is constructed from a set of terms by multiplying each term by a constant and adding the results [38]. The result of linear combination shows significant association with SRH in each domain—chronic disease, life stress, health behaviour and APOE gene.”

**Comment:** On p.9, the p value for APOE4 is 0.086 (Table 1). Since the sample size is relatively large, there is no reason to use 0.10 as the cutoff. Again, in the logistic regression analyses, the p value for APOE is 0.054 (model 1) and 0.053 (model 2), and should be regarded as insignificant. Conceptually there is no reason to believe that the APOE (unknown to older people) would directly affect self-reported health. If there is any effect, it is likely due to unmeasured health conditions associated with the APOE.

**Our Response:** Recently, many findings suggest that the APOE4 allele may play a multifaceted role in exacerbating a number of health outcomes associated with human aging, including mortality\(^1\), decline of cognitive function\(^3\), decreased functional status among elderly participants without dementia [19,20], and an earlier age of onset of Alzheimer’s disease and Parkinson’s disease [21,22].

**Comment:** The finding that cigarette smoking and older age were associated with lower risk of heart disease is against what we have known in many years of research. It is very likely that there are unknown issues in the data collection or statistical analysis. Please elaborate and explain what is going on.

**Response:** We now do so:

“Interestingly, cigarette smokers were less likely to report poor SRH (28.99%, P=0.012), even though cigarette smoking has been linked to poor health. Further examination of the data revealed that the proportion of smokers was appreciably lower in the population with heart disease. As shown in the independent variables, smoking behaviour was assessed for the six months prior to the interview. Therefore, people with heart disease may have been advised to stop smoking and did so some time before the interview.”

**Reviewer Dr. Karen Cheung**

**Comment:** It is good the authors have highlighted the research niche in this paragraph; however, they fail to define the physical health conditions and presume

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that the physical health conditions correspond to the presence of chronic diseases. Physical health can be measured by health problems, past and present diseases, hospitalization, etc. They should articulate that they focus on the presence of chronic diseases (past or present?) and the previous studies only focused on the context of Singapore or other Asian societies, such as HKSAR, NOT in Taiwan. How about any other related study that has been done in the context of Taiwan?

Response: Your point is well taken. We revised this section:

“The association of physical health conditions with SRH is well established but poorly understood. A thorough literature review indicates that previous studies provide evidence that self-assessments take into account physical health conditions including limited function, problems such as bodily pain and poor sleep, and hospitalizations [26, 27, 28, 29]. However, only a limited number of studies have incorporated chronic health conditions into the analytic framework so far. Chronic diseases tend to be prevalent among older adults. Illnesses such as coronary heart disease, diabetes, and a history of depression are associated with poor SRH, especially among the elderly people [30]. Therefore, our study specially focused on the association of experience of chronic diseases on SRH.”

All the chronic diseases were self-reported in response to the question “Have you ever had this illness?” Each condition was coded 1 if an individual said yes; 0 otherwise.

The effect of chronic diseases on SRH cannot be ignored among older people in Taiwan. We also reference Wang HP’s article.

Comment: The authors should provide at least a paragraph or a footnote clearly describe the content and the quality of the dataset even though the study design has been published elsewhere as shown in references #13 and 23. For instance the age range of the participants (mean and SD), the sampling method, the survey locations in Taiwan, the variables collected from the structured questionnaire, the survey period starting from when and ending from when…. In addition, the authors mentioned that each interview was conducted by a local public health nurse. What exactly is a local public health nurse? Are they registered nurses? Only one nurse did the whole interview, the medical examination including the physical examination and biospecimen collection? …How were the 12-hour urine sample and blood specimen collected and stored? In addition, the authors mentioned “Of the 1,713 selected Survey of Health and Living Status respondents, 1,497 (87.4%) participated in the Social Environment and Biomarkers of Aging Study interview and 1,023 of them completed the interview and the medical examination.” How were these 1,023 participants selected? Please provide the reference number of the ethical approval for this dataset and by which institute and organization and year of approval and the data user agreement (the date of data downloaded, etc.). As some readers may not familiar with this dataset, it is important that the authors should provide more basic information about the data and URL prior to data analysis. More related references for the data are needed as well.

Response: Thank you for this feedback. In response, we have added a description with more detail about the dataset:
Data utilized for this study are from the Social Environment and Biomarkers of Aging Study (SEBAS) in Taiwan, a national subsample selected randomly from the 1999 Taiwan Longitudinal Study of Aging (TLSA). The original TLSA survey began in 1989 with a multi-stage probability sample: 1) 56 townships (primary sampling units or PSUs) were randomly selected, 2) within each PSU, blocks were randomly selected, and 3) within each block, two eligible respondents were selected. Both PSUs and blocks were selected with probabilities proportional to the size of the population in the sampling unit [34].

