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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:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-049795
Article Type:	Original research
Date Submitted by the Author:	02-Feb-2021
Complete List of Authors:	<p>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, Institute of Population Sciences</p>
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

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TITLE

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

AUTHOR and AFFLIATION

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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

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4 gender, age, level of education, income, social participation, health behaviors and
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7 major comorbidities, age, poor income satisfaction, unemployment and constantly
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10 poor SRH were associated with increased risk of frailty, while constantly good SRH
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13 [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI
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16 (0.059-0.625)] were associated with reduced risks of frailty.

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

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34 **Strengths and Limitation of study:**

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37 1. To the best of our knowledge, this is the first long-term study to investigate the
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40 relationship between SRH trajectory and frailty among Asian population based on
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43 a nationally representative sample.
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46 2. Reporting bias could happen because all data were collected through
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49 self-reporting and not measured objectively.
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52 3. Frailty was defined according to a modified phenotype definition, assessed by
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55 using questionnaire data.
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3 **Key words:** self-rated health, frailty, trajectory, elderly
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For peer review only

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

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

44 *Data sources*

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

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3 highly trained interviewers. To ensure high data quality collection, careful supervision
4 is provided during data collection and data processing is conducted by a professional
5 data entry company.
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10 The TLISA was started in 1989 and six waves of data collection had been completed
11 by 2007. For this study, we used the 1999 sample, which included 2,130 subjects aged
12 53–69-years-old in 1999. We followed-up this cohort for 8 years and used data from
13 2007 to analyze outcomes. The Population Studies Center at the University of
14 Michigan reviewed the representativeness of the completed sample; the analysis
15 showed that the sample was highly representative, with a 90.6% response rate. Details
16 of the study design have been described elsewhere [23-25].
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29 *Study group identification*

30 We included the 1999 sample, which included 2,130 subjects aged 53–69-years-old in
31 1999. Individuals who had developed frailty in 1999 or who had any functional
32 disability in 1999 were excluded from the study. Thus, 1,956 subjects were included
33 in the final analysis.
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42 *Research variables*

43 For each eligible subject, we gathered data in 1999 on age, gender, level of education,
44 marital status, income level, SRH, social participation, employment status, smoking,
45 alcohol consumption, and chronic diseases. Level of education was classified into
46 four groups: illiterate (0 years), elementary school (1–6 years), junior to senior high
47 school (7–12 years), and college or above (> 12 years). Income level was determined
48 by asking individuals how they felt about their income level. The possible answers
49 were *very satisfied*, *satisfied*, *fair*, *unsatisfied*, and *very unsatisfied*. We classified the
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3 income levels as “good ” (rated *very satisfied, satisfied*) “fair” (rated *fair*) or “poor”
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5 (*unsatisfied* or *very unsatisfied*). SRH was determined by asking individuals how they
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7 rated their current health. Possible answers were *excellent, good, fair, poor, and very*
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9 *poor*. We classified the individuals into three groups based on SRH: good (rated
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11 *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*). Individuals who had either
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13 paid or voluntary work or who participated in community activities were considered
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15 as having social participation. The individuals were classified into two groups based
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17 on employment status in 1999: normally employed and unemployed. The number of
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19 chronic diseases suffered by each individual was recorded, including hypertension,
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21 diabetes, cardiovascular disease, stroke, cancer, chronic respiratory diseases, arthritis
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23 or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and kidney diseases.
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26 Data regarding frailty was collected in 2007 as the outcome measure. Frailty was
27
28 defined according to the Fried criteria [12]. Individuals who exhibited at least three of
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30 five traits (i.e., shrinking, weakness, exhaustion, slowness, and low physical activity)
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32 were considered frail. Individuals with only one or two of the five traits were regarded
33
34 as pre-frail. We used substitute evaluations for these five domains because we
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36 retrieved data from questionnaires, and this modified frailty definition have been used
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38 broadly and published before with validity [26-28]. The parameter decreased appetite
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40 was used instead of body weight loss to represent nutritional status. Participants who
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42 reported poor appetite often in the previous week were classified as having the trait of
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44 shrinking. For mobility, we used walking/moving in and around the house instead of
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46 gait speed. Participants who had difficulty or were unable to walk a distance of 200 to
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48 300 m were considered slow. For strength, we used the parameter of lifting heavy
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50 groceries instead of hand grip strength. Participants who had difficulty or were unable
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52 to carry 12 kg of groceries were considered weak. For physical activity, we used the
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3 duration of leisure time/physical activities per week instead of the level of physical
4 activity. Participants who did not take a walk, hike or jog, do gardening, or participate
5 in other outdoor activities at least once or twice a week were considered to have low
6 activity. We used the questionnaire of the Center for Epidemiologic Studies
7 Depression Scale (CES-D) to determine the level of energy. Participants who
8 reported, “*I could not get going*” or “*I felt everything I did was an effort*” often or
9 most of the time in the previous week were considered exhausted. Due to nearly all
10 elderly approaching end-of-life have functional disability and frailty, we regarded
11 those who deceased during study period as having frailty in our study[29]
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26 *Statistical analysis*

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30 A group-based analysis model was applied to determine the SRH trajectories. We
31 employed the Bayesian Information Criterion to identify the most appropriate model
32 groups[30]. Previous geriatric research studies have used this model[23, 27, 28, 31,
33 32]. For the descriptive analysis, we used analysis of variance and the chi-square test
34 to compare continuous and categorized variables, respectively. Logistic regression
35 was used to analyze the relationship between SRH trajectories and frailty, with
36 adjustments for age, gender, level of education, income level, marital status, number
37 of chronic diseases, social participation, smoking, alcohol consumption, and
38 employment status. Statistical significance was set at $p < 0.05$. All data were analyzed
39 using SPSS (version 22.0, IBM, Chicago, IL, USA).
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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 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. 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.

