BMJ Open

Trajectory of self-rated health on the incidence of frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-049795
Article Type:	Original research
Date Submitted by the Author:	02-Feb-2021
Complete List of Authors:	Chu, Wei-Min ; Taichung Veterans General Hospital, Department of Family Medicine; National Yang-Ming University, School of Medicine Ho, Hsin-En; Taichung Armed Forces General Hospital, Department of Family medicine; Chung Shan Medical University, Institution of Medicine Yeh, Chih-Jung; Chung Shan Medical University, School of Public Health Hsiao, Yu-han; Taichung Hospital, Department of Family Medicine; Chung Shan Medical University, School of Public Health Hsu, Pi-Shan; Taichung Veterans General Hospital, Department of Family Medicine Lee, Shu-Hsin; Chung Shan Medical University, School of Nursing Lee, Meng-Chih ; Taichung Hospital, Department of Family Medicine; National Health Research Institutes, Instiute of Population Sciences
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

TITLE

Trajectory of self-rated health on the incidence of frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

AUTHOR and AFFLITATION

Wei-Min Chu[1,2,3], Hsin-En Ho[4,5,6], Chih-Jung Yeh[7], Yu-han Hsiao[7,8], Pi-Shan Hsu[1], Shu-Hsin Lee[9,10], Meng-Chih Lee[8,11]

[1]Department of Family Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

[2]School of Medicine, Chung Shan Medical University, Taichung, Taiwan

[3]School of Medicine, National Yang-Ming University, Taipei, Taiwan

[4]Department of Family medicine, Taichung Armed Force General Hospital, Taichung, Taiwan.

[5]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan

[6]National Defense Medical Center, Taipei, Taiwan

[7]School of Public Health, Chung Shan Medical University, Taichung, Taiwan

[8]Department of Family Medicine, Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan

[9]School of Nursing, Chung Shan Medical University, Taichung, Taiwan

[10]Center for Education and Research on Geriatrics and Gerontology, Chung Shan Medical University, Taichung, Taiwan

[11]Instiute of Population Sciences, National Health Research Institutes, Miaoli County, Taiwan

Corresponding author:

Meng-Chih Lee, M.D., Ph.D., MPH

Department of Family Medicine

Taichung Hospital, Ministry of Health and Welfare

Taichung, Taiwan

Postal Address: No. 199, Sec. 1, Sanmin Rd., West Dist., Taichung City 403,

Taiwan (R.O.C.)

Phone: 04-22294411

mengchihlee@gmail.com

Word counts: 2429

ABSTRACT

Objectives: Self-rated health (SRH) is an assessment and predictor of health based on an individual's general condition, however evidence of the value of SRH for predicting frailty remains scarce for older Asian adults. This study aimed to evaluate the relationship between self-rated health (SRH) score trajectory and frailty among elderly individuals in Taiwan.

Design: An 8-year retrospective cohort study.

Setting: Data were retrieved from the Taiwan Longitudinal Study on Aging between 1999 to 2007.

Participants: Respondents aged 53 to 69-years-old who were not frail or disabled in 1999 (*n*=1956).

Primary and Secondary Outcome Measures: Frailty was defined using the Fried criteria. The group-based trajectory model was used to estimate SRH trajectories. Logistic regression analysis was used to examine the associations between changes in SRH and frailty.

Results: Four SRH trajectory classes were identified across the 8-year follow-up: 232 participants (11.9%) were classified into the constantly poor SRH group, 1123 (57.4%) into the constantly fair SRH group, 335 (17.1%) into the constantly good SRH group, and 266 (13.4%) into the good-to-fair SRH group. After adjusting for

gender, age, level of education, income, social participation, health behaviors and major comorbidities, age, poor income satisfaction, unemployment and constantly poor SRH were associated with increased risk of frailty, while constantly good SRH [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with reduced risks of frailty.

Conclusions: Constantly poor SRH is associated with an increased risk of frailty in older age. SRH in older adults should be recognized as a predictive tool for future frailty. Diet and exercise interventions may help to prevent frailty among high-risk elderly individuals with constantly low SRH.

Strengths and Limitation of study:

1. To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty among Asian population based on a nationally representative sample.
2. Reporting bias could happen because all data were collected through self-reporting and not measured objectively.
3. Frailty was defined according to a modified phenotype definition, assessed by using questionnaire data.

Key words: self-rated health, frailty, trajectory, elderly

BACKGROUND

Aging has become a serious challenge globally in both Western and developed Asian countries. The World Health Organization define an aged society as a population in which people over 65-years-old comprise more than 14% of the total population. According to the Department of Health of Taiwan, the proportion of people over 65 in Taiwan increased from 8.6% to 10.7% between 2000 and 2010 [1]. The Department of Development predict this number will rise to 20% by 2027 [2], which would represent the fastest rate of aging in the world. Due to the rapidly aging population, the annual crude mortality rate for Taiwanese citizens over 65 increased from 46.9% to 68.5% between 1981 to 2010 [1, 3].

Many key indicators can be used to predict the future health of the elderly, including the self-rated health (SRH) score. SRH is an assessment and predictor of health based on an individual's general condition and subjective feelings of their physical, psychological and social wellbeing, combined with objective measurements of health. Several studies have demonstrated consistency between SRH and individual health status and shown SRH can predict future mortality, disability and other adverse health outcomes [4-11]. In recent years,frailty has been proven to be one of the most important key indicators of the health of the elderly in recent decades. Frailty is a geriatric condition characterized by increased vulnerability and decreased capacity to

maintain homeostasis [12]. Frailty in later life has been proven to lead to a number of adverse health outcomes and a poor quality of life [13-17]. As frailty can be addressed by proper recognition and treatment, such as diet and exercise, it is important to identify risk factors for frailty in older adults [18]. Several studies have explored the relationship between SRH and frailty[19-21]. A population-based study of more than 2,000 healthy participants conducted in Finland by Huohvanainen et al. (2016) found that SRH in midlife could predict frailty, prefrailty and mortality in later life [22]. However, most of previous studies were implemented in Western countries, evidence of the value of SRH for predicting frailty remains scarce for older Asian adults, especially from long-term observation. The aim of this study was to explore the long-term relationships between SRH trajectories and future frailty in older Taiwanese adults using a national population cohort study.

METHODS

Data sources

We retrieved data from the Taiwan Longitudinal Study in Aging (TLSA), a population-based, national representative study initiated by the Bureau of Health Promotion of Taiwan, and the Population Studies Center and the Institute of Gerontology at the University of Michigan in the United States. Data are collected from systematically selected representative samples of the Taiwanese population, including institutionalized elderly people. Personal interviews are conducted by

highly trained interviewers. To ensure high data quality collection, careful supervision is provided during data collection and data processing is conducted by a professional data entry company.

The TLSA was started in 1989 and six waves of data collection had been completed by 2007. For this study, we used the 1999 sample, which included 2,130 subjects aged 53–69-years-old in 1999. We followed-up this cohort for 8 years and used data from 2007 to analyze outcomes. The Population Studies Center at the University of Michigan reviewed the representativeness of the completed sample; the analysis showed that the sample was highly representative, with a 90.6% response rate. Details of the study design have been described elsewhere [23-25].

Study group identification

We included the 1999 sample, which included 2,130 subjects aged 53–69-years-old in 1999. Individuals who had developed frailty in 1999 or who had any functional disability in 1999 were excluded from the study. Thus, 1,956 subjects were included in the final analysis.

Research variables

For each eligible subject, we gathered data in 1999 on age, gender, level of education, marital status, income level, SRH, social participation, employment status, smoking, alcohol consumption, and chronic diseases. Level of education was classified into four groups: illiterate (0 years), elementary school (1–6 years), junior to senior high school (7–12 years), and college or above (> 12 years). Income level was determined by asking individuals how they felt about their income level. The possible answers were *very satisfied*, *satisfied*, *fair*, *unsatisfied*, and *very unsatisfied*. We classified the

income levels as ‘‘good ’’ (rated *very satisfied*, *satisfied*) “fair” (rated *fair*) or ‘‘poor’’ (*unsatisfied* or *very unsatisfied*). SRH was determined by asking individuals how they rated their current health. Possible answers were *excellent*, *good*, *fair*, *poor*, and *very poor*. We classified the individuals into three groups based on SRH: good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*). Individuals who had either paid or voluntary work or who participated in community activities were considered as having social participation. The individuals were classified into two groups based on employment status in 1999: normally employed and unemployed. The number of chronic diseases suffered by each individual was recorded, including hypertension, diabetes, cardiovascular disease, stroke, cancer, chronic respiratory diseases, arthritis or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and kidney diseases.

Data regarding frailty was collected in 2007 as the outcome measure. Frailty was defined according to the Fried criteria [12]. Individuals who exhibited at least three of five traits (i.e., shrinking, weakness, exhaustion, slowness, and low physical activity) were considered frail. Individuals with only one or two of the five traits were regarded as pre-frail. We used substitute evaluations for these five domains because we retrieved data from questionnaires, and this modified frailty definition have been used broadly and published before with validity [26-28]. The parameter decreased appetite was used instead of body weight loss to represent nutritional status. Participants who reported poor appetite often in the previous week were classified as having the trait of shrinking. For mobility, we used walking/moving in and around the house instead of gait speed. Participants who had difficulty or were unable to walk a distance of 200 to 300 m were considered slow. For strength, we used the parameter of lifting heavy groceries instead of hand grip strength. Participants who had difficulty or were unable to carry 12 kg of groceries were considered weak. For physical activity, we used the

duration of leisure time/physical activities per week instead of the level of physical activity. Participants who did not take a walk, hike or jog, do gardening, or participate in other outdoor activities at least once or twice a week were considered to have low activity. We used the questionnaire of the Center for Epidemiologic Studies Depression Scale (CES-D) to determine the level of energy. Participants who reported, "*I could not get going*" or "*I felt everything I did was an effort*" often or most of the time in the previous week were considered exhausted. Due to nearly all elderly approaching end-of-life have functional disability and frailty, we regarded those who deceased during study period as having frailty in our study[29]

Statistical analysis

A group-based analysis model was applied to determine the SRH trajectories. We employed the Bayesian Information Criterion to identify the most appropriate model groups[30]. Previous geriatric research studies have used this model[23, 27, 28, 31, 32]. For the descriptive analysis, we used analysis of variance and the chi-square test to compare continuous and categorized variables, respectively. Logistic regression was used to analyze the relationship between SRH trajectories and frailty, with adjustments for age, gender, level of education, income level, marital status, number of chronic diseases, social participation, smoking, alcohol consumption, and employment status. Statistical significance was set at $p < 0.05$. All data were analyzed using SPSS (version 22.0, IBM, Chicago, IL, USA).

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting of our research. However, Taiwan Association of Gerontology and Geriatrics, who listens to and stands for geriatric patients, will help with dissemination plans of our research results.

RESULTS

Table 1 shows the descriptive data for all subjects. A total of 1,956 subjects with an average age of 61.46 years were included the final analysis. Most subjects had 1-6 years of education, had a fair income level, and were married. The average number of chronic diseases was 1.21. There were 232 participants (11.9%) in the constantly poor SRH group, 1123 participants (57.4%) in the constantly fair SRH group, 335 participants (17.1%) in the constantly good SRH group, and 266 participants (13.6%) in the good-to-fair SRH group (Figure 1). Age distribution, sex, level of education, income level, social participation, marriage status, alcohol consumption, and unemployment status were significantly different between each of the four SRH trajectory classes.

Univariate logistic regression of the associations between the demographic and clinical characteristics and frailty are presented in Table 2. All variables, except for marital status and smoking behavior, were significantly associated with frailty.

Table 3 illustrates multivariate logistic regression regarding the relationship between SRH trajectories and frailty. Afteradjustments for relevant factors, including age, gender, level of education, income level, social participation, alcohol consumption behavior, number of chronic diseases, and unemployment status, logistic regression analysis revealed age, poor income satisfaction, unemployment and constantly poor SRH was associated with an increased risk of frailty [OR 3.091, 95% CI (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with a decreased risk of frailty compared to constantly fair SRH.

DISCUSSION

In this population cohort study, we created a trajectory-based model for 1,956 Taiwanese adults aged 53–69-years-old in 1999. Based on their SRH trajectories over the 8-year follow-up, the cohort could be classified into four groups: constantly poor SRH, constantly fair SRH, constantly good SRH, and good-to fair SRH. Multivariate logistic regression demonstrated an elevated risk of frailty for the constantly poor SRH group. We also observed significant protective effects for the groups with constantly good SRH and good-to-fair SRH.

To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty. Our results are consistent with previous studies which investigated SRH at single time point. Huohvanainen et al. (2016) found that poor SRH in midlife was associated with prefrailty, frailty and mortality in later life after 26 years of follow-up in Finland [22]. A short-term study of 22 institutionalized elderly individuals by Gijzel et al. (2017) found that variance in the SRH score time series was significantly higher in frail participants across physical, mental and social domains [33]. Baddour et al. (2019) reported that SRH correlated moderately with frailty and found that good-to-excellent SRH was predictive of non-frail status and preservation of activities of daily living (ADL) [34].

We believe this study provides strong evidence of a causal relationship between SRH and frailty. First, this study was a well-designed cohort study with nationally representative subjects and we excluded those who had disability and frailty at baseline. Second, a significantly elevated risk of frailty was observed in the poor SRH group, even after adjusting for confounding factors related to frailty, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and employment status in multivariate regression

analysis. Third, in analysis of the relationship between SRH trajectory and frailty, the constantly poor SRH group had an elevated risk of frailty, and significant protective effects were observed for the constantly good SRH and good-to-fair SRH groups. Thus, a causal relationship may exist between SRH and frailty.

However, some studies stated that the relationship between SRH and frailty may be in different direction. Pinto et al. discovered that self-rated health is a mediator variable between physical and mental health, including frailty with life satisfaction[35]. The reasons could be that low level of daily activities prevent elderly from participating community activities, thus lead to poor subjective health and life satisfaction. Our study showed that constantly poor SRH would lead to increased incidence of frailty, and we believed that this causal relationship was true, because several studies have identified mechanisms that may possibly link SRH to frailty. Dysregulation of neuroendocrine processes and the immune system may lead to further vulnerability and lower resistance [36], and previous studies showed that inflammatory responses are related to SRH. Christian et al. (2011) found that poorer SRH was associated with elevated serum inflammatory markers, such as IL-6 and CRP, among generally healthy older adults [37]. These inflammatory markers have been associated with frailty. Low physical activity could also be a factor. Granger et al. (2017) reported that high levels of physical activity were positively associated with self-rated 'good health' status in European adolescents [38]. Additionally, Savela et al. (2013) found that a higher level of physical activity from midlife onwards was strongly associated with a lower risk of frailty in old age [39]. These studies suggested that the relationship between SRH and frailty is real under multifactorial mechanism. Further investigation is warranted to explore the intervention to prevent frailty for those people whose SRH are poor, and its cost-effectiveness.