The SEBAS 2000 was fielded from July through December 2000 using 27 original PSUs and 10 new townships; all respondents residing in a given PSU were selected for interviews. Data was collected from face-to-face interviews using a structured questionnaire, followed by a physical examination and biospecimen collection. This project was approved for human subjects by the institutional review boards at Princeton University, RAND, Georgetown University and the Bureau of Health Promotion in Taiwan.

The SEBAS 2000 in-home interview was conducted by a public health nurse, who was well-known and highly-respected in the local area. The questionnaire covered chronic conditions, physical functioning, psychological well-being, cognitive capacity, health services utilization and social networks/support. The interviewer then evaluated the respondent’s health in order to determine whether his or her health was suitable for blood drawing. The following health conditions disqualified respondents: living in an institution, seriously ill, catheter or diapery, on kidney dialysis, or presenting with other health conditions that would preclude a blood draw.

Among the 1,497 interview respondents, 7 percent were rejected for health reasons; 24 percent declined to participate; and 1,023 received physical exams at a nearby hospital several weeks later. The age range of the participants was 54–91 (Mean=68.33; SD=8.49); 63 percent of the sample were 65 or older; and 58 percent were males.

The night before the scheduled hospital appointment, a survey staff member together with an interviewer delivered the urine collection container to the respondent’s home. On the morning of the hospital appointment, a member of the survey staff picked up the participant at his or her home, collected the 12-hour urine specimen, and accompanied the participant to the hospital.

During the hospital visit, participants were asked about their health history, family disease history, health-related behaviours, and current long-term medications. Blood pressure and anthropometric measurements (i.e., respondent’s height, weight, waist and hip circumference) were performed and a blood specimen was taken for measurement of biomarkers.

Union Clinical Laboratories (UCL) took responsibility for immediate shipment of the specimens to their base in Taipei, followed standard laboratory protocols for conducting assays, and provided the results to the Bureau of Health Promotion (BHP, in the Department of Health of Taiwan) within two weeks. One genetic marker, Apolipoprotein E (APOE), was also obtained by blood specimen using the polymerase chain reaction amplification refractory mutation system (PCR-ARMS).
and polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) analysis. Data quality evaluations conducted during and after the fieldwork by BHP indicate that SEBAS rendered reliable data [35].”

The reference id is 114633. We’ve got the letter from Office of Human Research Ethics of University of North Carolina at Chapel Hill on December 13, 2012 as follows: “This is the letter you will need for your data use agreement. It is not a rejection letter, but a statement that the IRB has reviewed your application and your study does not require our oversight.” User guide shows this project was approved for human subjects by the institutional review boards at Princeton University, RAND, Georgetown University and the Bureau of Health Promotion in Taiwan.

And we’ve got the mailed Disk of dataset from Inter-university Consortium for Political and Social Research in university of Michigan in February 2013.

Comment: Why only focus on these four kinds of chronic diseases to measure overall physical health among the elderly? How did the question ask the participants about the chronic diseases have that they ever suffered? Was the chronic disease referred to self-report or medically diagnosed? ….More justifications and explanations are needed.

Response: We have expanded this section to explain why these four chronic diseases were chosen to measure overall physical health among the elderly.

“There are 14 illnesses or conditions reported: high blood pressure, diabetes, heart disease (does not include palpitations), stroke (cerebral haemorrhage), cancer or malignant tumour, bronchitis/ emphysema/ pneumonia/ lung disease/ asthma/ other lower respiratory tract diseases, arthritis/rheumatism, gastric ulcer/stomach ailment, liver or gall bladder disease, hip fracture, cataract, kidney disease (including stones), gout and spinal/vertebrae spur. All the chronic diseases were self-reported in response to the question “Have you ever had this illness?” Each condition was coded 1 if an individual said yes; 0 otherwise. For some of the diseases, the percentage having the illness is less than 10%. For example, the percentage for cancer is 3.15%, 3.28% for stroke, 7.86% for gout, 8.89% for liver disease and 9.16% for kidney disease. Among the seven diseases with percentages higher than 10%, hypertension was underreported through evaluation of the SEBAS 2000 self-reports by examination of consistency across waves or validation with laboratory results. Spinal/vertebrae spur, cataracts and arthritis/rheumatism did not have a significant impact on SRH through logistic regression and did not change the results substantially. Therefore, diabetes (BD), heart disease (HD), gastric ulcer (UL) and chronic obstructive pulmonary disease (COPD) were used to measure overall physical health in this study, and they may have an intermediate impact on SRH.”