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4 Table 3 illustrates multivariate logistic regression regarding the relationship between
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7 SRH trajectories and frailty. After adjustments for relevant factors, including age,
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10 gender, level of education, income level, social participation, alcohol consumption
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13 behavior, number of chronic diseases, and unemployment status, logistic regression
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16 analysis revealed age, poor income satisfaction, unemployment and constantly poor
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19 SRH was associated with an increased risk of frailty [OR 3.091, 95% CI
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22 (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95%
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25 CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were
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28 associated with a decreased risk of frailty compared to constantly fair SRH.
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1 DISCUSSION

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

9 To the best of our knowledge, this is the first long-term study to investigate the
10 relationship between SRH trajectory and frailty. Our results are consistent with
11 previous studies which investigated SRH at single time point. Huohvanainen et al.
12 (2016) found that poor SRH in midlife was associated with prefrailty, frailty and
13 mortality in later life after 26 years of follow-up in Finland [22]. A short-term study
14 of 22 institutionalized elderly individuals by Gijzel et al. (2017) found that variance in
15 the SRH score time series was significantly higher in frail participants across physical,
16 mental and social domains [33]. Baddour et al. (2019) reported that SRH correlated
17 moderately with frailty and found that good-to-excellent SRH was predictive of
18 non-frail status and preservation of activities of daily living (ADL) [34].

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

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3 1 analysis. Third, in analysis of the relationship between SRH trajectory and frailty, the
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5 2 constantly poor SRH group had an elevated risk of frailty, and significant protective
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7 3 effects were observed for the constantly good SRH and good-to-fair SRH groups.
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9 4 Thus, a causal relationship may exist between SRH and frailty.
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11 5 However, some studies stated that the relationship between SRH and frailty may be in
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13 6 different direction. Pinto et al. discovered that self-rated health is a mediator variable
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15 7 between physical and mental health, including frailty with life satisfaction[35]. The
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17 8 reasons could be that low level of daily activities prevent elderly from participating
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19 9 community activities, thus lead to poor subjective health and life satisfaction. Our
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21 10 study showed that constantly poor SRH would lead to increased incidence of frailty,
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23 11 and we believed that this causal relationship was true, because several studies have
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25 12 identified mechanisms that may possibly link SRH to frailty. Dysregulation of
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27 13 neuroendocrine processes and the immune system may lead to further vulnerability
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29 14 and lower resistance [36], and previous studies showed that inflammatory responses
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31 15 are related to SRH. Christian et al. (2011) found that poorer SRH was associated with
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33 16 elevated serum inflammatory markers, such as IL-6 and CRP, among generally
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35 17 healthy older adults [37]. These inflammatory markers have been associated with
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37 18 frailty. Low physical activity could also be a factor. Granger et al. (2017) reported that
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39 19 high levels of physical activity were positively associated with self-rated 'good
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41 20 health' status in European adolescents [38]. Additionally, Savela et al. (2013) found
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43 21 that a higher level of physical activity from midlife onwards was strongly associated
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45 22 with a lower risk of frailty in old age [39]. These studies suggested that the
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47 23 relationship between SRH and frailty is real under multifactorial mechanism. Further
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49 24 investigation is warranted to explore the intervention to prevent frailty for those
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51 25 people whose SRH are poor, and its cost-effectiveness.
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1 *Strengths and Limitations*

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

23 24 **CONCLUSION**

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3 1 Poor SRH in older adults is associated with a higher risk of frailty in the future, and
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5 2 constantly poor SRH possesses more risk of frailty in the elderly. Moreover,
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7 3 maintaining stable, good SRH may help to prevent frailty in later life. Thus, we
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9 4 suggest governments should design and implement programs to regularly screen SRH
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11 5 in older adults.. Further studies are necessary to define practical strategies to reduce
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13 6 the risk of disability and death among older adults with constantly poor SRH and thus
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15 7 improve the quality of life of elderly people.
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3 **FIGURE**

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6 **Figure 1.** Flow chart of the study design¹

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

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

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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.