Strengths and Limitations

This study has several advantages. First, this eight-year retrospective cohort study was based on a nationally representative sample with extremely high survey response rates. The database was based on a large, randomly selected population; thus, external validity is high. Second, our analysis of SRH trajectory as a predictor of frailty strengthens the evidence of a causal relationship between SRH and frailty. Moreover, the study design of trajectory-based model analysis minimized the possibility of misclassification bias, as SRH can change over time. Third, we adjusted for numerous confounding factors, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and unemployment status. However, this study also has several limitations. First, all data were collected through self-reporting and not measured objectively, which could result in reporting bias. Additionally, proxy respondents completed the follow-up questionnaire for subjects who were severely ill, which may possibly generate reporting bias. Secondly, we used serial SRH reports, though some participants may have experienced low SRH due to unidentified causes. For example, a subject may feel poor SRH due to health reasons. However, we attempted to address this possibility by excluding people with frailty and/or disability at baseline, as both frailty and/or disability could substantially affect the outcome. The design of this study also helped to eliminate the possibility of reverse causality. We also adjusted for a number of major chronic diseases to reduce the influence of bias. Because the study was conducted in Taiwan, generalisation of the results to other ethnic group should be made with caution.

CONCLUSION

Poor SRH in older adults is associated with a higher risk of frailty in the future, and constantly poor SRH possesses more risk of frailty in the elderly. Moreover, maintaining stable, good SRH may help to prevent frailty in later life. Thus, we suggest governments should design and implement programs to regularly screen SRH in older adults.. Further studies are necessary to define practical strategies to reduce the risk of disability and death among older adults with constantly poor SRH and thus improve the quality of life of elderly people.

FIGURE

Figure 1. Flow chart of the study design1

Flow chart showing the patient inclusion and exclusion processes, and the process of group-based trajectory analysis. SRH, self-rated health.

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

After group-based trajectory analysis, there were 232 participants (11.9%, group 1) in the constant poor SRH group, 1123 participants (57.4%, group 2) in the constant fair SRH group, 335 participants (17.1%, group 3) were in the constant good SRH group, and 266 participants (13.6%, group 4) were in the good to fair SRH group.

ABBREVIATIONS

SRH Self-rated Health

TLSA Taiwan Longitudinal Study on Aging

CES-D Center for Epidemiologic Studies Depression Scale

ADL Activities of Daily Living

DECLARATIONS

Ethics approval and consent to participate

The current study was approved by the Institutional Review Board of Health Promotion Administration, Ministry of Health and Warfare. (Approval no. BHP-2007-002). Before recruitment, all participants received a proper explanation about the study and provided consent for inclusion in the study. Participants who could read and write signed the written consent documents; those who could not read nor write impressed the name stamps or handprint with the assistance of their family members. In addition, legal guardian/representative provided consent on behalf of the participants with cognitive decline or stroke

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are not publicity available, but are available from the corresponding author on reasonable request with the permission of the Ministry of Health and Welfare, Taiwan.

Competing interests

The authors declare no conflicts of interests.

Funding

This work was supported by Ministry of Health and Welfare, Taiwan (Grant number: M06M2346 awarded to M.-C.L.).

Author Contributions

Each author's individual contributions: Meng-Chih Lee conceived of the study and supervised all aspects of its implementation. Wei-Min Chu completed the analyses and drafted the content. Yu-han Hsiao, Shu-Hsin Lee and Pi-Shan Hsu assisted with the study design and revised the content. Hsin-En Ho and Chih-Jung Yeh assisted with the statistical analysis and revised the content. All authors helped to conceptualize ideas, interpret findings, and review drafts of the manuscript.

Acknowledgements

We thank our colleagues from Chun Shan Medical University, Taichung, Taiwan for providing supports in statistical analysis. The sponsor has no role in the design, methods, subject recruitment, data collections, analysis and preparation of paper.

REFERENCES

1. Department of Health EY T: **Taiwan public health report 2017**. 2018.
2. National Development Council T: **Population projections for Taiwan: 2018-2065**. 2018.
3. Department of Health EY T: **The statistical analysis of mortality in 2010**. 2011.
4. Wu S, Wang R, Zhao Y, Ma X, Wu M, Yan X, He J: **The relationship between self-rated health and objective health status: a population-based study**. *BMC public health* 2013, **13**:320.
5. Bopp M, Braun J, Gutzwiller F, Faeh D: **Health risk or resource? Gradual and independent association between self-rated health and mortality persists over 30 years**. *PloS one* 2012, **7**(2):e30795.
6. Giltay EJ, Vollaard AM, Kromhout D: **Self-rated health and physician-rated health as independent predictors of mortality in elderly men**. *Age and ageing* 2012, **41**(2):165-171.
7. Halford C, Wallman T, Welin L, Rosengren A, Bardel A, Johansson S, Eriksson H, Palmer E, Wilhelmsen L, Svardsudd K: **Effects of self-rated health on sick leave, disability pension, hospital admissions and mortality. A population-based longitudinal study of nearly 15,000 observations among Swedish women and men**. *BMC public health* 2012, **12**:1103.
8. Jylha M: **What is self-rated health and why does it predict mortality? Towards a unified conceptual model**. *Social science & medicine (1982)* 2009, **69**(3):307-316.
9. Mavaddat N, Kinmonth AL, Sanderson S, Surtees P, Bingham S, Khaw KT: **What determines Self-Rated Health (SRH)? A cross-sectional study of SF-36 health domains in the EPIC-Norfolk cohort**. *Journal of epidemiology and community health* 2011, **65**(9):800-806.
10. Sargent-Cox KA, Anstey KJ, Luszcz MA: **The choice of self-rated health measures matter when predicting mortality: evidence from 10 years follow-up of the Australian longitudinal study of ageing**. *BMC geriatrics* 2010, **10**:18.
11. Stenholm S, Pentti J, Kawachi I, Westerlund H, Kivimaki M, Vahtera J: **Self-rated health in the last 12 years of life compared to matched surviving controls: the Health and Retirement Study**. *PloS one* 2014, **9**(9):e107879.
12. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G *et al*: **Frailty in older adults: evidence for a phenotype**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2001, **56**(3):M146-156.
13. Bartley MM, Geda YE, Christianson TJ, Pankratz VS, Roberts RO, Petersen RC: **Frailty and Mortality Outcomes in Cognitively Normal Older People: Sex Differences in a Population-Based Study**. *Journal of the American Geriatrics Society* 2016, **64**(1):132-137.
14. At J, Bryce R, Prina M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JJ, Salas A, Sosa AL *et al*: **Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study**. *BMC medicine* 2015, **13**:138.

15. Lin SY, Lee WJ, Chou MY, Peng LN, Chiou ST, Chen LK: **Frailty Index Predicts All-Cause Mortality for Middle-Aged and Older Taiwanese: Implications for Active-Aging Programs**. *PloS one* 2016, **11**(8):e0161456.
16. Kulmala J, Nykanen I, Hartikainen S: **Frailty as a predictor of all-cause mortality in older men and women**. *Geriatrics & gerontology international* 2014, **14**(4):899-905.
17. Vermeiren S, Vella-Azzopardi R, Beckwee D, Habbig AK, Scafoglieri A, Jansen B, Bautmans I: **Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis**. *Journal of the American Medical Directors Association* 2016, **17**(12):1163.e1161-1163.e1117.
18. Walston J, Buta B, Xue QL: **Frailty Screening and Interventions: Considerations for Clinical Practice**. *Clinics in geriatric medicine* 2018, **34**(1):25-38.
19. Franse CB, van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H: **Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens**. *PloS one* 2017, **12**(11):e0187946.
20. Lau BH, Kwan J, Cheung KS: **Overlap of Frailty, Comorbidity, Disability, and Poor Self-Rated Health in Community-Dwelling Near-Centenarians and Centenarians**. *Journal of the American Geriatrics Society* 2016, **64**(4):900-901.
21. Obaidi MA, Giri S, Mir N, Kenzik K, McDonald AM, Smith CY, Gbolahan OB, Paluri RK, Bhatia S, Williams GR: **Use of self-rated health to identify frailty and predict mortality in older adults with cancer. Results from the care study**. *Journal of Clinical Oncology* 2020, **38**(15_suppl):12046-12046.
22. Huohvanainen E, Strandberg AY, Stenholm S, Pitkala KH, Tilvis RS, Strandberg TE: **Association of Self-Rated Health in Midlife With Mortality and Old Age Frailty: A 26-Year Follow-Up of Initially Healthy Men**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2016, **71**(7):923-928.
23. Liang J, Wang CN, Xu X, Hsu HC, Lin HS, Lin YH: **Trajectory of functional status among older Taiwanese: Gender and age variations**. *Social science & medicine (1982)* 2010, **71**(6):1208-1217.
24. Pu C, Tang GJ, Huang N, Chou YJ: **Predictive power of self-rated health for subsequent mortality risk during old age: analysis of data from a nationally representative survey of elderly adults in Taiwan**. *J Epidemiol* 2011, **21**(4):278-284.
25. Martin LG, Zimmer Z, Hurng BS: **Trends in late-life disability in Taiwan, 1989-2007: the roles of education, environment, and technology**. *Popul Stud (Camb)* 2011, **65**(3):289-304.
26. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Nijhuis-van der Sanden MW: **Outcome instruments to measure frailty: a systematic review**. *Ageing research reviews* 2011, **10**(1):104-114.
27. Hsu HC, Chang WC: **Trajectories of frailty and related factors of the older people in Taiwan**. *Experimental aging research* 2015, **41**(1):104-114.
28. Ho HE, Yeh CJ, Chu WM, Lee MC: **Midlife Body Mass Index Trajectory and Risk of Frailty 8 Years Later in Taiwan**. *The journal of nutrition, health & aging* 2019, **23**(9):849-855.
29. Covinsky KE, Eng C, Lui LY, Sands LP, Yaffe K: **The last 2 years of life:**

functional trajectories of frail older people. *Journal of the American Geriatrics Society* 2003, **51**(4):492-498.

30. Nagin DS, Odgers CL: **Group-based trajectory modeling in clinical research**. *Annual review of clinical psychology* 2010, **6**:109-138.

31. Dhana K, van Rosmalen J, Vistisen D, Ikram MA, Hofman A, Franco OH, Kavousi M: **Trajectories of body mass index before the diagnosis of cardiovascular disease: a latent class trajectory analysis**. *European journal of epidemiology* 2016, **31**(6):583-592.

32. Murayama H, Liang J, Bennett JM, Shaw BA, Botoseneanu A, Kobayashi E, Fukaya T, Shinkai S: **Trajectories of Body Mass Index and Their Associations With Mortality Among Older Japanese: Do They Differ From Those of Western Populations?** *American journal of epidemiology* 2015, **182**(7):597-605.

33. Gijzel SMW, van de Leemput IA, Scheffer M, Roppolo M, Olde Rikkert MGM, Melis RJF: **Dynamical Resilience Indicators in Time Series of Self-Rated Health Correspond to Frailty Levels in Older Adults**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2017, **72**(7):991-996.

34. Baddour NA, Robinson-Cohen C, Lipworth L, Bian A, Stewart TG, Jhamb M, Siew ED, Abdel-Kader K: **The Surprise Question and Self-Rated Health Are Useful Screens for Frailty and Disability in Older Adults with Chronic Kidney Disease**. *Journal of palliative medicine* 2019, **22**(12):1522-1529.

35. Pinto JM, Fontaine AM, Neri AL: **The influence of physical and mental health on life satisfaction is mediated by self-rated health: A study with Brazilian elderly**. *Archives of gerontology and geriatrics* 2016, **65**:104-110.

36. Lutgendorf SK, Costanzo ES: **Psychoneuroimmunology and health psychology: an integrative model**. *Brain, behavior, and immunity* 2003, **17**(4):225-232.

37. Christian LM, Glaser R, Porter K, Malarkey WB, Beversdorf D, Kiecolt-Glaser JK: **Poorer self-rated health is associated with elevated inflammatory markers among older adults**. *Psychoneuroendocrinology* 2011, **36**(10):1495-1504.

38. Granger E, Williams G, Di Nardo F, Harrison A, Verma A: **The relationship between physical activity and self-rated health status in European adolescents: Results of the EURO-URHIS 2 survey**. *European journal of public health* 2017, **27**(suppl_2):107-111.

39. Savela SL, Koistinen P, Stenholm S, Tilvis RS, Strandberg AY, Pitkala KH, Salomaa VV, Strandberg TE: **Leisure-time physical activity in midlife is related to old age frailty**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2013, **68**(11):1433-1438.

TABLES

Table 1. Demographic and clinical characteristics of the participants grouped by SRH trajectories

Characteristics		Total n=1956	SRH Trajectory Group 1 n=232	Group 2 n=1123	Group 3 n=335	Group 4 n=266	P value
Age		61.46(4.8)	62.42(4.5)	61.56(4.8)	60.75(4.8)	61.11(4.9)	0.0003*
Sex							<0.0001*
	Male	1025(52.4%)	104(44.8%)	547(48.7%)	210(62.7%)	164(61.65%)	
	Female	931(47.6%)	128(55.2%)	576(51.3%)	125(37.3%)	102(38.35%)	
Level of education							<0.0001*
	illiterate	473(24.18%)	82(35.3%)	301(26.8%)	41(12.2%)	49(18.4%)	
	1~6 yrs	987(50.46%)	120(51.7%)	573(51%)	164(49%)	130(48.9%)	
	7~12 yrs	374(19.12%)	26(11.2%)	191(17%)	93(27.8%)	64(24.1%)	
	>12 yrs	122(6.24%)	4(1.7%)	58(5.2%)	37(11%)	23(8.7%)	
Income							<0.0001*
	Poor	416(21.81%)	76(33.9%)	246(22.5%)	43(13.1%)	51(19.8%)	
	Fair	860(45.1%)	102(45.5%)	513(46.8%)	143(43.5%)	102(39.5%)	
	Good	631(33.09%)	46(20.5%)	337(30.8%)	143(43.5%)	105(40.7%)	
Social participation							0.0003*
	No	475(24.28%)	61(26.3%)	305(27.2%)	56(16.7%)	53(19.9%)	
	Yes	1481(75.72%)	171(73.7%)	818(72.8%)	279(83.3%)	213(80.1%)	
Marriage							0.0316*
	No	356(18.2%)	46(19.8%)	215(19.2%)	42(12.5%)	53(19.9%)	

	Yes	1600(81.8%)	186(80.2%)	908(80.9%)	293(87.5%)	213(80.1%)	
Smoking							0.0876*
	No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	
	Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	
Alcohol consumption							<0.0001*
	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	
	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
Unemployment							<0.0001*
	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	
	Yes	1135(58.18%)	155(67.4%)	689(61.5%)	157(46.9%)	134(50.4%)	
Number of diseases		1.21(1.29)	1.92(1.55)	1.35(1.31)	0.63(0.92)	0.74(0.89)	<0.0001*

Notes. Data in tables are numbers(%) for categorical variables and means (SD) for continuous variables. Group 1 refers to constant poor SRH group; Group 2 refers to constant fair SRH group; Group 3 refers to constant good SRH group; Group 4 refers to good to fair SRH group

* P<0.05

Table 2. Univariate logistic regression of demographic and clinical characteristics predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.118*	1.077-1.161	<.0001
Sex				
	Male	Ref		<.0001
	Female	2.063*	1.441-2.954	
Level of education				
	illiterate	Ref		
	1~6 years	0.556*	0.384-0.805	0.0019
	7~12 years	0.240*	0.126-0.456	<0.0001
	>12 years	0.058*	0.008-0.424	0.005
Income satisfaction				
	Good	Ref		
	Fair	1.408	0.909-2.181	0.1259
	Poor	2.324*	1.447-3.734	0.0005
Social participation				
	Yes	0.642*	0.443-0.931	<0.0001
	No	Ref		
Marriage				
	Yes	Ref		
	No	1.276	0.830-1.962	0.2665
Smoking				
	Yes	0.7	0.458-1.069	0.0991