Comment: Since the authors are the secondary data users, they have to clearly explain how reliable the data are. How was the genetic analysis done? A proper reference and citation is needed.

Response: We have added a description with more detail in the Dataset section. See p. 3 of this response letter.
**Comment:** Did the authors say the 1999 earthquake occurred in the whole territory of Taiwan or just a location or community? …Any death tolls…? Secondly using the number of people living together (i.e., household size) and whether or not a respondent lives in a bad (poor or very poor) neighbourhood as measures of life stress are problematic because we don’t know to what extent the participants would encounter life stress. What is the cutoff of the household size being considered as life stress? By the same token, how bad would the neighbourhood have to be to be considered stressful? For the finances variable, the authors need to provide the exact question they asked participants. For family separation, as the authors cite in reference #13, they should provide more accurate information about the number of elderly people moved from mainland China to Taiwan. And in the literature review, they should highlight that life stress can be also measured by family separation due to political instability or wars.

**Response:** We have added more information about these independent variables:

“Life stress is measured by traumatic events and chronic stress. Experiencing housing damage during the 1999 earthquake, which was a year before the survey was conducted, is used to measure life stress due to a traumatic event. The 7.3 Ms or 7.6-7.7 Mw earthquake occurred in Jiji, Nantou County, Taiwan on 21 September 1999. It was the greatest disaster in the late 21st century Taiwan. Some 2,415 people were killed, 11,305 injured. The question asked was “Any damage or loss to the house in which you usually lived prior to earthquake?”

Living conditions were measured by the number of people living together, with the question “How many people usually live in this house (including yourself)?” We cited two references on using household size as a life stress factor [16, 25].

Community living was measured by self-reported neighbourhood environment. The question was “What do you think about your neighborhood and area around where you live? Is it very good, good, average, poor or very poor?” Responses were coded 1 if the assessment was “poor” or “very poor”; 0 otherwise.

Financial condition was measured by the question “Do you (and your spouse) have enough money or any difficulty meeting monthly living expenses or other expenditures?” Possible responses were: “enough money, with some left over; just enough money, no difficulty; some difficulty; much difficulty.” Responses were coded 1 if the individual selected one of the first two items, 0 otherwise.

As many as 2.2 million elderly people moved from mainland China to Taiwan during the Chinese Civil War 1946-1949 [36], and they have been separated from their original families on mainland China for more than half a century. Consequently, almost all the mainland participants were older than 55 since they were forced to come to Taiwan either as an adult or as a child with parents. We believed that this group of elderly may have suffered from chronic stress as a result.”

We also added to the literature review as this reviewer suggested. Thanks.

“In addition, life stress can be also measured by family separation due to political instability or wars. Previous research has indicated that those who were forced to
leave mainland of China for Taiwan during the Chinese Civil War may have suffered from chronic stress after being isolated from their original families for half a century [16].”

**Comment:** Are you referring to past- or current-smoking? Similar problems result from the abuse of alcohol or a poor physical exercise regime. The authors need to provide the exact question for these health behaviours.

**Response:** Sure. We added more detailed information about these health-related behaviours.

“Health behaviours studied included smoking, drinking, physical exercise and diet. Based on the two questions—“In the past six months, did you smoke?” and “If smoke every day, on average ___ cigarettes?”—we categorized smoking as: non-smoker, <=20 cigarettes per day and 20+. For the question “On average, how many times do you exercise each week?”, we categorized “number of times per week” into <=1, 2–5 and 6+. Other health behaviours such as alcohol use, daily milk intake and diet were recoded into binary variables measured by the following questions: “In the past six months, did you drink alcohol?” “Do you drink milk every day?” And, “Do you eat at least three servings of vegetables and two servings of fruit every day?”

**Comment:** On p. 8, “Obesity, defined as body mass index (BMI) greater than 25--weight/height (kg/m)2--was also included to measure physical condition.” A proper citation and reference is required.

**Response:** We found an error in the original version of our paper. Obesity was defined as body mass index (BMI) greater than 23 instead of 25. The descriptive analyses of BMI are as follows: mean=20.4, min=15.4, max=25, SD=1.51. We also have added the citation of Choo V’s article for BMI.

**Comment:** Multilevel models (also hierarchical linear models, nested models, mixed models, random coefficient, random-effects models, random parameter models, or split-plot designs) are statistical models of parameters that vary at more than one level (Bryk and Raudenbush, 2002). So which exact model did they use? Random-effects models or hierarchical models?

**Response:** We have made this part more clear. Thanks.

“Because the SEBAS survey design involved multi-stage cluster sampling, multi-level random-effects logistic regression was used to examine the association of SRH and chronic health conditions, the APOE4 gene, life stress factors and health behaviours by correcting for potential intra-cluster relatedness.