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1 **ABBREVIATIONS**

2 SRH Self-rated Health

3 TLSA Taiwan Longitudinal Study on Aging

4 CES-D Center for Epidemiologic Studies Depression Scale

5 ADL Activities of Daily Living

6

For peer review only

1 **DECLARATIONS**

2 **Ethics approval and consent to participate**

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

12 **Consent for publication**

13 Not applicable.

15 **Availability of data and materials**

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

20 **Competing interests**

21 The authors declare no conflicts of interests.

23 **Funding**

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

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3 1
45 2 **Author Contributions**
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7 3 Each author's individual contributions: Meng-Chih Lee conceived of the study and
8 supervised all aspects of its implementation. Wei-Min Chu completed the analyses
9 4 and drafted the content. Yu-han Hsiao, Shu-Hsin Lee and Pi-Shan Hsu assisted with
10 5 the study design and revised the content. Hsin-En Ho and Chih-Jung Yeh assisted
11 6 with the statistical analysis and revised the content. All authors helped to
12 7 conceptualize ideas, interpret findings, and review drafts of the manuscript.
13 8

9

10 10 **Acknowledgements**

11 11 We thank our colleagues from Chun Shan Medical University, Taichung, Taiwan for
12 12 providing supports in statistical analysis. The sponsor has no role in the design,
13 13 methods, subject recruitment, data collections, analysis and preparation of paper.

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1 TABLES

2

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

Characteristics	Total n=1956	SRH Trajectory				P value
		Group 1 n=232	Group 2 n=1123	Group 3 n=335	Group 4 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	No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	0.0876*
	Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	
Alcohol consumption	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	<0.0001*
	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
Unemployment	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	<0.0001*
	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

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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

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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

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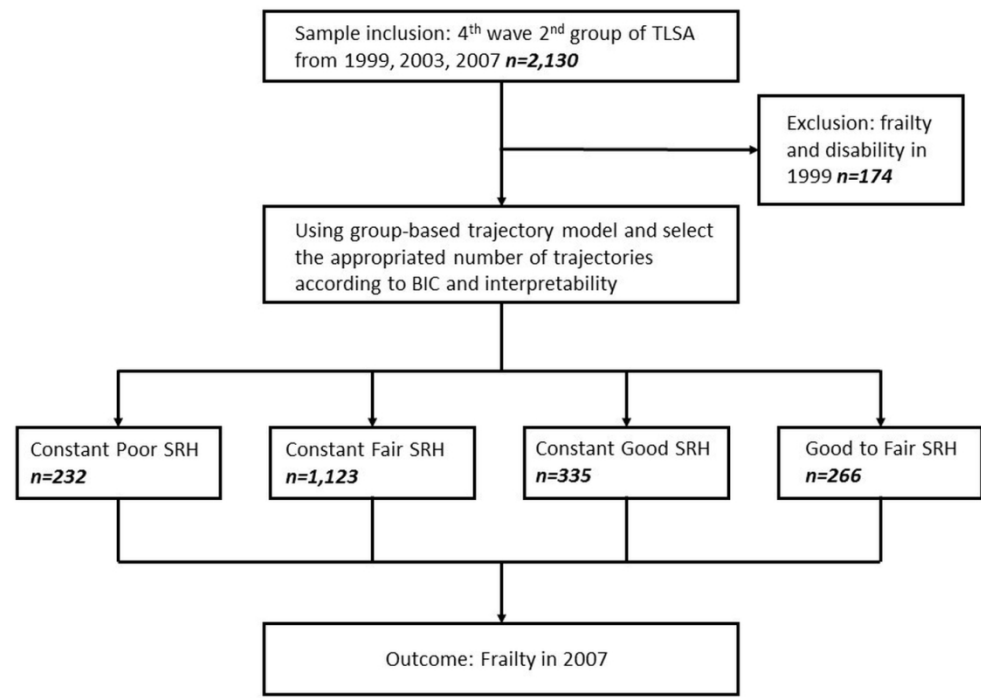