	No	Ref		
Alcohol consumption				
	Yes	0.566*	0.371-0.863	0.0082
	No	Ref		
Unemployment				
	Yes	2.889*	1.914-4.359	<0.0001
	No	Ref		
Self-Rated Health				
	Good	0.169*	0.106-0.269	<0.0001
	Fair	0.426	0.285-0.638	<0.0001
	Poor	Ref		
Number of diseases		1.407*	1.248-1.587	<.0001

* P<0.05

1

Table 3. Multivariate logistic regression of SRH trajectories predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.104*	1.056-1.155	<.0001
Sex				
	Male	Ref		
	Female	1.291*	0.812-2.052	0.2803
Level of education				
	illiterate	Ref		
	1~6 years	0.791	0.517-1.211	0.2811
	7~12 years	0.492	0.241-1.007	0.0523
	>12 years	0.185	0.024-1.430	0.1058
Income satisfaction				
	Good	Ref		
	Fair	1.039	0.645-1.674	0.8746
	Poor	1.731*	1.022-2.933	0.0413
Social Participation				
	Yes	1.295	0.829-2.024	0.2558
	No	Ref		
Alcohol consumption				
	Yes	1.055	0.632-1.761	0.8382
	No	Ref		
Unemployment				
	Yes	1.997*	1.221-3.267	0.0059

	No	Ref		
Self Rated Health trajectory				
	Group 1	3.091*	2.036-4.692	<.0001
	Group 2	Ref		
	Group 3	0.044*	0.006-0.323	0.0021
	Group 4	0.192*	0.059-0.625	0.0061
Number of diseases		1.103	0.961-1.267	0.1645

Notes. Group 1 refers to constant poor SRH group; Group 2 refers to constant fair SRH group; Group 3 refers to constant good SRH group; Group 4 refers to good to fair SRH group

* P<0.05

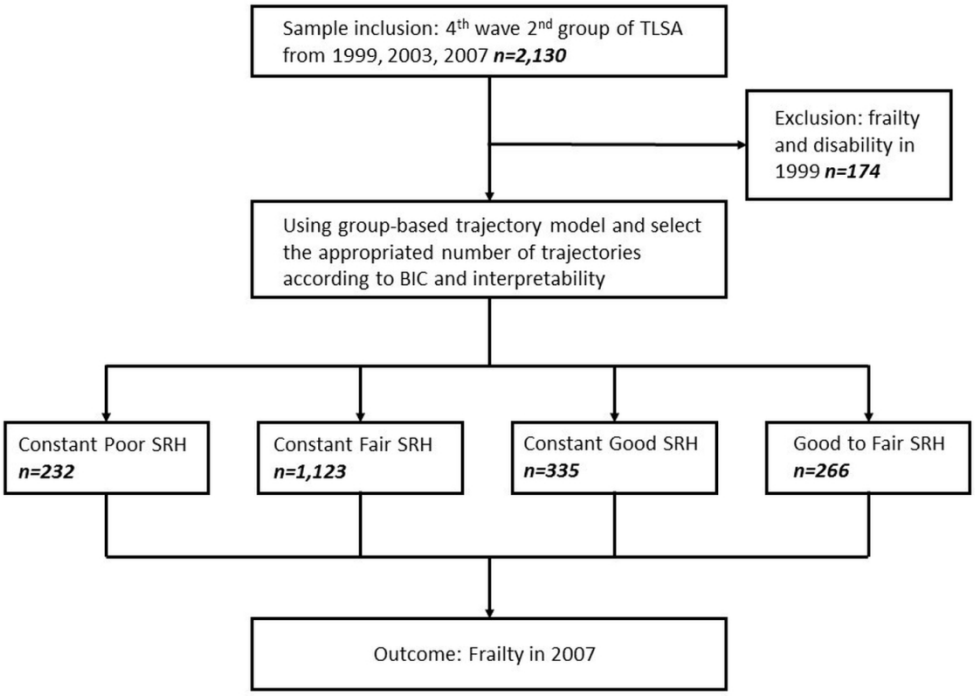

Figure 1. Flow chart of the study design

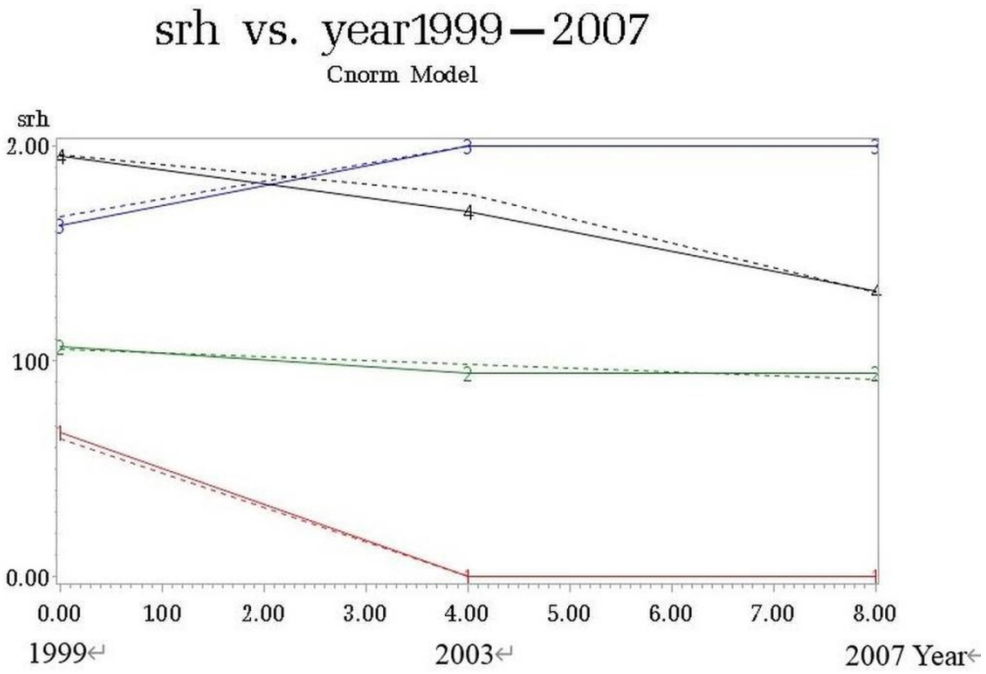

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	#3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods	6

		of recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7
Bias	#9	Describe any efforts to address potential sources of bias	7
Study size	#10	Explain how the study size was arrived at	7
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	8
Statistical methods	#12c	Explain how missing data were addressed	8
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	8
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible,	9

		included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	9
Participants	#13c	Consider use of a flow diagram	9
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	n/a
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
Main results	#16b	Report category boundaries when continuous variables were categorized	9
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9

Discussion

Key results	#18	Summarise key results with reference to study objectives	11
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13
Generalisability	#21	Discuss the generalisability (external validity) of the study results	14
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

This checklist was completed on 01. February 2021 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Trajectory of self-rated health on the incidence of frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-049795.R1
Article Type:	Original research
Date Submitted by the Author:	20-May-2021
Complete List of Authors:	Chu, Wei-Min ; Taichung Veterans General Hospital, Department of Family Medicine; National Yang-Ming University, School of Medicine Ho, Hsin-En; Taichung Armed Forces General Hospital, Department of Family medicine; Chung Shan Medical University, Institution of Medicine Yeh, Chih-Jung; Chung Shan Medical University, School of Public Health Hsiao, Yu-han; Taichung Hospital, Department of Family Medicine; Chung Shan Medical University, School of Public Health Hsu, Pi-Shan; Taichung Veterans General Hospital, Department of Family Medicine Lee, Shu-Hsin; Chung Shan Medical University, School of Nursing Lee, Meng-Chih ; Taichung Hospital, Department of Family Medicine; National Health Research Institutes, Instiute of Population Sciences
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

TITLE

Trajectory of self-rated health on the incidence of frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

AUTHOR and AFFLITATION

Wei-Min Chu[1,2,3], Hsin-En Ho[4,5,6], Chih-Jung Yeh[7], Yu-han Hsiao[7,8], Pi-Shan Hsu[1], Shu-Hsin Lee[9,10], Meng-Chih Lee[8,11]

[1]Department of Family Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

[2]School of Medicine, Chung Shan Medical University, Taichung, Taiwan

[3]School of Medicine, National Yang-Ming University, Taipei, Taiwan

[4]Department of Family medicine, Taichung Armed Force General Hospital, Taichung, Taiwan.

[5]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan

[6]National Defense Medical Center, Taipei, Taiwan

[7]School of Public Health, Chung Shan Medical University, Taichung, Taiwan

[8]Department of Family Medicine, Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan

[9]School of Nursing, Chung Shan Medical University, Taichung, Taiwan

[10]Center for Education and Research on Geriatrics and Gerontology, Chung Shan Medical University, Taichung, Taiwan

[11]Instiute of Population Sciences, National Health Research Institutes, Miaoli County, Taiwan

Corresponding author:

Meng-Chih Lee, M.D., Ph.D., MPH

Department of Family Medicine

Taichung Hospital, Ministry of Health and Welfare

Taichung, Taiwan

Postal Address: No. 199, Sec. 1, Sanmin Rd., West Dist., Taichung City 403, Taiwan (R.O.C.)

Phone: 04-22294411

mengchihlee@gmail.com

Word counts: 2995

ABSTRACT

Objectives: Self-rated health (SRH) is an assessment and predictor of health based on an individual's general condition, however evidence of the value of SRH for predicting frailty remains scarce for older Asian adults. This study aimed to evaluate the relationship between self-rated health (SRH) score trajectory and frailty among older individuals in Taiwan.

Design: An 8-year retrospective cohort study.

Setting: Data were retrieved from the Taiwan Longitudinal Study on Aging between 1999 to 2007.

Participants: Respondents aged 53 to 69-years-old who were not frail or disabled in 1999 (*n*=1956).

Primary and Secondary Outcome Measures: Frailty was defined using the Fried criteria. The group-based trajectory modelling (GBTM) technique was used to estimate SRH trajectories. Logistic regression analysis was used to examine the associations between changes in SRH and frailty.

Results: Four SRH trajectory classes were identified across the 8-year follow-up: 232 participants (11.9%) were classified into the constantly poor SRH group, 1123 (57.4%) into the constantly fair SRH group, 335 (17.1%) into the constantly good SRH group, and 266 (13.4%) into the good-to-fair SRH group. After adjusting for

gender, age, level of education, income, social participation, health behaviors and major comorbidities, age, poor income satisfaction, unemployment and constantly poor SRH were associated with increased risk of frailty, while constantly good SRH [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with reduced risks of frailty.

Conclusions: Constantly poor SRH is associated with an increased risk of frailty in older age. SRH in older adults should be recognized as a predictive tool for future frailty. Diet and exercise interventions may help to prevent frailty among high-risk older individuals with constantly low SRH.

Strengths and Limitation of study:

1. To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty among Asian population based on a nationally representative sample.
2. Reporting bias could happen because all data were collected through self-reporting and not measured objectively.
3. Frailty was defined according to a modified phenotype definition, assessed by using questionnaire data.

Key words: self-rated health, frailty, trajectory, older adults

BACKGROUND

Aging has become a serious challenge globally in both Western and developed Asian countries. The World Health Organization define an aged society as a population in which people over 65-years-old comprise more than 14% of the total population. According to the Department of Health of Taiwan, the proportion of people over 65 in Taiwan increased from 8.6% to 10.7% between 2000 and 2010 [1]. The Department of Development predict this number will rise to 20% by 2027 [2], which would represent the fastest rate of aging in the world. Due to the rapidly aging population, the annual crude mortality rate for Taiwanese citizens over 65 increased from 46.9% to 68.5% between 1981 to 2010 [1, 3].

Many key indicators can be used to predict the future health of the older adults, including the self-rated health (SRH) score. SRH refers to a single question such as "in general, would you say that your health is excellent, very good, good, fair, or poor?" [4]. SRH is an assessment and predictor of health based on an individual's general condition and subjective feelings of their physical, psychological and social wellbeing, combined with objective measurements of health. Several studies have demonstrated consistency between SRH and individual health status and shown SRH can predict future mortality, disability and other adverse health outcomes [5-12]. Frailty has been proven to be one of the most important key indicators of the health of

the elderly in recent decades. Frailty is a geriatric condition characterized by increased vulnerability and decreased capacity to maintain homeostasis, and pre-frailty refers to when one or two of the elements of the Fried frailty phenotype are detected [13]. Frailty in later life has been proven to lead to a number of adverse health outcomes and a poor quality of life [14-18]. As frailty can be addressed by proper recognition and treatment, such as diet and exercise, it is important to identify risk factors for frailty in older adults [19]. Several studies have explored the relationship between SRH and frailty[20-22]. A population-based study of more than 2,000 healthy participants conducted in Finland by Huohvanainen et al. (2016) found that SRH in midlife could predict frailty, prefrailty and mortality in later life [23]. However, most of previous studies were implemented in Western countries, evidence of the value of SRH for predicting frailty remains scarce for older Asian adults, especially from long-term observation. Also, more and more researchers used trajectories of SRH as indicators to explore the change of SRH through time and its consequences [24, 25]. The aim of this study was to explore the long-term relationships between SRH trajectories and future frailty in older Taiwanese adults using a national population cohort study.

METHODS

Data sources

We retrieved data from the Taiwan Longitudinal Study in Aging (TLSA), a population-based, national representative study initiated by the Bureau of Health Promotion of Taiwan, and the Population Studies Center and the Institute of Gerontology at the University of Michigan in the United States. Data are collected from systematically selected representative samples of the Taiwanese population, including institutionalized older people. In TLSA, a three-stage systematic random sampling design was used for the selection of an equal probability sample [26]. We believe that TLSA hold high sample representative and revealed true population structure under this kind of sampling method. Personal interviews are conducted by highly trained interviewers. To ensure high data quality collection, careful supervision is provided during data collection and data processing is conducted by a professional data entry company.

The TLSA was started in 1989 and six waves of data collection had been completed by 2007. For this study, we used the 1999 sample, which included 2,130 subjects aged 53–69-years-old in 1999. We followed-up this cohort for 8 years and used data from 2007 to analyze outcomes. The Population Studies Center at the University of Michigan reviewed the representativeness of the completed sample; the analysis showed that the sample was highly representative, with a 90.6% response rate. Details of the study design have been described elsewhere [27-29].

Study group identification

We included the 1999 sample, which included 2,130 subjects aged 53–69-years-old in 1999. Individuals who had developed frailty in 1999 or who had any functional disability in 1999 were excluded from the study. Functional disability was ascertained

if participants had trouble with at least one activity of daily living, including bathing, dressing, eating, getting out of bed, walking, and using the bathroom [30]. Thus, 1,956 subjects were included in the final analysis.

Research variables

Demographics

For each eligible subject, we gathered data in 1999 on age, gender, level of education, marital status, income level, social participation, employment status, smoking, alcohol consumption, and chronic diseases. We gathered data of SRH in 1999, 2003 and 2007. Level of education was classified into four groups: illiterate (0 years), elementary school (1–6 years), junior to senior high school (7–12 years), and college or above (> 12 years). Income level was determined by asking individuals how they felt about their income level. The possible answers were *very satisfied*, *satisfied*, *fair*, *unsatisfied*, and *very unsatisfied*. We classified the income levels as ‘‘good ’’ (rated *very satisfied*, *satisfied*) “fair” (rated *fair*) or ‘‘poor’’ (*unsatisfied* or *very unsatisfied*).