We first estimated a multiple random-effect logistic regression model of the APOE4 allele, life stress factors and health behaviours with poor SRH while controlling for socio-demographic factors (Model 1). We then incorporated chronic diseases to see how the association of these factors in Model 1 changed (Model 2).”

**Comment:** Comment: Did the authors use “listwise deletion” to handle the missing data? Please specify.
Response: We did use “listwise deletion” to handle the missing data and made it clear in the revised version of our paper. Thanks.

“By listwise deletion, of the 1,023 individuals who completed the survey, 1,005 subjects without missing values were kept.”

Comment: On p. 10: “Based on final model (Model 3) adjusting for potential endogeneity, we tested for combined effect of four group variables-- chronic diseases, life stress factors, health behaviours and APOE4 gene, which showed significant association with SRH. We found that chronic diseases combined together are mostly associated with SRH (OR=3.26, P=3.5 x10-15); …Should add “Table 4” in the above paragraph, if needed.

Response: We have done so.

“Based on Model 3 and adjusting for potential endogeneity, we tested for the combined effect of four group variables—chronic diseases, life stress factors, health behaviours and the APOE4 gene—which showed significant association with SRH in Table 4. We found that chronic diseases combined are mostly associated with SRH (OR=3.26, P=3.5 x10-15).”

Comment: It seems those descriptive analyses (i.e. mean, min, max, SD) are redundant in the table. To make it simple, Table 4 should suppress as the results also described in page 10.

Response: We have simplified Table 4, deleting descriptive analyses.

Comment: The authors failed to explain why they used these four major chronic diseases in their analysis, not others. How about other chronic diseases such as cancer and stroke? Would they also play important roles in explaining the variation of poor SRH? The effects of other independent variables such as ADL difficulties and intergenerational support could play important roles in explaining the variation on SRH.

Response: We added more information about chronic diseases in this study. See p. 5 of our response. We agree that several measures such as ADL difficulties and intergenerational support could play important roles in explaining the variation on SRH and should be considered. However, the dataset does not contain relevant variables of intergenerational support; and only 3.1% respondents underlying ADL difficulties.

Comment: The results presented in this paper have a potential to contribute the literature and provide a better understanding of SRH. The findings are also very close to what Zhang et al. (2008) found in their paper, “Apolipoprotein E polymorphism, life stress and self-reported health among older adults”. The authors should discuss thoughtfully the similarities and differences between their findings and Zhang’s results. For instance, they found the apolipoprotein E4 (APOE4) allele was significantly associated with poor SRH overall (odds ratio (OR) 1.54, 95% confidence interval (CI) 1.03 to 2.35), but the association was stronger in women (OR 2.13, 95%
CI 1.17 to 3.88) than in men. In the present paper, it seems the gender doesn’t play a role.

**Response:** We were enlightened by Zhang and colleagues’ work since we use the same dataset and discuss the same topic—self-reported health among the elderly. Their study’s strength is that it includes APOE genetic marker from a population-based survey and showed the association of SRH and genetic factors at the population level. Before their study, few studies associated SRH with a specific genetic marker. We kept this improvement on interdisciplinary research, an the genetic marker also showed a significant association with SRH again.

Zhang’s study mentions that chronic conditions are known to influence SRH; however they did not include information on chronic disease status in the model because some chronic diseases may be affected by the APOE gene or by socio-behavioural factors. Their concern is that including chronic disease information in the same model may cause endogeneity, consequently reducing the statistical power of the results. Our strength is that our paper integrated chronic disease information in the analytic model of SRH, adjusted the potential endogeneity and assessed the relative importance of chronic diseases, the APOE4 gene, life stress factors and health behaviours.

Our study also found the apolipoprotein E4 (APOE4) allele was significantly associated with poor SRH overall (odds ratio (OR) 1.52, 95% confidence interval (CI) 1.00 to 2.33), but we did not discuss the gender difference of the association. Instead, we focus on the change of the association before and after integrating chronic disease information, as well as the relative importance of four groups of factors—chronic diseases, the APOE4 gene, life stress factors and health behaviours. Our future research may take a look at the battle of sexes in relation to SRH over the life course and overall health outcomes.

**Dr. Fengyu Zhang**  
**Comment:**  
- “life stress or life stresses factors; life stressful event or stressful life events”  
- “Times of exercise per week” in the Table is confusing, but I do see “number of exercise per week in the main text”  
- “Data was analyzed using multilevel logistic regression model while controlling for unobserved heterogeneity at community level”  
- In conclusion, our data suggested that ….  

**Response:** All the expressions mentioned above have been revised and we have also made a major effort to improve the writing of our manuscript.