Figure 1. Flow chart of the study design

srh vs. year1999–2007

Cnorm Model

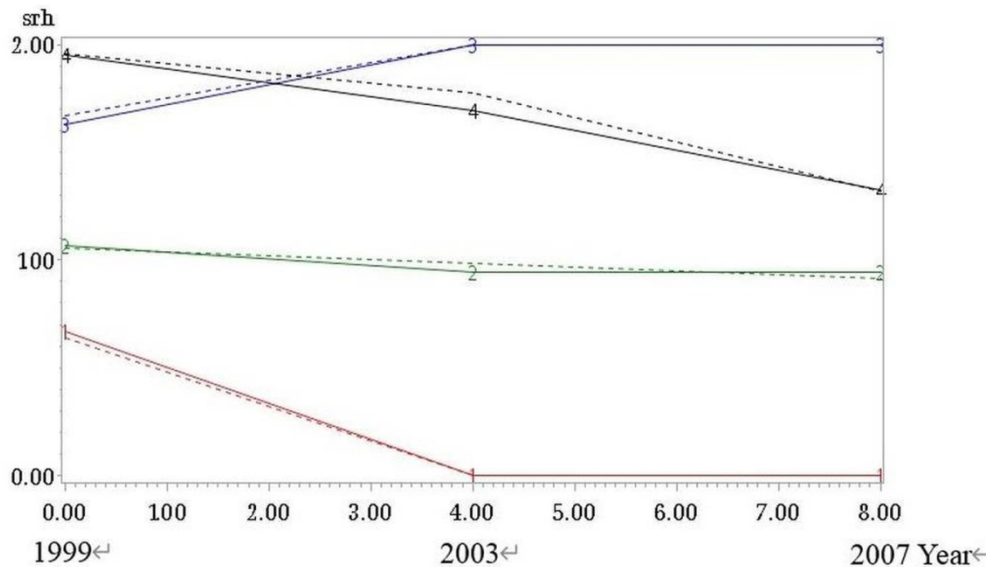


Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

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 cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche 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	
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3	Eligibility criteria	#6a Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7
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6	Eligibility criteria	#6b For matched studies, give matching criteria and number of exposed and unexposed	n/a
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10	Variables	#7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
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15	Data sources /		
16	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
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22	Bias	#9 Describe any efforts to address potential sources of bias	7
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24	Study size	#10 Explain how the study size was arrived at	7
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27	Quantitative		
28	variables	#11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7
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31	Statistical		
32	methods	#12a Describe all statistical methods, including those used to control for confounding	
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37	Statistical	#12b Describe any methods used to examine subgroups and interactions	8
38	methods		
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41	Statistical	#12c Explain how missing data were addressed	8
42	methods		
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44	Statistical	#12d If applicable, explain how loss to follow-up was addressed	8
45	methods		
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48	Statistical	#12e Describe any sensitivity analyses	
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54	Results		
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57	Participants	#13a Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible,	9
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included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.

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5	Participants	#13b	Give reasons for non-participation at each stage 9
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7	Participants	#13c	Consider use of a flow diagram
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12	Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, 9
13			social) and information on exposures and potential confounders. Give
14			information separately for exposed and unexposed groups if
15			applicable.
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19	Descriptive data	#14b	Indicate number of participants with missing data for each variable of
20			interest
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23	n/a		
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25	Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)
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30	Outcome data	#15	Report numbers of outcome events or summary measures over time.
31			Give information separately for exposed and unexposed groups if
32			applicable.
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38	Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted 9
39			estimates and their precision (eg, 95% confidence interval). Make
40			clear which confounders were adjusted for and why they were
41			included
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44	Main results	#16b	Report category boundaries when continuous variables were 9
45			categorized
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48	Main results	#16c	If relevant, consider translating estimates of relative risk into absolute
49			risk for a meaningful time period
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52	n/a		
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54	Other analyses	#17	Report other analyses done—eg analyses of subgroups and 9
55			interactions, and sensitivity analyses
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57			

Discussion

1	Key results	#18	Summarise key results with reference to study objectives	11
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3	Limitations	#19	Discuss limitations of the study, taking into account sources of	13
4			potential bias or imprecision. Discuss both direction and magnitude of	
5			any potential bias.	
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8	Interpretation	#20	Give a cautious overall interpretation considering objectives,	13
9			limitations, multiplicity of analyses, results from similar studies, and	
10			other relevant evidence.	
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14	Generalisability	#21	Discuss the generalisability (external validity) of the study results	14
15				
16	Other			
17	Information			
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20	Funding	#22	Give the source of funding and the role of the funders for the present	16
21			study and, if applicable, for the original study on which the present	
22			article is based	
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 26 This checklist was completed on 01. February 2021 using <https://www.goodreports.org/>, a tool made by the
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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:	<i>BMJ Open</i>
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, Institute of Population Sciences
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

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2
3 1 **TITLE**
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5 2 Trajectory of self-rated health on the incidence of frailty among community-dwelling
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7 3 older adults: evidence from the Taiwan Longitudinal Study on Aging (TLSA)
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37 **12 Word counts: 2995**
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3 **1 ABSTRACT**
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6 **2 Objectives:** Self-rated health (SRH) is an assessment and predictor of health based on
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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.

7 **Design:** An 8-year retrospective cohort study.

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

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

12 **Primary and Secondary Outcome Measures:** Frailty was defined using the Fried
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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.

16 **Results:** Four SRH trajectory classes were identified across the 8-year follow-up: 232
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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

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4 1 gender, age, level of education, income, social participation, health behaviors and
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7 2 major comorbidities, age, poor income satisfaction, unemployment and constantly
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10 3 poor SRH were associated with increased risk of frailty, while constantly good SRH
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13 4 [OR 0.044, 95% CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI
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16 5 (0.059-0.625)] were associated with reduced risks of frailty.

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19 6 **Conclusions:** Constantly poor SRH is associated with an increased risk of frailty in
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22 7 older age. SRH in older adults should be recognized as a predictive tool for future
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25 8 frailty. Diet and exercise interventions may help to prevent frailty among high-risk
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28 9 older individuals with constantly low SRH.

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34 11 **Strengths and Limitation of study:**

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37 12 1. To the best of our knowledge, this is the first long-term study to investigate the
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40 13 relationship between SRH trajectory and frailty among Asian population based on
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43 14 a nationally representative sample.

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46 15 2. Reporting bias could happen because all data were collected through
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49 16 self-reporting and not measured objectively.

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52 17 3. Frailty was defined according to a modified phenotype definition, assessed by
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55 18 using questionnaire data.