Health factors

SRH was determined by asking individuals how they rated their current health. Possible answers were *excellent*, *good*, *fair*, *poor*, and *very poor*. We reclassified the individuals into three groups based on SRH: good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*). Individuals who had either paid or voluntary work or who participated in community activities were considered as having social participation. The individuals were classified into two groups based on employment status in 1999: normally employed and unemployed [31]. “Normally employed” was referred to as participants chose the answer of “ I had a job whether it was fulltime or par time job” or “I had a job but took a leave temporarily.”; “Unemployed” was referred to as

participants chose the answer of "I had no job and was looking for a job." or "I did not doing any job." The number of chronic diseases suffered by each individual was recorded, including hypertension, diabetes, cardiovascular disease, stroke, cancer, chronic respiratory diseases, arthritis or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and kidney diseases. Information about chronic conditions was ascertained by a positive answer to the question "have you ever been told by a doctor that you suffer from…".

Outcome

Data regarding frailty was collected in 2007 as the outcome measure. Frailty was defined according to the Fried criteria [13]. Individuals who exhibited at least three of five traits (i.e., weight loss, exhaustion, low physical activity, slowness and weakness) were considered frail. Individuals with only one or two of the five traits of Fried frailty criteria were regarded as pre-frail. We used substitute evaluations for these five domains because we retrieved data from questionnaires, and this modified frailty definition have been used broadly and published before with validity [32-34]. The parameter decreased appetite was used instead of body weight loss to represent nutritional status. Participants who reported poor appetite often in the previous week were classified as having the trait of shrinking. For mobility, we used walking/moving in and around the house instead of gait speed. Participants who had difficulty or were unable to walk a distance of 200 to 300 m were considered slow. For strength, we used the parameter of lifting heavy groceries instead of hand grip strength. Participants who had difficulty or were unable to carry 12 kg of groceries were considered weak. For physical activity, we used the duration of leisure time/physical activities per week instead of the level of physical activity. Participants who did not take a walk, hike or jog, do gardening, or participate in other outdoor activities at least

once or twice a week were considered to have low activity. We used the questionnaire of the Center for Epidemiologic Studies Depression Scale (CES-D) to determine the level of energy. Participants who reported, "*I could not get going*" or "*I felt everything I did was an effort*" often or most of the time in the previous week were considered exhausted. Due to nearly all elderly approaching end-of-life have functional disability and frailty, we regarded those who deceased during study period as having frailty in our study [35]

Statistical analysis

A group-based trajectory modelling (GBTM) was applied to determine the SRH trajectories. GBTM is a finite mixture model and also a semi-parametric model for longitudinal data. We chose this model because it postulates discrete distribution of the population and thus makes it possible to distinguish, in the population, groups/classes of homogeneous individuals [36]. We used the three groups based on SRH: good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*) as indicators to generate the model and employed the Bayesian Information Criterion to identify the most appropriate model groups[37]. Previous geriatric research studies have used this model [27, 33, 34, 38, 39]. For the descriptive analysis, we used analysis of variance and the chi-square test to compare continuous and categorized variables, respectively. Logistic regression was used to analyze the relationship between SRH trajectories and frailty, with adjustments for age, gender, level of

education, income level, marital status, number of chronic diseases, social participation, smoking, alcohol consumption, and employment status. Statistical significance was set at $p < 0.05$. All data were analyzed using SPSS (version 22.0, IBM, Chicago, IL, USA).

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting of our research. However, Taiwan Association of Gerontology and Geriatrics, who listens to and stands for geriatric patients, will help with dissemination plans of our research results.

RESULTS

Figure 1 shows the flow chart of this study, including data collection from 1999, 2003 and 2007. Table 1 shows the descriptive data for all subjects. A total of 1,956 subjects with an average age of 61.46 years were included the final analysis. Most subjects had 1-6 years of education, had a fair income level, and were married. The average number of chronic diseases was 1.21. After GBTM was applied, 4 trajectories of SRH was generated from 1999 to 2007 (Figure 2). There were 232 participants (11.9%) in the constantly poor SRH group, 1123 participants (57.4%) in the constantly fair SRH

group, 335 participants (17.1%) in the constantly good SRH group, and 266 participants (13.6%) in the good-to-fair SRH group. Age distribution, sex, level of education, income level, social participation, marriage status, alcohol consumption, and unemployment status were significantly different between each of the four SRH trajectory classes.

Univariate logistic regression of the associations between the demographic and clinical characteristics and frailty are presented in Table 2. All variables, except for marital status and smoking behavior, were significantly associated with frailty.

Table 3 illustrates multivariate logistic regression regarding the relationship between SRH trajectories and frailty. After adjustments for relevant factors, including age, gender, level of education, income level, social participation, alcohol consumption behavior, number of chronic diseases, and unemployment status, logistic regression analysis revealed age, poor income satisfaction, unemployment and constantly poor SRH was associated with an increased risk of frailty [OR 3.091, 95% CI (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with a decreased risk of frailty compared to constantly fair SRH.

DISCUSSION

In this population cohort study, we created a trajectory-based model for 1,956 Taiwanese adults aged 53–69-years-old in 1999. Based on their SRH trajectories over the 8-year follow-up, the cohort could be classified into four groups: constantly poor SRH, constantly fair SRH, constantly good SRH, and good-to fair SRH. Multivariate logistic regression demonstrated an elevated risk of frailty for the constantly poor SRH group. We also observed significant protective effects for the groups with constantly good SRH and good-to-fair SRH.

To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty. Our results are consistent with previous studies which investigated SRH at single time point. Huohvanainen et al. (2016) found that poor SRH in midlife was associated with prefrailty, frailty and mortality in later life after 26 years of follow-up in Finland [23]. A short-term study of 22 institutionalized older individuals by Gijzel et al. (2017) found that variance in the SRH score time series was significantly higher in frail participants across physical, mental and social domains [40]. Baddour et al. (2019) reported that SRH correlated moderately with frailty and found that good-to-excellent SRH was predictive of non-frail status and preservation of activities of daily living (ADL) [41].

We believe this study provides strong evidence of a causal relationship between SRH and frailty. First, this study was a well-designed cohort study with nationally representative subjects and we excluded those who had disability and frailty at baseline. Second, a significantly elevated risk of frailty was observed in the poor SRH group, even after adjusting for confounding factors related to frailty, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and employment status in multivariate regression

analysis. Third, in analysis of the relationship between SRH trajectory and frailty, the constantly poor SRH group had an elevated risk of frailty, and significant protective effects were observed for the constantly good SRH and good-to-fair SRH groups. Thus, a causal relationship may exist between SRH and frailty.

However, some studies stated that the relationship between SRH and frailty may be in different direction. Pinto et al. discovered that self-rated health is a mediator variable between physical and mental health, including frailty with life satisfaction [42]. The reasons could be that low level of daily activities prevent older adults from participating community activities, thus lead to poor subjective health and life satisfaction. Our study showed that constantly poor SRH would lead to increased incidence of frailty, and we believed that this causal relationship was true, because several studies have identified mechanisms that may possibly link SRH to frailty. Dysregulation of neuroendocrine processes and the immune system may lead to further vulnerability and lower resistance [43], and previous studies showed that inflammatory responses are related to SRH. Christian et al. (2011) found that poorer SRH was associated with elevated serum inflammatory markers, such as IL-6 and CRP, among generally healthy older adults [44]. These inflammatory markers have been associated with frailty. Low physical activity could also be a factor. Granger et al. (2017) reported that high levels of physical activity were positively associated with self-rated ‘good health’ status in European adolescents [45]. Additionally, Savela et al. (2013) found that a higher level of physical activity from midlife onwards was strongly associated with a lower risk of frailty in old age [46]. Further investigation is warranted to explore the intervention to prevent frailty for those people whose SRH are poor, and its cost-effectiveness.

Strengths and Limitations

This study has several advantages. First, this eight-year retrospective cohort study was based on a nationally representative sample with extremely high survey response rates. The database was based on a large, randomly selected population; thus, external validity is high. Second, our analysis of SRH trajectory as a predictor of frailty strengthens the evidence of a causal relationship between SRH and frailty. Moreover, the study design of trajectory-based model analysis minimized the possibility of misclassification bias, as SRH can change over time. Third, we adjusted for numerous confounding factors, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and unemployment status.

However, this study also has several limitations. First, all data were collected through self-reporting and not measured objectively, which could result in reporting bias. Additionally, proxy respondents completed the follow-up questionnaire for subjects who were severely ill, which may possibly generate reporting bias. Second, the associations between SRH and frailty could be bi-directional. For example, a subject may feel poor SRH due to frailty. However, we attempted to address this possibility by using a longitudinal study design and excluding people with frailty and/or disability at baseline, as both frailty and/or disability could substantially affect the outcome. The design of this study also helped to eliminate the possibility of reverse causality. We also adjusted for a number of major chronic diseases to reduce the influence of bias. Third, when GBTM was applied, differences between subgroups could be discussed, but not differences within subgroups. This was because that GBTM assumed that all individuals in a trajectory class have the same behavior [47]. Thus, different trajectory modelling techniques could be applied to examine the difference in specific SRH trajectory in future study. Fourth, we used subjective

assessment for variables such as self-rated health or income level, and such subjective assessment could be influenced by mood states such as depression [48] or cognitive function such as dementia. Thus, we believed that future study is still warranted to explore the relationship between SRH, depression, dementia and frailty. Fifth, interaction effects may affect the results, such as women consistently report poorer SRH compared to men in previous studies. Future study should put emphasis on this issue. Lastly, survival bias could have occurred due to multiple subjects being lost to follow-up, which is a common problem in cohort studies. However, our study used a prospective design and a nationally representative sample, which should have compensated for this limitation.

CONCLUSION

Poor SRH in older adults is associated with a higher risk of frailty in the future, and constantly poor SRH possesses more risk of frailty in the older adults. Moreover, maintaining stable, good SRH may help to prevent frailty in later life. Thus, we suggest governments should design and implement programs to regularly screen SRH in older adults. Further studies are necessary to define practical strategies to reduce the risk of disability and death among older adults with constantly poor SRH and thus improve the quality of life of older people.

FIGURE

Figure 1. Flow chart of the study design1

Flow chart showing the patient inclusion and exclusion processes, and the process of group-based trajectory analysis. SRH, self-rated health.

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

After group-based trajectory analysis, there were 232 participants (11.9%, group 1) in the constant poor SRH group, 1123 participants (57.4%, group 2) in the constant fair SRH group, 335 participants (17.1%, group 3) were in the constant good SRH group, and 266 participants (13.6%, group 4) were in the good to fair SRH group.

ABBREVIATIONS

SRH Self-rated Health

TLSA Taiwan Longitudinal Study on Aging

CES-D Center for Epidemiologic Studies Depression Scale

ADL Activities of Daily Living

DECLARATIONS

Ethics approval and consent to participate

The current study was approved by the Institutional Review Board of Health Promotion Administration, Ministry of Health and Warfare. (Approval no. BHP-2007-002). Before recruitment, all participants received a proper explanation about the study and provided consent for inclusion in the study. Participants who could read and write signed the written consent documents; those who could not read nor write impressed the name stamps or handprint with the assistance of their family members. In addition, legal guardian/representative provided consent on behalf of the participants with cognitive decline or stroke

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are not publicity available, but are available from the corresponding author on reasonable request with the permission of the Ministry of Health and Welfare, Taiwan.

Competing interests

The authors declare no conflicts of interests.

Funding

This work was supported by Ministry of Health and Welfare, Taiwan (Grant number: M06M2346 awarded to M.-C.L.).

Author Contributions

Each author's individual contributions: Meng-Chih Lee conceived of the study and supervised all aspects of its implementation. Wei-Min Chu completed the analyses and drafted the content. Yu-han Hsiao, Shu-Hsin Lee and Pi-Shan Hsu assisted with the study design and revised the content. Hsin-En Ho and Chih-Jung Yeh assisted with the statistical analysis and revised the content. All authors helped to conceptualize ideas, interpret findings, and review drafts of the manuscript.

Acknowledgements

We thank our colleagues from Chun Shan Medical University, Taichung, Taiwan for providing supports in statistical analysis. The sponsor has no role in the design, methods, subject recruitment, data collections, analysis and preparation of paper.

REFERENCES

1. Department of Health EY T: **Taiwan public health report 2017**. 2018.
2. National Development Council T: **Population projections for Taiwan: 2018-2065**. 2018.
3. Department of Health EY T: **The statistical analysis of mortality in 2010**. 2011.
4. Idler EL, Benyamini Y: **Self-rated health and mortality: a review of twenty-seven community studies**. *Journal of health and social behavior* 1997, **38**(1):21-37.
5. Wu S, Wang R, Zhao Y, Ma X, Wu M, Yan X, He J: **The relationship between self-rated health and objective health status: a population-based study**. *BMC public health* 2013, **13**:320.
6. Bopp M, Braun J, Gutzwiller F, Faeh D: **Health risk or resource? Gradual and independent association between self-rated health and mortality persists over 30 years**. *PloS one* 2012, **7**(2):e30795.
7. Giltay EJ, Vollaard AM, Kromhout D: **Self-rated health and physician-rated health as independent predictors of mortality in elderly men**. *Age and ageing* 2012, **41**(2):165-171.
8. Halford C, Wallman T, Welin L, Rosengren A, Bardel A, Johansson S, Eriksson H, Palmer E, Wilhelmsen L, Svardsudd K: **Effects of self-rated health on sick leave, disability pension, hospital admissions and mortality. A population-based longitudinal study of nearly 15,000 observations among Swedish women and men**. *BMC public health* 2012, **12**:1103.
9. Jylha M: **What is self-rated health and why does it predict mortality? Towards a unified conceptual model**. *Social science & medicine (1982)* 2009, **69**(3):307-316.
10. Mavaddat N, Kinmonth AL, Sanderson S, Surtees P, Bingham S, Khaw KT: **What determines Self-Rated Health (SRH)? A cross-sectional study of SF-36 health domains in the EPIC-Norfolk cohort**. *Journal of epidemiology and community health* 2011, **65**(9):800-806.
11. Sargent-Cox KA, Anstey KJ, Luszcz MA: **The choice of self-rated health measures matter when predicting mortality: evidence from 10 years follow-up of the Australian longitudinal study of ageing**. *BMC geriatrics* 2010, **10**:18.
12. Stenholm S, Pentti J, Kawachi I, Westerlund H, Kivimaki M, Vahtera J: **Self-rated health in the last 12 years of life compared to matched surviving controls: the Health and Retirement Study**. *PloS one* 2014, **9**(9):e107879.
13. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G *et al*: **Frailty in older adults: evidence for a phenotype**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2001, **56**(3):M146-156.
14. Bartley MM, Geda YE, Christianson TJ, Pankratz VS, Roberts RO, Petersen RC: **Frailty and Mortality Outcomes in Cognitively Normal Older People: Sex Differences in a Population-Based Study**. *Journal of the American Geriatrics Society* 2016, **64**(1):132-137.
15. At J, Bryce R, Prina M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JJ,

Salas A, Sosa AL *et al*: **Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study**. *BMC medicine* 2015, **13**:138.

16. Lin SY, Lee WJ, Chou MY, Peng LN, Chiou ST, Chen LK: **Frailty Index Predicts All-Cause Mortality for Middle-Aged and Older Taiwanese: Implications for Active-Aging Programs**. *PloS one* 2016, **11**(8):e0161456.
17. Kulmala J, Nykanen I, Hartikainen S: **Frailty as a predictor of all-cause mortality in older men and women**. *Geriatrics & gerontology international* 2014, **14**(4):899-905.
18. Vermeiren S, Vella-Azzopardi R, Beckwee D, Habbig AK, Scafoglieri A, Jansen B, Bautmans I: **Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis**. *Journal of the American Medical Directors Association* 2016, **17**(12):1163.e1161-1163.e1117.
19. Walston J, Buta B, Xue QL: **Frailty Screening and Interventions: Considerations for Clinical Practice**. *Clinics in geriatric medicine* 2018, **34**(1):25-38.
20. Franse CB, van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H: **Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens**. *PloS one* 2017, **12**(11):e0187946.
21. Lau BH, Kwan J, Cheung KS: **Overlap of Frailty, Comorbidity, Disability, and Poor Self-Rated Health in Community-Dwelling Near-Centenarians and Centenarians**. *Journal of the American Geriatrics Society* 2016, **64**(4):900-901.
22. Obaidi MA, Giri S, Mir N, Kenzik K, McDonald AM, Smith CY, Gbolahan OB, Paluri RK, Bhatia S, Williams GR: **Use of self-rated health to identify frailty and predict mortality in older adults with cancer. Results from the care study**. *Journal of Clinical Oncology* 2020, **38**(15_suppl):12046-12046.
23. Huohvanainen E, Strandberg AY, Stenholm S, Pitkala KH, Tilvis RS, Strandberg TE: **Association of Self-Rated Health in Midlife With Mortality and Old Age Frailty: A 26-Year Follow-Up of Initially Healthy Men**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2016, **71**(7):923-928.
24. Lee J, Cho SI, Chun H, Jung-Choi K, Kang M, Jang SN: **Life course indices for social determinants of self-rated health trajectory in Korean elderly**. *Archives of gerontology and geriatrics* 2017, **70**:186-194.
25. Falconer J, Quesnel-Vallée A: **Pathway from poor self-rated health to mortality: Explanatory power of disease diagnosis**. *Social science & medicine (1982)* 2017, **190**:227-236.
26. Tai CJ, Chen JH, Tseng TG, Lin YT, Hsiao YH, Lee MC, Yang YH: **Prediction of Frailty and Dementia Using Oral Health Impact Profile from a Population-Based Survey**. *International journal of environmental research and public health* 2020, **17**(6).
27. Liang J, Wang CN, Xu X, Hsu HC, Lin HS, Lin YH: **Trajectory of functional status among older Taiwanese: Gender and age variations**. *Social science & medicine (1982)* 2010, **71**(6):1208-1217.
28. Pu C, Tang GJ, Huang N, Chou YJ: **Predictive power of self-rated health for subsequent mortality risk during old age: analysis of data from a nationally representative survey of elderly adults in Taiwan**. *J Epidemiol* 2011,

21(4):278-284.
29. Martin LG, Zimmer Z, Hurng BS: **Trends in late-life disability in Taiwan, 1989-2007: the roles of education, environment, and technology**. *Popul Stud (Camb)* 2011, **65**(3):289-304.
30. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW: **STUDIES OF ILLNESS IN THE AGED. THE INDEX OF ADL: A STANDARDIZED MEASURE OF BIOLOGICAL AND PSYCHOSOCIAL FUNCTION**. *JAMA* 1963, **185**:914-919.
31. Chu WM, Ho HE, Yeh CJ, Tsan YT, Lee SH, Lee MC: **Late-career unemployment and risk of frailty among older adults in Taiwan: An 8-year population-based cohort study**. *Geriatrics & gerontology international* 2021, **21**(4):353-358.
32. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Nijhuis-van der Sanden MW: **Outcome instruments to measure frailty: a systematic review**. *Ageing research reviews* 2011, **10**(1):104-114.
33. Hsu HC, Chang WC: **Trajectories of frailty and related factors of the older people in Taiwan**. *Experimental aging research* 2015, **41**(1):104-114.
34. Ho HE, Yeh CJ, Chu WM, Lee MC: **Midlife Body Mass Index Trajectory and Risk of Frailty 8 Years Later in Taiwan**. *The journal of nutrition, health & aging* 2019, **23**(9):849-855.
35. Covinsky KE, Eng C, Lui LY, Sands LP, Yaffe K: **The last 2 years of life: functional trajectories of frail older people**. *Journal of the American Geriatrics Society* 2003, **51**(4):492-498.
36. Nguena Nguefack HL, Pagé MG, Katz J, Choinière M, Vanasse A, Dorais M, Samb OM, Lacasse A: **Trajectory Modelling Techniques Useful to Epidemiological Research: A Comparative Narrative Review of Approaches**. *Clinical epidemiology* 2020, **12**:1205-1222.
37. Nagin DS, Odgers CL: **Group-based trajectory modeling in clinical research**. *Annual review of clinical psychology* 2010, **6**:109-138.
38. Dhana K, van Rosmalen J, Vistisen D, Ikram MA, Hofman A, Franco OH, Kavousi M: **Trajectories of body mass index before the diagnosis of cardiovascular disease: a latent class trajectory analysis**. *European journal of epidemiology* 2016, **31**(6):583-592.
39. Murayama H, Liang J, Bennett JM, Shaw BA, Botoseneanu A, Kobayashi E, Fukaya T, Shinkai S: **Trajectories of Body Mass Index and Their Associations With Mortality Among Older Japanese: Do They Differ From Those of Western Populations?** *American journal of epidemiology* 2015, **182**(7):597-605.
40. Gijzel SMW, van de Leemput IA, Scheffer M, Roppolo M, Olde Rikkert MGM, Melis RJF: **Dynamical Resilience Indicators in Time Series of Self-Rated Health Correspond to Frailty Levels in Older Adults**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2017, **72**(7):991-996.
41. Baddour NA, Robinson-Cohen C, Lipworth L, Bian A, Stewart TG, Jhamb M, Siew ED, Abdel-Kader K: **The Surprise Question and Self-Rated Health Are Useful Screens for Frailty and Disability in Older Adults with Chronic Kidney Disease**. *Journal of palliative medicine* 2019, **22**(12):1522-1529.
42. Pinto JM, Fontaine AM, Neri AL: **The influence of physical and mental health**

on life satisfaction is mediated by self-rated health: A study with Brazilian elderly. *Archives of gerontology and geriatrics* 2016, **65**:104-110.

43. Lutgendorf SK, Costanzo ES: **Psychoneuroimmunology and health psychology: an integrative model**. *Brain, behavior, and immunity* 2003, **17**(4):225-232.

44. Christian LM, Glaser R, Porter K, Malarkey WB, Beversdorf D, Kiecolt-Glaser JK: **Poorer self-rated health is associated with elevated inflammatory markers among older adults**. *Psychoneuroendocrinology* 2011, **36**(10):1495-1504.

45. Granger E, Williams G, Di Nardo F, Harrison A, Verma A: **The relationship between physical activity and self-rated health status in European adolescents: Results of the EURO-URHIS 2 survey**. *European journal of public health* 2017, **27**(suppl_2):107-111.

46. Savela SL, Koistinen P, Stenholm S, Tilvis RS, Strandberg AY, Pitkala KH, Salomaa VV, Strandberg TE: **Leisure-time physical activity in midlife is related to old age frailty**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2013, **68**(11):1433-1438.

47. Muthén B, Muthén LK: **Integrating person-centered and variable-centered analyses: growth mixture modeling with latent trajectory classes**. *Alcoholism, clinical and experimental research* 2000, **24**(6):882-891.

48. Chu WM, Liao WC, Li CR, Lee SH, Tang YJ, Ho HE, Lee MC: **Late-career unemployment and all-cause mortality, functional disability and depression among the older adults in Taiwan: A 12-year population-based cohort study**. *Archives of gerontology and geriatrics* 2016, **65**:192-198.

TABLES

Table 1. Demographic and clinical characteristics of the participants grouped by SRH trajectories

Characteristics		Total n=1956	SRH Trajectory Group 1 n=232	Group 2 n=1123	Group 3 n=335	Group 4 n=266	P value
Age		61.46(4.8)	62.42(4.5)	61.56(4.8)	60.75(4.8)	61.11(4.9)	0.0003*
Sex							<0.0001*
	Male	1025(52.4%)	104(44.8%)	547(48.7%)	210(62.7%)	164(61.65%)	
	Female	931(47.6%)	128(55.2%)	576(51.3%)	125(37.3%)	102(38.35%)	
Level of education							<0.0001*
	illiterate	473(24.18%)	82(35.3%)	301(26.8%)	41(12.2%)	49(18.4%)	
	1~6 yrs	987(50.46%)	120(51.7%)	573(51%)	164(49%)	130(48.9%)	
	7~12 yrs	374(19.12%)	26(11.2%)	191(17%)	93(27.8%)	64(24.1%)	
	>12 yrs	122(6.24%)	4(1.7%)	58(5.2%)	37(11%)	23(8.7%)	
Income							<0.0001*
	Poor	416(21.81%)	76(33.9%)	246(22.5%)	43(13.1%)	51(19.8%)	
	Fair	860(45.1%)	102(45.5%)	513(46.8%)	143(43.5%)	102(39.5%)	
	Good	631(33.09%)	46(20.5%)	337(30.8%)	143(43.5%)	105(40.7%)	
Social participation							0.0003*
	No	475(24.28%)	61(26.3%)	305(27.2%)	56(16.7%)	53(19.9%)	
	Yes	1481(75.72%)	171(73.7%)	818(72.8%)	279(83.3%)	213(80.1%)	
Marriage							0.0316*
	No	356(18.2%)	46(19.8%)	215(19.2%)	42(12.5%)	53(19.9%)	

	Yes	1600(81.8%)	186(80.2%)	908(80.9%)	293(87.5%)	213(80.1%)	
Smoking							0.0876*
	No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	
	Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	
Alcohol consumption							<0.0001*
	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	
	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
Unemployment							<0.0001*
	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	
	Yes	1135(58.18%)	155(67.4%)	689(61.5%)	157(46.9%)	134(50.4%)	
Number of diseases		1.21(1.29)	1.92(1.55)	1.35(1.31)	0.63(0.92)	0.74(0.89)	<0.0001*

Notes. Data in tables are numbers(%) for categorical variables and means (SD) for continuous variables. Group 1 refers to constant poor SRH group; Group 2 refers to constant fair SRH group; Group 3 refers to constant good SRH group; Group 4 refers to good to fair SRH group

* P<0.05

Table 2. Univariate logistic regression of demographic and clinical characteristics predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.12*	1.08-1.16	<.0001
Sex				
	Male	Ref		<.0001
	Female	2.06*	1.44-2.95	
Level of education				
	illiterate	Ref		
	1~6 years	0.57*	0.38-0.81	0.0019
	7~12 years	0.24*	0.13-0.46	<0.0001
	>12 years	0.06*	0.01-0.42	0.005
Income satisfaction				
	Good	Ref		
	Fair	1.41	0.91-2.18	0.1259
	Poor	2.32*	1.45-3.73	0.0005
Social participation				
	Yes	0.64*	0.44-0.93	<0.0001
	No	Ref		
Marriage				
	Yes	Ref		
	No	1.28	0.83-1.96	0.2665
Smoking				
	Yes	0.7	0.46-1.07	0.0991

	No	Ref		
Alcohol consumption				
	Yes	0.57*	0.37-0.86	0.0082
	No	Ref		
Unemployment				
	Yes	2.89*	1.91-4.36	<0.0001
	No	Ref		
Self-Rated Health				
	Good	0.17*	0.17-0.27	<0.0001
	Fair	0.43	0.29-0.64	<0.0001
	Poor	Ref		
Number of diseases		1.41*	1.25-1.59	<.0001

* P<0.05

1

Table 3. Multivariate logistic regression of SRH trajectories predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.10*	1.06-1.16	<.0001
Sex				
	Male	Ref		
	Female	1.29*	0.81-2.05	0.2803
Level of education				
	illiterate	Ref		
	1~6 years	0.79	0.52-1.21	0.2811
	7~12 years	0.49	0.24-1.08	0.0523
	>12 years	0.16	0.02-1.43	0.1058
Income satisfaction				
	Good	Ref		
	Fair	1.04	0.65-1.67	0.8746
	Poor	1.73*	1.02-2.93	0.0413
Social Participation				
	Yes	1.30	0.83-2.02	0.2558
	No	Ref		
Alcohol consumption				
	Yes	1.06	0.63-1.76	0.8382
	No	Ref		
Unemployment				
	Yes	2.00*	1.22-3.27	0.0059

	No	Ref		
Self-Rated Health trajectory				
	Group 1	3.09*	2.04-4.69	<.0001
	Group 2	Ref		
	Group 3	0.04*	0.01-0.32	0.0021
	Group 4	0.19*	0.06-0.63	0.0061
Number of diseases		1.10	0.96-1.27	0.1645

Notes. Group 1 refers to constant poor SRH group; Group 2 refers to constant fair SRH group; Group 3 refers to constant good SRH group; Group 4 refers to good to fair SRH group