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3 1 **Key words:** self-rated health, frailty, trajectory, older adults
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For peer review only

1 BACKGROUND

2 Aging has become a serious challenge globally in both Western and developed Asian
3 countries. The World Health Organization define an aged society as a population in
4 which people over 65-years-old comprise more than 14% of the total population.

5 According to the Department of Health of Taiwan, the proportion of people over 65 in
6 Taiwan increased from 8.6% to 10.7% between 2000 and 2010 [1]. The Department
7 of Development predict this number will rise to 20% by 2027 [2], which would
8 represent the fastest rate of aging in the world. Due to the rapidly aging population,
9 the annual crude mortality rate for Taiwanese citizens over 65 increased from 46.9%
10 to 68.5% between 1981 to 2010 [1, 3].

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

19 Frailty has been proven to be one of the most important key indicators of the health of

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4 1 the elderly in recent decades. Frailty is a geriatric condition characterized by
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7 2 increased vulnerability and decreased capacity to maintain homeostasis, and
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10 3 pre-frailty refers to when one or two of the elements of the Fried frailty phenotype are
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13 4 detected [13]. Frailty in later life has been proven to lead to a number of adverse
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16 5 health outcomes and a poor quality of life [14-18]. As frailty can be addressed by
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19 6 proper recognition and treatment, such as diet and exercise, it is important to identify
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22 7 risk factors for frailty in older adults [19]. Several studies have explored the
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25 8 relationship between SRH and frailty[20-22]. A population-based study of more than
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28 9 2,000 healthy participants conducted in Finland by Huohvanainen et al. (2016) found
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31 10 that SRH in midlife could predict frailty, prefrailty and mortality in later life [23].
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34 11 However, most of previous studies were implemented in Western countries, evidence
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37 12 of the value of SRH for predicting frailty remains scarce for older Asian adults,
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40 13 especially from long-term observation. Also, more and more researchers used
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43 14 trajectories of SRH as indicators to explore the change of SRH through time and its
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46 15 consequences [24, 25]. The aim of this study was to explore the long-term
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49 16 relationships between SRH trajectories and future frailty in older Taiwanese adults
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52 17 using a national population cohort study.
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58 19 **METHODS**

1 *Data sources*

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

14 The TLSA was started in 1989 and six waves of data collection had been completed
15 by 2007. For this study, we used the 1999 sample, which included 2,130 subjects aged
16 53–69-years-old in 1999. We followed-up this cohort for 8 years and used data from
17 2007 to analyze outcomes. The Population Studies Center at the University of
18 Michigan reviewed the representativeness of the completed sample; the analysis
19 showed that the sample was highly representative, with a 90.6% response rate. Details
20 of the study design have been described elsewhere [27-29].

21 *Study group identification*

22 We included the 1999 sample, which included 2,130 subjects aged 53–69-years-old in
23 1999. Individuals who had developed frailty in 1999 or who had any functional
24 disability in 1999 were excluded from the study. Functional disability was ascertained
25

1 if participants had trouble with at least one activity of daily living, including bathing,
2 dressing, eating, getting out of bed, walking, and using the bathroom [30]. Thus,
3 1,956 subjects were included in the final analysis.

4 5 *Research variables*

6 *Demographics*

7 For each eligible subject, we gathered data in 1999 on age, gender, level of education,
8 marital status, income level, social participation, employment status, smoking, alcohol
9 consumption, and chronic diseases. We gathered data of SRH in 1999, 2003 and
10 2007. Level of education was classified into four groups: illiterate (0 years),
11 elementary school (1–6 years), junior to senior high school (7–12 years), and college
12 or above (> 12 years). Income level was determined by asking individuals how they
13 felt about their income level. The possible answers were *very satisfied*, *satisfied*, *fair*,
14 *unsatisfied*, and *very unsatisfied*. We classified the income levels as “good ” (rated
15 *very satisfied*, *satisfied*) “fair” (rated *fair*) or “poor” (*unsatisfied* or *very unsatisfied*).

16 *Health factors*

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

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

8 *Outcome*

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

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3 1 once or twice a week were considered to have low activity. We used the questionnaire
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5 2 of the Center for Epidemiologic Studies Depression Scale (CES-D) to determine the
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7 3 level of energy. Participants who reported, “*I could not get going*” or “*I felt everything*
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9 4 *I did was an effort*” often or most of the time in the previous week were considered
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12 5 exhausted. Due to nearly all elderly approaching end-of-life have functional disability
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14 6 and frailty, we regarded those who deceased during study period as having frailty in
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16 7 our study [35]

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21 9 *Statistical analysis*

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26 10 A group-based trajectory modelling (GBTM) was applied to determine the SRH
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28 11 trajectories. GBTM is a finite mixture model and also a semi-parametric model for
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30 12 longitudinal data. We chose this model because it postulates discrete distribution of
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32 13 the population and thus makes it possible to distinguish, in the population,
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34 14 groups/classes of homogeneous individuals [36]. We used the three groups based on
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36 15 SRH: good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*) as
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38 16 indicators to generate the model and employed the Bayesian Information Criterion to
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40 17 identify the most appropriate model groups[37]. Previous geriatric research studies
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42 18 have used this model [27, 33, 34, 38, 39]. For the descriptive analysis, we used
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44 19 analysis of variance and the chi-square test to compare continuous and categorized
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46 20 variables, respectively. Logistic regression was used to analyze the relationship
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48 21 between SRH trajectories and frailty, with adjustments for age, gender, level of
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4 1 education, income level, marital status, number of chronic diseases, social
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7 2 participation, smoking, alcohol consumption, and employment status. Statistical
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10 3 significance was set at $p < 0.05$. All data were analyzed using SPSS (version 22.0,
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13 4 IBM, Chicago, IL, USA).