* P<0.0

1

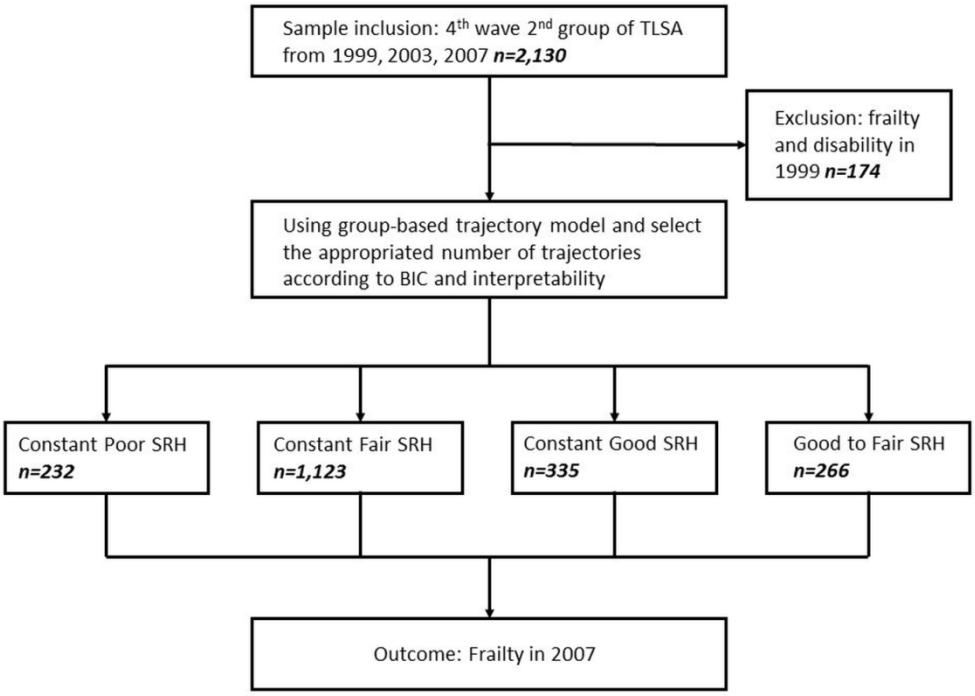

Figure 1. Flow chart of the study design

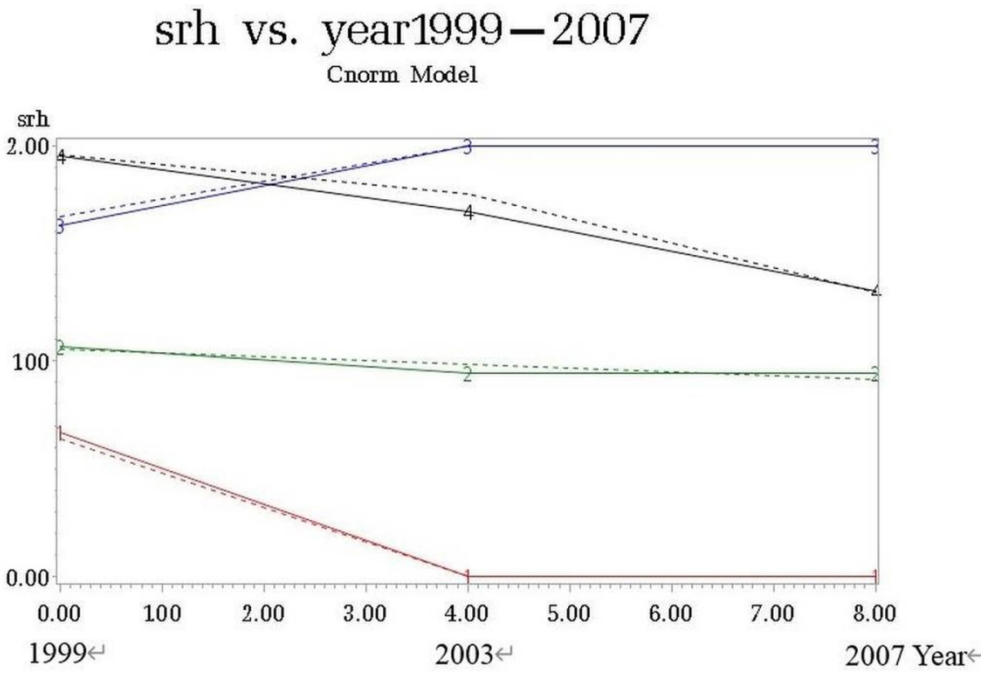

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary	3

		of what was done and what was found	
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	#3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7

Bias	#9	Describe any efforts to address potential sources of bias	7
Study size	#10	Explain how the study size was arrived at	7
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	8
Statistical methods	#12c	Explain how missing data were addressed	8
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	8
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and	9

		unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	9
Participants	#13c	Consider use of a flow diagram	9
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	12
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
Main results	#16b	Report category boundaries when continuous variables were	9

		categorized	
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
n/a			
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	#18	Summarise key results with reference to study objectives	11
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13
Generalisability	#21	Discuss the generalisability (external validity) of the study results	14
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

BMJ Open

Self-rated health trajectory and frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-049795.R2
Article Type:	Original research
Date Submitted by the Author:	02-Jul-2021
Complete List of Authors:	Chu, Wei-Min ; Taichung Veterans General Hospital, Department of Family Medicine; National Yang-Ming University, School of Medicine Ho, Hsin-En; Taichung Armed Forces General Hospital, Department of Family medicine; Chung Shan Medical University, Institution of Medicine Yeh, Chih-Jung; Chung Shan Medical University, School of Public Health Hsiao, Yu-han; Taichung Hospital, Department of Family Medicine; Chung Shan Medical University, School of Public Health Hsu, Pi-Shan; Taichung Veterans General Hospital, Department of Family Medicine Lee, Shu-Hsin; Chung Shan Medical University, School of Nursing Lee, Meng-Chih ; Taichung Hospital, Department of Family Medicine; National Health Research Institutes, Instiute of Population Sciences
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

TITLE

Self-rated health trajectory and frailty among community-dwelling older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)

AUTHORS and AFFILIATIONS

Wei-Min Chu[1,2,3], Hsin-En Ho[4,5,6], Chih-Jung Yeh[7], Yu-han Hsiao[7,8], Pi-Shan Hsu[1], Shu-Hsin Lee[9,10], Meng-Chih Lee[8,11]

[1]Department of Family Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

[2]School of Medicine, Chung Shan Medical University, Taichung, Taiwan

[3]School of Medicine, National Yang-Ming University, Taipei, Taiwan

[4]Department of Family Medicine, Taichung Armed Force General Hospital, Taichung, Taiwan.

[5]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan

[6]National Defense Medical Center, Taipei, Taiwan

[7]School of Public Health, Chung Shan Medical University, Taichung, Taiwan

[8]Department of Family Medicine, Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan

[9]School of Nursing, Chung Shan Medical University, Taichung, Taiwan

[10]Center for Education and Research on Geriatrics and Gerontology, Chung Shan Medical University, Taichung, Taiwan

[11]Institute of Population Sciences, National Health Research Institutes, Miaoli County, Taiwan

Corresponding author:

Meng-Chih Lee, M.D., Ph.D., MPH

Department of Family Medicine

Taichung Hospital, Ministry of Health and Welfare

Taichung, Taiwan

Postal Address: No. 199, Sec. 1, Sanmin Rd., West Dist., Taichung City 403, Taiwan (R.O.C.)

Phone: 04-22294411

mengchihlee@gmail.com

Word counts: 3087

ABSTRACT

Objectives: Self-rated health (SRH) is an assessment and predictor of health based on an individual's general condition; however, evidence of the value of SRH for predicting frailty remains scarce for older Asian adults. This study aimed to evaluate the relationship between self-rated health (SRH) score trajectory and frailty among older individuals in Taiwan.

Design: An 8-year retrospective cohort study.

Setting: Data were retrieved from the Taiwan Longitudinal Study on Aging from 1999 to 2007.

Participants: Respondents aged 53 to 69 years old who were not frail or disabled in 1999 (*n*=1956).

Primary and Secondary Outcome Measures: Frailty was defined using the Fried criteria. The group-based trajectory modelling (GBTM) technique was used to estimate SRH trajectories. Logistic regression analysis was used to examine the associations between changes in SRH and frailty.

Results: Four SRH trajectory classes were identified across the 8-year follow-up: 232 participants (11.9%) were classified into the constantly poor SRH group, 1123 (57.4%) into the constantly fair SRH group, 335 (17.1%) into the constantly good SRH group, and 266 (13.4%) into the good-to-fair SRH group. After adjusting for gender, age, level of education, income, social participation, health behaviors, and major comorbidities, it was found that age, poor income satisfaction, without job, and constantly poor SRH were associated with increased risk of frailty, while constantly good SRH [OR 0.04, 95% CI (0.01-0.32)] and good-to-fair SRH [OR 0.19, 95% CI (0.06-0.63)] were associated with reduced risks of frailty.

Conclusions: Constantly poor SRH was associated with an increased risk of frailty in older age.

SRH in older adults should be recognized as a predictive tool for future frailty. Diet and exercise interventions may help to prevent frailty among high-risk older individuals with constantly low SRH.

Strengths and Limitation of study:

1. To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty in an Asian population based on a nationally representative sample.
2. Reporting bias could have occurred because all data were collected through self-reporting and not measured objectively.
3. Frailty was defined according to a modified phenotype definition, and assessed using questionnaire data.

Key words: self-rated health, frailty, trajectory, older adults

BACKGROUND

Aging has become a serious challenge globally in both Western and developed Asian countries. The World Health Organization defines an aged society as a population in which people over 65 years old comprise more than 14% of the total population. According to the Department of Health of Taiwan, the proportion of people over 65 in Taiwan increased from 8.6% to 10.7% between 2000 and 2010 [1]. The Department of Development predicts this figure will rise to 20% by 2027 [2], which would represent the fastest rate of aging in the world. Due to the rapidly aging population, the annual crude mortality rate for Taiwanese citizens over 65 increased from 46.9% to 68.5% between 1981 and 2010 [1, 3].

Many key indicators can be used to predict the future health of older adults, such as the self-rated health (SRH) score. SRH refers to a single question, such as, “In general, would you say that your health is excellent, very good, good, fair, or poor?” [4]. SRH is an assessment and predictor of health based on an individual’s general condition and subjective feelings about their physical, psychological, and social well-being, combined with objective measurements of health. Several studies have demonstrated consistency between SRH and individual health status and have shown SRH can predict future mortality, disability, and other adverse health outcomes [5-12]. Frailty has been proven to be one of the most important key indicators of the health of older people in recent decades. Frailty is a geriatric condition characterized by increased vulnerability and decreased capacity to maintain homeostasis, and pre-frailty refers to a condition that meets one or two of the criteria for the Fried frailty phenotype [13]. Frailty in later life has been proven to lead to a number of adverse health outcomes and a poor quality of life [14-18]. As frailty can be addressed by proper recognition and treatment, such as diet and exercise, it is important to identify risk factors

for frailty in older adults [19]. Several studies have explored the relationship between SRH and frailty[20-22]. A population-based study of more than 2,000 healthy participants conducted in Finland by Huohvanainen et al. (2016) found that SRH in midlife could predict frailty, pre-frailty, and mortality in later life [23]. However, most previous studies were conducted in Western countries; evidence of the value of SRH for predicting frailty remains scarce for older Asian adults, especially from long-term observation. The problem with long-term observations of older adults is that rapid changes in biological function and psychosocial processes occur over time in this population, and it is not possible to detect these changes using traditional statistical methods. Thus, the group-based trajectory model (GBTM) was developed, which provides a statistical standard for establishing the influence of life trajectory [24, 25]. The aim of this study was to explore the long-term relationships between SRH trajectories and future frailty in older Taiwanese adults using a national population cohort study.

METHODS

Data sources

We retrieved data from the Taiwan Longitudinal Study in Aging (TLSA), a population-based, national representative study initiated by Taiwan's Bureau of Health Promotion, and the University of Michigan's Population Studies Center and Institute of Gerontology in the United States. Data were collected from systematically selected representative samples of the Taiwanese population, including institutionalized older people. In the TLSA, a three-stage systematic random sampling design was used for the selection of an equal probability sample [26]. We believe that the TLSA contains samples that are highly representative of the true population structure under this kind of sampling method. Personal interviews were conducted by highly trained interviewers. To ensure high data quality collection, careful supervision was provided during data collection and data processing was conducted by a professional data entry company.

The TLSA was started in 1989 and six waves of data collection had been completed by 2007. For this study, we used the 1999 sample, which included 2,130 subjects aged 53–69 years old in 1999. We followed up this cohort for 8 years and used data from 2007 to analyze outcomes. The Population Studies Center at the University of Michigan reviewed the representativeness of the completed sample, and the analysis showed that the sample was highly representative, with a 90.6% response rate. Details of the study design have been described elsewhere [27-29].

Study group identification

We analyzed the 1999 sample, which included 2,130 subjects aged 53–69 years old in 1999. Individuals who had developed frailty in 1999 or who had any functional disability in 1999 were

excluded from the study. A participant was deemed to have functional disability if he or she had trouble with at least one activity of daily living, including bathing, dressing, eating, getting out of bed, walking, and using the bathroom [30]. The reason that we excluded people with frailty or disability at baseline was because both frailty and disability could have substantially affected the outcome. Thus, 1,956 subjects were included in the final analysis.

Research variables

Demographics

For each eligible subject, we gathered data in 1999 on age, gender, level of education, marital status, income level, social participation, employment status, smoking, alcohol consumption, and chronic diseases. We gathered SRH data in 1999, 2003, and 2007. Level of education was classified into four groups: illiterate (0 years), elementary school (1–6 years), junior to senior high school (7–12 years), and college or above (> 12 years). Income level was determined by asking individuals how they felt about their income level. The possible answers were *very satisfied*, *satisfied*, *fair*, *unsatisfied*, and *very unsatisfied*. We classified the income levels as ‘‘good ’’ (rated *very satisfied*, *satisfied*), “fair” (rated *fair*), or ‘‘poor’’ (*unsatisfied* or *very unsatisfied*).

Health factors

SRH was determined by asking individuals how they rated their current health. Possible answers were *excellent*, *good*, *fair*, *poor*, and *very poor*. We reclassified the individuals into three groups based on SRH: good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*). We reclassified SRH from 5 groups to 3 groups so that there were enough participants in each group to provide sufficient statistical power.

Social participation was determined based on whether individuals performed either paid or voluntary work or participated in community activities. The individuals were classified into two groups based on job status in 1999: with a job and without job [31]. Participants were considered to be employed ("With a job") if they chose the response " I had a job whether it was fulltime or part-time job" or "I had a job but took a leave temporarily." Participants were considered to be unemployed ("Without job") if they chose the response, "I had no job and was looking for a job." or "I did not do any job." The number of chronic diseases suffered by each individual was recorded, including hypertension, diabetes, cardiovascular disease, stroke, cancer, chronic respiratory diseases, arthritis or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and kidney diseases. Information about chronic conditions was ascertained by a positive answer to the question, "Have you ever been told by a doctor that you suffer from…".

Outcome

Data regarding frailty was collected in 2007 as the outcome measure. Frailty was defined according to the Fried criteria [13]. Individuals who exhibited at least three of five traits (i.e., weight loss, exhaustion, low physical activity, slowness, and weakness) were considered frail. Individuals meeting only one or two of the five traits of the Fried frailty criteria were regarded as pre-frail. We used substitute evaluations for these five traits because we retrieved data from questionnaires, and this modified frailty definition has been widely used and previously published with validity [32-34]. The parameter "decreased appetite" was used instead of "body weight loss" to represent nutritional status. Hence, participants who reported poor appetite often in the previous week were classified as having the trait "shrinking". For mobility, we used walking/moving in and around the house instead of gait speed. Participants who had difficulty or were unable to walk a

distance of 200 to 300 m were considered slow. For strength, we used the "lifting heavy groceries" parameter instead of "hand grip strength". Participants who had difficulty or were unable to carry 12 kg of groceries were considered weak. For physical activity, we used the duration of leisure time/physical activities per week instead of the level of physical activity. Participants who did not take a walk, hike or jog, do gardening, or participate in other outdoor activities at least once or twice a week were considered to have low activity. We used the questionnaire of the Center for Epidemiologic Studies Depression Scale (CES-D) to determine the level of energy. Participants who reported, "*I could not get going*" or "*I felt everything I did was an effort*" often or most of the time in the previous week were considered to be exhausted. As nearly all older people approaching end of life have functional disability and frailty, we regarded those who died during the study period as having frailty in our study [35]

Statistical analysis

Group-based trajectory modelling (GBTM) was applied to determine the SRH trajectories. GBTM is a finite mixture model and also a semi-parametric model for longitudinal data. We chose this model because it postulates a discrete distribution of the population, which makes it possible to distinguish groups/classes of homogeneous individuals within the population [36]. We used the three groups based on SRH, good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*), as indicators to generate the model and employed the Bayesian Information Criterion to identify the most appropriate model groups[37]. Previous geriatric research studies have used this model [27, 33, 34, 38, 39]. For the descriptive analysis, we used analysis of variance and the chi-square test to compare continuous and categorical variables, respectively. Logistic regression was used to

analyze the relationship between SRH trajectories and frailty, with adjustments for age, gender, level of education, income level, marital status, number of chronic diseases, social participation, smoking, alcohol consumption, and employment status. Statistical significance was set at $p < 0.05$. All data were analyzed using SPSS (version 22.0, IBM, Chicago, IL, USA).

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting of our research. However, the Taiwan Association of Gerontology and Geriatrics, who listens to and represents geriatric patients, will help to disseminate our plans, which are based on our research results.

RESULTS

Figure 1 shows the flow chart of this study, including data collection from 1999, 2003, and 2007. Table 1 shows the descriptive data for all subjects. A total of 1,956 subjects with an average age of 61.46 years were included in the final analysis. Most subjects had 1-6 years of education, had a fair income level, and were married. The average number of chronic diseases was 1.21. After GBTM was applied, 4 trajectories of SRH were generated from 1999 to 2007 (Figure 2). There were 232 participants (11.9%) in the constantly poor SRH group, 1123 participants (57.4%) in the constantly fair SRH group, 335 participants (17.1%) in the constantly good SRH group, and 266 participants (13.6%) in the good-to-fair SRH group. Age distribution, sex, level of education, income level, social participation, marriage status, alcohol consumption, and job status were significantly different among the four SRH trajectory classes.

Univariate logistic regression of the associations between the demographic and clinical characteristics and frailty are presented in Table 2. All variables, except for marital status and smoking behavior, were significantly associated with frailty.

Table 3 illustrates the results of the multivariate logistic regression analysis of the relationships between SRH trajectories and frailty. After adjustments for relevant factors, including age, gender, level of education, income level, social participation, alcohol consumption behavior, number of chronic diseases, and job status, logistic regression analysis revealed age, poor income satisfaction, without job, and constantly poor SRH was associated with an increased risk of frailty [OR 3.091, 95% CI (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with a decreased risk of frailty compared to constantly fair SRH.

DISCUSSION

In this population cohort study, we created a trajectory-based model for 1,956 Taiwanese adults aged 53–69 years old in 1999. Based on their SRH trajectories over the 8-year follow-up, the cohort could be classified into four groups: constantly poor SRH, constantly fair SRH, constantly good SRH, and good-to-fair SRH. Multivariate logistic regression demonstrated an elevated risk of frailty for the constantly poor SRH group. We also observed significant protective effects for the groups with constantly good SRH and good-to-fair SRH.

To the best of our knowledge, this is the first long-term study to investigate the relationship between SRH trajectory and frailty. Our results are consistent with previous studies which investigated SRH at a single time point. Huohvanainen et al. (2016) found that poor SRH in midlife was associated with pre-frailty, frailty, and mortality in later life after 26 years of follow-up in Finland [23]. A short-term study of 22 institutionalized older individuals by Gijzel et al. (2017) found that variance in the SRH score time series was significantly higher in frail participants across physical, mental, and social domains [40]. Baddour et al. (2019) reported that SRH correlated moderately with frailty and found that good-to-excellent SRH was predictive of non-frail status and preservation of activities of daily living (ADL) [41].

We believe this study provides strong evidence of a causal relationship between SRH and frailty. First, this study was a well-designed cohort study with nationally representative subjects and we excluded those who had disability and frailty at baseline. Second, a significantly elevated risk of frailty was observed in the poor SRH group, even after adjusting for confounding factors related to frailty, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and employment status in the multivariate regression analysis.

Third, in the analysis of the relationships between SRH trajectory and frailty, the constantly poor SRH group had an elevated risk of frailty, and significant protective effects were observed for the constantly good SRH and good-to-fair SRH groups. Thus, a causal relationship may exist between SRH and frailty.

However, some studies have suggested that in the relationship between SRH and frailty, the direction of causality may be different. Pinto et al. discovered that self-rated health is a mediator variable between physical and mental health and life satisfaction [42]. Possibly, low-level daily activities prevent older adults from participating in community activities, leading to poor subjective health and life satisfaction. Our study showed that constantly poor SRH would lead to increased incidence of frailty, and we believe that this causal relationship does exist, because several studies have identified mechanisms that potentially link SRH to frailty. Dysregulation of neuroendocrine processes and the immune system may lead to further vulnerability and lower resistance [43], and previous studies showed that inflammatory responses are related to SRH. Christian et al. (2011) found that poorer SRH was associated with elevated serum inflammatory markers, such as IL-6 and CRP, among generally healthy older adults [44]. These inflammatory markers have been associated with frailty. Low physical activity could also be a factor. Granger et al. (2017) reported that high levels of physical activity were positively associated with self-rated 'good health' status in European adolescents [45]. Additionally, Savela et al. (2013) found that a higher level of physical activity from midlife onwards was strongly associated with a lower risk of frailty in old age [46]. Further investigation is warranted to explore this intervention for the prevention of frailty in people whose SRH is poor, and to evaluate its cost-effectiveness.

Strengths and Limitations

This study has several strengths. First, this eight-year retrospective cohort study was based on a nationally representative sample with extremely high survey response rates. The database contained data from a large, randomly selected population; thus, the external validity is high. Second, our analysis of SRH trajectory as a predictor of frailty strengthens the evidence of a causal relationship between SRH and frailty. Moreover, the study design included a trajectory-based model analysis, which minimized the possibility of misclassification bias, as SRH can change over time. Third, we adjusted for numerous confounding factors, including age, gender, level of education, income level, marital status, major disease, health behaviors, social participation, and job status.

However, this study also has several limitations. First, all data were collected through self-reporting and were not measured objectively, which could have resulted in reporting bias. Additionally, proxy respondents completed the follow-up questionnaire for subjects who were severely ill, which possibly generated reporting bias. Second, the associations between SRH and frailty could be bi-directional. For example, a subject may experience poor SRH due to frailty. However, we attempted to address this issue by using a longitudinal study design and excluding people with frailty and/or disability at baseline, as frailty and/or disability could substantially affect the outcome. The design of this study also helped to eliminate the possibility of reverse causality. We also adjusted for a number of major chronic diseases to reduce the influence of bias. Third, when GBTM was applied, differences between subgroups could be determined, but not differences within subgroups. This was because in GBTM it was assumed that all individuals in a trajectory class had the same behavior [47]. Thus, different trajectory modelling techniques could

be applied to examine any differences in a specific SRH trajectory in future research. Fourth, we used subjective assessment for variables such as self-rated health or income level, and these measurements could therefore have been influenced by mood states such as depression [48] or poor cognitive function, which may occur in certain diseases, such as dementia. Thus, further study is warranted to explore the relationships among SRH, depression, dementia, and frailty. Fifth, interaction effects may have affected the results. For example, women have consistently reported poorer SRH compared to men in previous studies. Future research should take this issue into consideration. Lastly, survival bias could have occurred due to multiple subjects being lost to follow-up, which is a common problem in cohort studies.

CONCLUSION

Poor SRH in older adults was associated with a higher risk of developing frailty, and constantly poor SRH appeared to confer a greater risk of frailty in older adults. Moreover, maintaining stable, good SRH may help to prevent frailty in later life. Thus, we suggest that policymakers design and implement programs to regularly screen SRH in older adults. Further studies are necessary to define practical strategies for reducing the risk of disability and death among older adults with constantly poor SRH, thereby improving the quality of life of older people.

FIGURE

Figure 1. Flow chart of the study design

Flow chart showing the patient inclusion and exclusion processes, and the process of group-based trajectory analysis. SRH, self-rated health.

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

After group-based trajectory analysis, there were 232 participants (11.9%, group 1) in the constant poor SRH group, 1123 participants (57.4%, group 2) in the constant fair SRH group, 335 participants (17.1%, group 3) in the constant good SRH group, and 266 participants (13.6%, group 4) in the good-to-fair SRH group.

ABBREVIATIONS

SRH Self-rated Health

TLSA Taiwan Longitudinal Study on Aging

CES-D Center for Epidemiologic Studies Depression Scale

ADL Activities of Daily Living

DECLARATIONS

Ethics approval and consent to participate

The current study was approved by the Institutional Review Board of Health Promotion Administration, Ministry of Health and Welfare (Approval no. BHP-2007-002). Before recruitment, all participants received a proper explanation about the study and provided consent for inclusion in the study. Participants who could read and write signed the written consent documents; those who could not read nor write used a name chop or handprint [thumb print? fingerprint?] with the assistance of their family members. In addition, a legal guardian/representative provided consent on behalf of participants with cognitive decline or stroke.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request with the permission of the Ministry of Health and Welfare, Taiwan.

Competing interests

The authors declare no conflicts of interests.

Funding

This work was supported by the Ministry of Health and Welfare, Taiwan (Grant number: M06M2346 awarded to M.-C.L.).

Author Contributions

The individual contributions of all authors: Meng-Chih Lee conceived of the study and supervised all aspects of its implementation. Wei-Min Chu completed the analyses and drafted the content. Yu-han Hsiao, Shu-Hsin Lee, and Pi-Shan Hsu assisted with the study design and revised the content. Hsin-En Ho and Chih-Jung Yeh assisted with the statistical analysis and revised the content. All authors helped to conceptualize ideas, interpret findings, and review drafts of the manuscript.

Acknowledgements

We thank our colleagues from Chung Shan Medical University, Taichung, Taiwan for assisting with the statistical analysis. The sponsor had no role in the design, methods, subject recruitment, data collection, analysis, or preparation of paper.

REFERENCES

1. Department of Health EY T: **Taiwan public health report 2017**. 2018.

2. National Development Council T: **Population projections for Taiwan: 2018-2065**. 2018.

3. Department of Health EY T: **The statistical analysis of mortality in 2010**. 2011.

4. Idler EL, Benyamini Y: **Self-rated health and mortality: a review of twenty-seven community studies**. *Journal of health and social behavior* 1997, **38**(1):21-37.

5. Wu S, Wang R, Zhao Y, Ma X, Wu M, Yan X, He J: **The relationship between self-rated health and objective health status: a population-based study**. *BMC public health* 2013, **13**:320.

6. Bopp M, Braun J, Gutzwiller F, Faeh D: **Health risk or resource? Gradual and independent association between self-rated health and mortality persists over 30 years**. *PloS one* 2012, **7**(2):e30795.

7. Giltay EJ, Vollaard AM, Kromhout D: **Self-rated health and physician-rated health as independent predictors of mortality in elderly men**. *Age and ageing* 2012, **41**(2):165-171.

8. Halford C, Wallman T, Welin L, Rosengren A, Bardel A, Johansson S, Eriksson H, Palmer E, Wilhelmsen L, Svardsudd K: **Effects of self-rated health on sick leave, disability pension, hospital admissions and mortality. A population-based longitudinal study of nearly 15,000 observations among Swedish women and men**. *BMC public health* 2012, **12**:1103.

9. Jylha M: **What is self-rated health and why does it predict mortality? Towards a unified conceptual model**. *Social science & medicine (1982)* 2009, **69**(3):307-316.

10. Mavaddat N, Kinmonth AL, Sanderson S, Surtees P, Bingham S, Khaw KT: **What determines Self-Rated Health (SRH)? A cross-sectional study of SF-36 health domains in the EPIC-Norfolk cohort**. *Journal of epidemiology and community health* 2011, **65**(9):800-806.

11. Sargent-Cox KA, Anstey KJ, Luszcz MA: **The choice of self-rated health measures matter when predicting mortality: evidence from 10 years follow-up of the Australian longitudinal study of ageing**. *BMC geriatrics* 2010, **10**:18.

12. Stenholm S, Pentti J, Kawachi I, Westerlund H, Kivimaki M, Vahtera J: **Self-rated health in the last 12 years of life compared to matched surviving controls: the Health and Retirement Study**. *PloS one* 2014, **9**(9):e107879.

13. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G *et al*: **Frailty in older adults: evidence for a phenotype**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2001, **56**(3):M146-156.

14. Bartley MM, Geda YE, Christianson TJ, Pankratz VS, Roberts RO, Petersen RC: **Frailty and Mortality Outcomes in Cognitively Normal Older People: Sex Differences in a Population-Based Study**. *Journal of the American Geriatrics Society* 2016, **64**(1):132-137.

15. At J, Bryce R, Prina M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JJ, Salas A, Sosa AL *et al*: **Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study**. *BMC medicine* 2015, **13**:138.

16. Lin SY, Lee WJ, Chou MY, Peng LN, Chiou ST, Chen LK: **Frailty Index Predicts All-Cause**

Mortality for Middle-Aged and Older Taiwanese: Implications for Active-Aging Programs. *PloS one* 2016, **11**(8):e0161456.

17. Kulmala J, Nykanen I, Hartikainen S: **Frailty as a predictor of all-cause mortality in older men and women**. *Geriatrics & gerontology international* 2014, **14**(4):899-905.

18. Vermeiren S, Vella-Azzopardi R, Beckwee D, Habbig AK, Scafoglieri A, Jansen B, Bautmans I: **Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis**. *Journal of the American Medical Directors Association* 2016, **17**(12):1163.e1161-1163.e1117.

19. Walston J, Buta B, Xue QL: **Frailty Screening and Interventions: Considerations for Clinical Practice**. *Clinics in geriatric medicine* 2018, **34**(1):25-38.

20. Franse CB, van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H: **Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens**. *PloS one* 2017, **12**(11):e0187946.

21. Lau BH, Kwan J, Cheung KS: **Overlap of Frailty, Comorbidity, Disability, and Poor Self-Rated Health in Community-Dwelling Near-Centenarians and Centenarians**. *Journal of the American Geriatrics Society* 2016, **64**(4):900-901.

22. Obaidi MA, Giri S, Mir N, Kenzik K, McDonald AM, Smith CY, Gbolahan OB, Paluri RK, Bhatia S, Williams GR: **Use of self-rated health to identify frailty and predict mortality in older adults with cancer. Results from the care study**. *Journal of Clinical Oncology* 2020, **38**(15_suppl):12046-12046.

23. Huohvanainen E, Strandberg AY, Stenholm S, Pitkala KH, Tilvis RS, Strandberg TE:

Association of Self-Rated Health in Midlife With Mortality and Old Age Frailty: A 26-Year Follow-Up of Initially Healthy Men. *The journals of gerontology Series A, Biological sciences and medical sciences* 2016, **71**(7):923-928.

24. Lee J, Cho SI, Chun H, Jung-Choi K, Kang M, Jang SN: **Life course indices for social determinants of self-rated health trajectory in Korean elderly**. *Archives of gerontology and geriatrics* 2017, **70**:186-194.

25. Nagin DS, Odgers CL: **Group-based trajectory modeling in clinical research.** *Annu Rev Clin Psychol. 2010, **6**:109-38.*

26. Tai CJ, Chen JH, Tseng TG, Lin YT, Hsiao YH, Lee MC, Yang YH: **Prediction of Frailty and Dementia Using Oral Health Impact Profile from a Population-Based Survey**. *International journal of environmental research and public health* 2020, **17**(6).

27. Liang J, Wang CN, Xu X, Hsu HC, Lin HS, Lin YH: **Trajectory of functional status among older Taiwanese: Gender and age variations**. *Social science & medicine (1982)* 2010, **71**(6):1208-1217.

28. Pu C, Tang GJ, Huang N, Chou YJ: **Predictive power of self-rated health for subsequent mortality risk during old age: analysis of data from a nationally representative survey of elderly adults in Taiwan**. *J Epidemiol* 2011, **21**(4):278-284.