15 16 5 *Patient and Public Involvement*

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21 6 Patients or the public were not involved in the design, or conduct, or reporting of our
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24 7 research. However, Taiwan Association of Gerontology and Geriatrics, who listens to
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27 8 and stands for geriatric patients, will help with dissemination plans of our research
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35 36 37 38 11 **RESULTS**

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41 12 Figure 1 shows the flow chart of this study, including data collection from 1999, 2003
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44 13 and 2007. Table 1 shows the descriptive data for all subjects. A total of 1,956 subjects
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47 14 with an average age of 61.46 years were included the final analysis. Most subjects had
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50 15 1-6 years of education, had a fair income level, and were married. The average
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53 16 number of chronic diseases was 1.21. After GBTM was applied, 4 trajectories of SRH
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56 17 was generated from 1999 to 2007 (Figure 2). There were 232 participants (11.9%) in
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59 18 the constantly poor SRH group, 1123 participants (57.4%) in the constantly fair SRH
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1 group, 335 participants (17.1%) in the constantly good SRH group, and 266
2 participants (13.6%) in the good-to-fair SRH group. Age distribution, sex, level of
3 education, income level, social participation, marriage status, alcohol consumption,
4 and unemployment status were significantly different between each of the four SRH
5 trajectory classes.

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

9 Table 3 illustrates multivariate logistic regression regarding the relationship between
10 SRH trajectories and frailty. After adjustments for relevant factors, including age,
11 gender, level of education, income level, social participation, alcohol consumption
12 behavior, number of chronic diseases, and unemployment status, logistic regression
13 analysis revealed age, poor income satisfaction, unemployment and constantly poor
14 SRH was associated with an increased risk of frailty [OR 3.091, 95% CI
15 (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95%
16 CI (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were
17 associated with a decreased risk of frailty compared to constantly fair SRH.

1 DISCUSSION

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

9 To the best of our knowledge, this is the first long-term study to investigate the
10 relationship between SRH trajectory and frailty. Our results are consistent with
11 previous studies which investigated SRH at single time point. Huohvanainen et al.
12 (2016) found that poor SRH in midlife was associated with prefrailty, frailty and
13 mortality in later life after 26 years of follow-up in Finland [23]. A short-term study
14 of 22 institutionalized older individuals by Gijzel et al. (2017) found that variance in
15 the SRH score time series was significantly higher in frail participants across physical,
16 mental and social domains [40]. Baddour et al. (2019) reported that SRH correlated
17 moderately with frailty and found that good-to-excellent SRH was predictive of
18 non-frail status and preservation of activities of daily living (ADL) [41].

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

1 analysis. Third, in analysis of the relationship between SRH trajectory and frailty, the
2 constantly poor SRH group had an elevated risk of frailty, and significant protective
3 effects were observed for the constantly good SRH and good-to-fair SRH groups.
4 Thus, a causal relationship may exist between SRH and frailty.
5 However, some studies stated that the relationship between SRH and frailty may be in
6 different direction. Pinto et al. discovered that self-rated health is a mediator variable
7 between physical and mental health, including frailty with life satisfaction [42]. The
8 reasons could be that low level of daily activities prevent older adults from
9 participating community activities, thus lead to poor subjective health and life
10 satisfaction. Our study showed that constantly poor SRH would lead to increased
11 incidence of frailty, and we believed that this causal relationship was true, because
12 several studies have identified mechanisms that may possibly link SRH to frailty.
13 Dysregulation of neuroendocrine processes and the immune system may lead to
14 further vulnerability and lower resistance [43], and previous studies showed that
15 inflammatory responses are related to SRH. Christian et al. (2011) found that poorer
16 SRH was associated with elevated serum inflammatory markers, such as IL-6 and
17 CRP, among generally healthy older adults [44]. These inflammatory markers have
18 been associated with frailty. Low physical activity could also be a factor. Granger et
19 al. (2017) reported that high levels of physical activity were positively associated with
20 self-rated 'good health' status in European adolescents [45]. Additionally, Savela et
21 al. (2013) found that a higher level of physical activity from midlife onwards was
22 strongly associated with a lower risk of frailty in old age [46]. Further investigation is
23 warranted to explore the intervention to prevent frailty for those people whose SRH
24 are poor, and its cost-effectiveness.