29. Martin LG, Zimmer Z, Hurng BS: **Trends in late-life disability in Taiwan, 1989-2007: the roles of education, environment, and technology**. *Popul Stud (Camb)* 2011, **65**(3):289-304.

30. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW: **STUDIES OF ILLNESS IN THE AGED. THE INDEX OF ADL: A STANDARDIZED MEASURE OF BIOLOGICAL AND PSYCHOSOCIAL FUNCTION**. *JAMA* 1963, **185**:914-919.

31. Chu WM, Ho HE, Yeh CJ, Tsan YT, Lee SH, Lee MC: **Late-career unemployment and risk of frailty among older adults in Taiwan: An 8-year population-based cohort study**. *Geriatrics & gerontology international* 2021, **21**(4):353-358.

32. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Nijhuis-van der Sanden MW: **Outcome instruments to measure frailty: a systematic review**. *Ageing research reviews* 2011, **10**(1):104-114.

33. Hsu HC, Chang WC: **Trajectories of frailty and related factors of the older people in Taiwan**. *Experimental aging research* 2015, **41**(1):104-114.

34. Ho HE, Yeh CJ, Chu WM, Lee MC: **Midlife Body Mass Index Trajectory and Risk of Frailty 8 Years Later in Taiwan**. *The journal of nutrition, health & aging* 2019, **23**(9):849-855.

35. Covinsky KE, Eng C, Lui LY, Sands LP, Yaffe K: **The last 2 years of life: functional trajectories of frail older people**. *Journal of the American Geriatrics Society* 2003, **51**(4):492-498.

36. Nguena Nguefack HL, Pagé MG, Katz J, Choinière M, Vanasse A, Dorais M, Samb OM, Lacasse A: **Trajectory Modelling Techniques Useful to Epidemiological Research: A Comparative Narrative Review of Approaches**. *Clinical epidemiology* 2020, **12**:1205-1222.

37. Nagin DS, Odgers CL: **Group-based trajectory modeling in clinical research**. *Annual review*

of clinical psychology 2010, **6**:109-138.

38. Dhana K, van Rosmalen J, Vistisen D, Ikram MA, Hofman A, Franco OH, Kavousi M: **Trajectories of body mass index before the diagnosis of cardiovascular disease: a latent class trajectory analysis**. *European journal of epidemiology* 2016, **31**(6):583-592.

39. Murayama H, Liang J, Bennett JM, Shaw BA, Botoseneanu A, Kobayashi E, Fukaya T, Shinkai S: **Trajectories of Body Mass Index and Their Associations With Mortality Among Older Japanese: Do They Differ From Those of Western Populations?** *American journal of epidemiology* 2015, **182**(7):597-605.

40. Gijzel SMW, van de Leemput IA, Scheffer M, Roppolo M, Olde Rikkert MGM, Melis RJF: **Dynamical Resilience Indicators in Time Series of Self-Rated Health Correspond to Frailty Levels in Older Adults**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2017, **72**(7):991-996.

41. Baddour NA, Robinson-Cohen C, Lipworth L, Bian A, Stewart TG, Jhamb M, Siew ED, Abdel-Kader K: **The Surprise Question and Self-Rated Health Are Useful Screens for Frailty and Disability in Older Adults with Chronic Kidney Disease**. *Journal of palliative medicine* 2019, **22**(12):1522-1529.

42. Pinto JM, Fontaine AM, Neri AL: **The influence of physical and mental health on life satisfaction is mediated by self-rated health: A study with Brazilian elderly**. *Archives of gerontology and geriatrics* 2016, **65**:104-110.

43. Lutgendorf SK, Costanzo ES: **Psychoneuroimmunology and health psychology: an**

integrative model. *Brain, behavior, and immunity* 2003, **17**(4):225-232.

44. Christian LM, Glaser R, Porter K, Malarkey WB, Beversdorf D, Kiecolt-Glaser JK: **Poorer self-rated health is associated with elevated inflammatory markers among older adults**. *Psychoneuroendocrinology* 2011, **36**(10):1495-1504.

45. Granger E, Williams G, Di Nardo F, Harrison A, Verma A: **The relationship between physical activity and self-rated health status in European adolescents: Results of the EURO-URHIS 2 survey**. *European journal of public health* 2017, **27**(suppl_2):107-111.

46. Savela SL, Koistinen P, Stenholm S, Tilvis RS, Strandberg AY, Pitkala KH, Salomaa VV, Strandberg TE: **Leisure-time physical activity in midlife is related to old age frailty**. *The journals of gerontology Series A, Biological sciences and medical sciences* 2013, **68**(11):1433-1438.

47. Muthén B, Muthén LK: **Integrating person-centered and variable-centered analyses: growth mixture modeling with latent trajectory classes**. *Alcoholism, clinical and experimental research* 2000, **24**(6):882-891.

48. Chu WM, Liao WC, Li CR, Lee SH, Tang YJ, Ho HE, Lee MC: **Late-career unemployment and all-cause mortality, functional disability and depression among the older adults in Taiwan: A 12-year population-based cohort study**. *Archives of gerontology and geriatrics* 2016, **65**:192-198.

TABLES

Table 1. Demographic and clinical characteristics of the participants grouped by SRH trajectories

Characteristics		Total	SRH Trajectory				P value
			Group 1	Group 2	Group 3	Group 4	
		n=1956	n=232	n=1123	n=335	n=266	
Age		61.46(4.8)	62.42(4.5)	61.56(4.8)	60.75(4.8)	61.11(4.9)	0.0003*
Sex							<0.0001*
	Male	1025(52.4%)	104(44.8%)	547(48.7%)	210(62.7%)	164(61.65%)	
	Female	931(47.6%)	128(55.2%)	576(51.3%)	125(37.3%)	102(38.35%)	
Level of education							<0.0001*
	illiterate	473(24.18%)	82(35.3%)	301(26.8%)	41(12.2%)	49(18.4%)	
	1~6 yrs	987(50.46%)	120(51.7%)	573(51%)	164(49%)	130(48.9%)	
	7~12 yrs	374(19.12%)	26(11.2%)	191(17%)	93(27.8%)	64(24.1%)	

	>12 yrs	122(6.24%)	4(1.7%)	58(5.2%)	37(11%)	23(8.7%)	
Income							<0.0001*
	Poor	416(21.81%)	76(33.9%)	246(22.5%)	43(13.1%)	51(19.8%)	
	Fair	860(45.1%)	102(45.5%)	513(46.8%)	143(43.5%)	102(39.5%)	
	Good	631(33.09%)	46(20.5%)	337(30.8%)	143(43.5%)	105(40.7%)	
Social participation							0.0003*
	No	475(24.28%)	61(26.3%)	305(27.2%)	56(16.7%)	53(19.9%)	
	Yes	1481(75.72%)	171(73.7%)	818(72.8%)	279(83.3%)	213(80.1%)	
Marriage							0.0316*
	No	356(18.2%)	46(19.8%)	215(19.2%)	42(12.5%)	53(19.9%)	
	Yes	1600(81.8%)	186(80.2%)	908(80.9%)	293(87.5%)	213(80.1%)	
Smoking							0.0876*
	No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	
	Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	

Alcohol consumption						<0.0001*
	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	
	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
Without job						<0.0001*
	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	
	Yes	1135(58.18%)	155(67.4%)	689(61.5%)	157(46.9%)	134(50.4%)	
Number of diseases		1.21(1.29)	1.92(1.55)	1.35(1.31)	0.63(0.92)	0.74(0.89)	<0.0001*

Notes. Data in tables are numbers(%) for categorical variables and means (SD) for continuous variables. Group 1 refers to constant poor SRH group; Group 2 refers to constant fair SRH group; Group 3 refers to constant good SRH group; Group 4 refers to good-to-fair SRH group

* P<0.05

Table 2. Univariate logistic regression of demographic and clinical characteristics predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.12*	1.08-1.16	<.0001
Sex				
	Male	Ref		<.0001
	Female	2.06*	1.44-2.95	
Level of education				
	illiterate	Ref		
	1~6 years	0.57*	0.38-0.81	0.0019
	7~12 years	0.24*	0.13-0.46	<0.0001
	>12 years	0.06*	0.01-0.42	0.005
Income satisfaction				
	Good	Ref		

	Fair	1.41	0.91-2.18	0.1259
	Poor	2.32*	1.45-3.73	0.0005
Social participation				
	Yes	0.64*	0.44-0.93	<0.0001
	No	Ref		
Marriage				
	Yes	Ref		
	No	1.28	0.83-1.96	0.2665
Smoking				
	Yes	0.7	0.46-1.07	0.0991
	No	Ref		
Alcohol consumption				
	Yes	0.57*	0.37-0.86	0.0082
	No	Ref		

Without job				
	Yes	2.89*	1.91-4.36	<0.0001
	No	Ref		
Self-Rated Health				
	Good	0.17*	0.17-0.27	<0.0001
	Fair	0.43	0.29-0.64	<0.0001
	Poor	Ref		
Number of diseases		1.41*	1.25-1.59	<.0001

* P<0.05

Table 3. Multivariate logistic regression of SRH trajectories predicting frailty

		Frailty		
		OR	95%CI	P value
Age		1.10*	1.06-1.16	<.0001
Sex				
	Male	Ref		
	Female	1.29*	0.81-2.05	0.2803
Level of education				
	illiterate	Ref		
	1~6 years	0.79	0.52-1.21	0.2811
	7~12 years	0.49	0.24-1.08	0.0523
	>12 years	0.16	0.02-1.43	0.1058
Income satisfaction				
	Good	Ref		

	Fair	1.04	0.65-1.67	0.8746
	Poor	1.73*	1.02-2.93	0.0413
Social Participation				
	Yes	1.30	0.83-2.02	0.2558
	No	Ref		
Alcohol consumption				
	Yes	1.06	0.63-1.76	0.8382
	No	Ref		
Without job				
	Yes	2.00*	1.22-3.27	0.0059
	No	Ref		
Self-Rated Health trajectory				
	Group 1	3.09*	2.04-4.69	<.0001
	Group 2	Ref		

	Group 3	0.04*	0.01-0.32	0.0021
	Group 4	0.19*	0.06-0.63	0.0061
Number of diseases		1.10	0.96-1.27	0.1645

Notes. Group 1 refers to constantly poor SRH group; Group 2 refers to constantly fair SRH group; Group 3 refers to constantly good SRH group; Group 4 refers to good-to-fair SRH group

* P<0.05

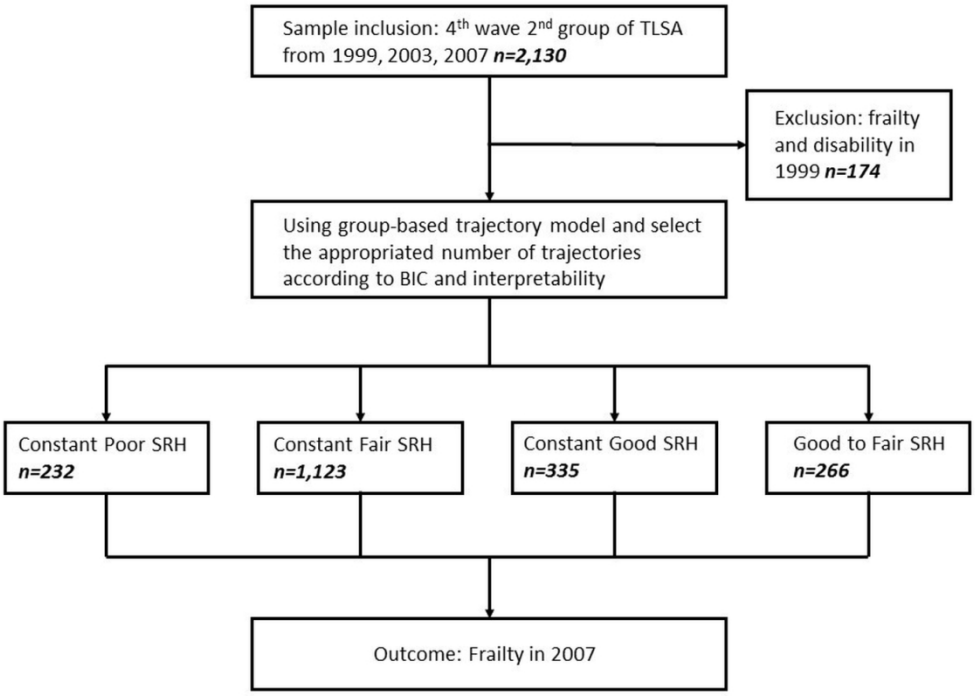

Figure 1. Flow chart of the study design

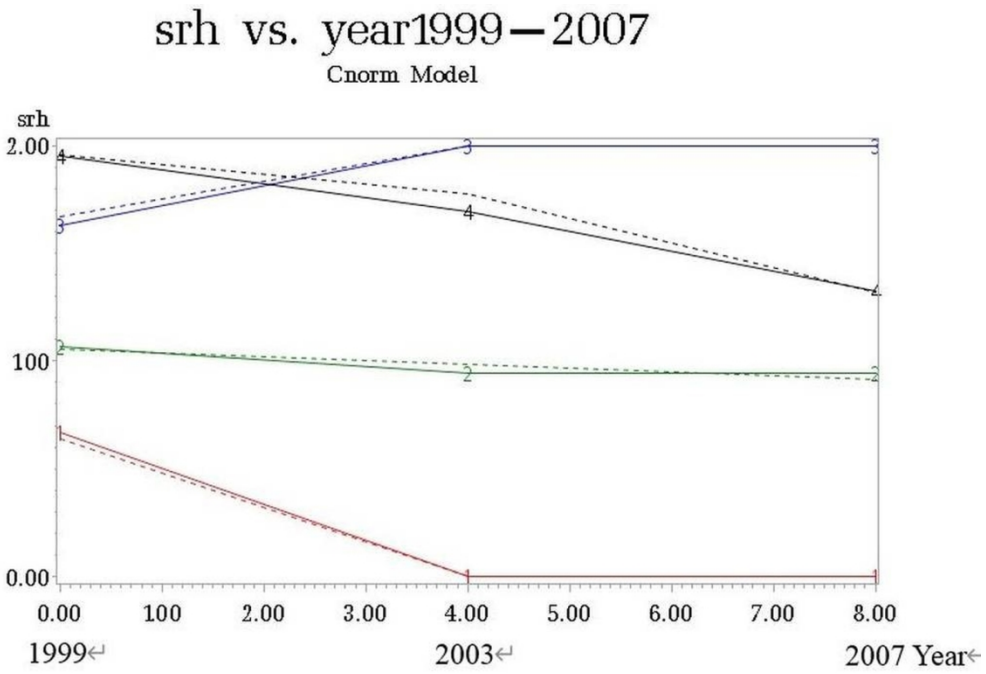

Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary	3

		of what was done and what was found	
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	#3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7

Bias	#9	Describe any efforts to address potential sources of bias	7
Study size	#10	Explain how the study size was arrived at	7
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	8
Statistical methods	#12c	Explain how missing data were addressed	8
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	8
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and	9

		unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	9
Participants	#13c	Consider use of a flow diagram	9
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	12
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
Main results	#16b	Report category boundaries when continuous variables were	9

		categorized	
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
n/a			
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	#18	Summarise key results with reference to study objectives	11
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13
Generalisability	#21	Discuss the generalisability (external validity) of the study results	14
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16