25

1 *Strengths and Limitations*

2 This study has several advantages. First, this eight-year retrospective cohort study was
3 based on a nationally representative sample with extremely high survey response
4 rates. The database was based on a large, randomly selected population; thus, external
5 validity is high. Second, our analysis of SRH trajectory as a predictor of frailty
6 strengthens the evidence of a causal relationship between SRH and frailty. Moreover,
7 the study design of trajectory-based model analysis minimized the possibility of
8 misclassification bias, as SRH can change over time. Third, we adjusted for numerous
9 confounding factors, including age, gender, level of education, income level, marital
10 status, major disease, health behaviors, social participation, and unemployment status.
11 However, this study also has several limitations. First, all data were collected through
12 self-reporting and not measured objectively, which could result in reporting bias.
13 Additionally, proxy respondents completed the follow-up questionnaire for subjects
14 who were severely ill, which may possibly generate reporting bias. Second, the
15 associations between SRH and frailty could be bi-directional. For example, a subject
16 may feel poor SRH due to frailty. However, we attempted to address this possibility
17 by using a longitudinal study design and excluding people with frailty and/or
18 disability at baseline, as both frailty and/or disability could substantially affect the
19 outcome. The design of this study also helped to eliminate the possibility of reverse
20 causality. We also adjusted for a number of major chronic diseases to reduce the
21 influence of bias. Third, when GBTM was applied, differences between subgroups
22 could be discussed, but not differences within subgroups. This was because that
23 GBTM assumed that all individuals in a trajectory class have the same behavior [47].
24 Thus, different trajectory modelling techniques could be applied to examine the
25 difference in specific SRH trajectory in future study. Fourth, we used subjective

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

11

12 **CONCLUSION**

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

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3 **1 FIGURE**

4 **2**
5 **3 Figure 1.** Flow chart of the study design¹

6 **4**
7 **5** Flow chart showing the patient inclusion and exclusion processes, and the process of
8 **6** group-based trajectory analysis. SRH, self-rated health.

9 **7**
10 **8 Figure 2.** Trajectories of Self-Rated Health score between 1999 and 2007

11 **9**
12 **10** After group-based trajectory analysis, there were 232 participants (11.9%, group 1) in
13 **11** the constant poor SRH group, 1123 participants (57.4%, group 2) in the constant fair
14 **12** SRH group, 335 participants (17.1%, group 3) were in the constant good SRH group,
15 **13** and 266 participants (13.6%, group 4) were in the good to fair SRH group.
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3 **1 ABBREVIATIONS**
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5 2 SRH Self-rated Health
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7 3 TLSA Taiwan Longitudinal Study on Aging
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9 4 CES-D Center for Epidemiologic Studies Depression Scale
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12 5 ADL Activities of Daily Living
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For peer review only

1 **DECLARATIONS**

2 **Ethics approval and consent to participate**

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

12 **Consent for publication**

13 Not applicable.

15 **Availability of data and materials**

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

20 **Competing interests**

21 The authors declare no conflicts of interests.

23 **Funding**

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

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45 2 **Author Contributions**
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7
8 3 Each author's individual contributions: Meng-Chih Lee conceived of the study and
9
10 4 supervised all aspects of its implementation. Wei-Min Chu completed the analyses
11
12 5 and drafted the content. Yu-han Hsiao, Shu-Hsin Lee and Pi-Shan Hsu assisted with
13
14 6 the study design and revised the content. Hsin-En Ho and Chih-Jung Yeh assisted
15
16 7 with the statistical analysis and revised the content. All authors helped to
17
18 8 conceptualize ideas, interpret findings, and review drafts of the manuscript.
19
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2223
24 10 **Acknowledgements**
25

26 11 We thank our colleagues from Chun Shan Medical University, Taichung, Taiwan for
27
28 12 providing supports in statistical analysis. The sponsor has no role in the design,
29
30 13 methods, subject recruitment, data collections, analysis and preparation of paper.
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1 TABLES

2

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

Characteristics	Total n=1956	SRH Trajectory				P value
		Group 1 n=232	Group 2 n=1123	Group 3 n=335	Group 4 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	No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	0.0876*
	Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	
Alcohol consumption	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	<0.0001*
	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
Unemployment	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	<0.0001*
	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

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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

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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

1 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;
 2 Group 4 refers to good to fair SRH group
 3 * P<0.0

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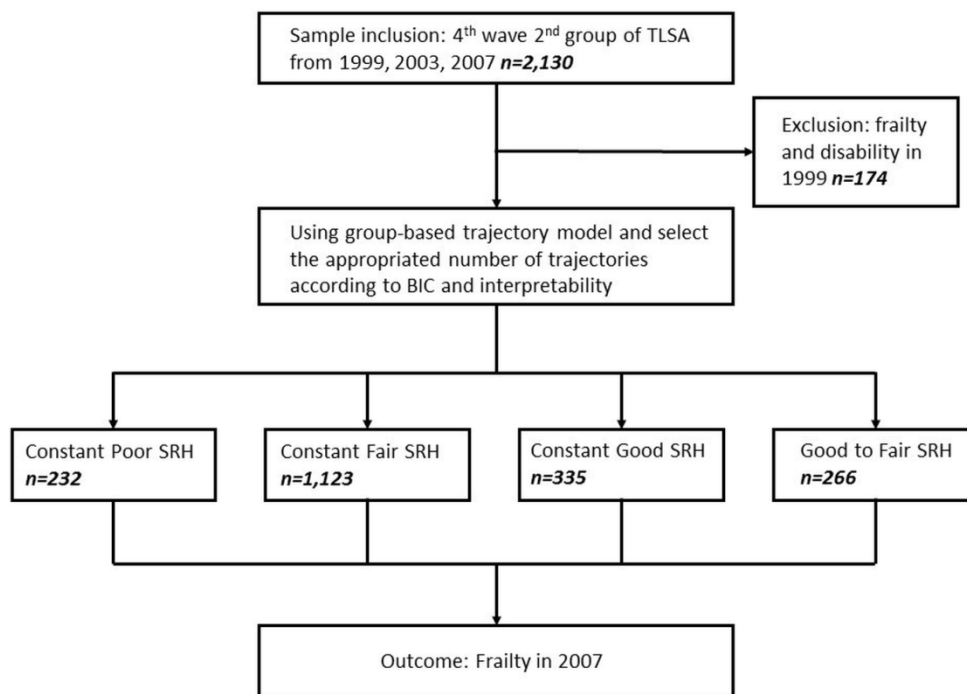


Figure 1. Flow chart of the study design

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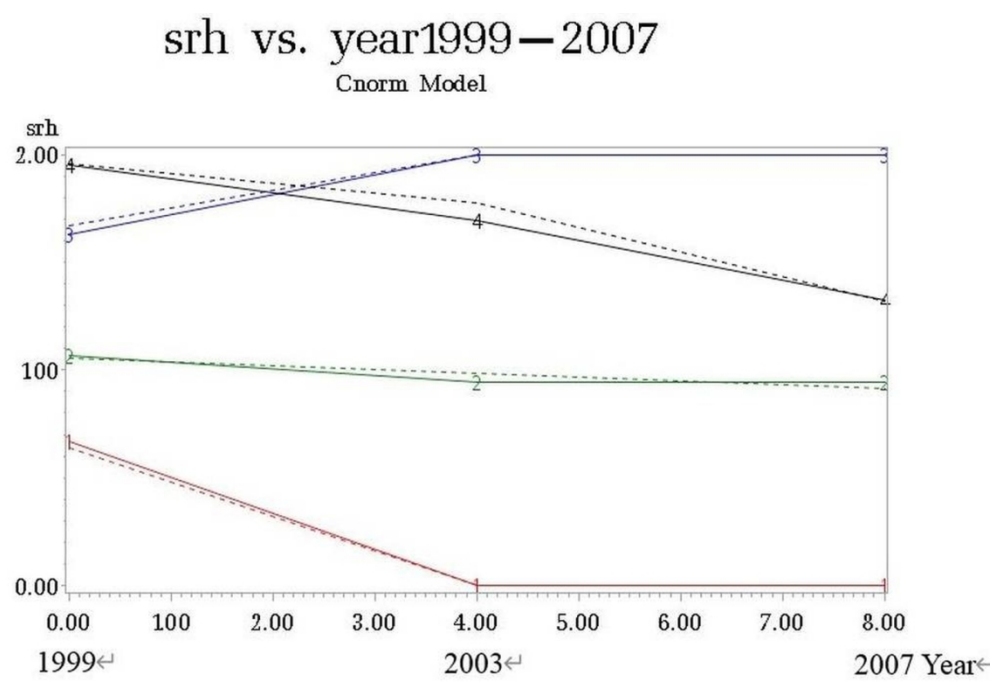


Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

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.

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

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			Page
		Reporting Item	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 / [#2](#) Explain the scientific background and rationale for the 5
rationale investigation being reported

Objectives [#3](#) State specific objectives, including any prespecified 6
hypotheses

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 6
periods of recruitment, exposure, follow-up, and data collection

Eligibility criteria [#6a](#) Give the eligibility criteria, and the sources and methods of 7
selection of participants. Describe methods of follow-up.

Eligibility criteria [#6b](#) For matched studies, give matching criteria and number of 7
exposed and unexposed n/a

Variables [#7](#) Clearly define all outcomes, exposures, predictors, potential 7
confounders, and effect modifiers. Give diagnostic criteria, if
applicable

Data sources / [#8](#) For each variable of interest give sources of data and details of 7
measurement 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.

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

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4	Participants	#13b	Give reasons for non-participation at each stage 9
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13	Descriptive data	#14a	Give characteristics of study participants (eg demographic, 9
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15			clinical, social) and information on exposures and potential
16			confounders. Give information separately for exposed and
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23			variable of interest
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31	Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)
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37	Outcome data	#15	Report numbers of outcome events or summary measures
38			over time. Give information separately for exposed and
39			unexposed groups if applicable.
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48	Main results	#16a	Give unadjusted estimates and, if applicable, confounder- 9
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50			adjusted estimates and their precision (eg, 95% confidence
51			interval). Make clear which confounders were adjusted for and
52			why they were included
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58	Main results	#16b	Report category boundaries when continuous variables were 9
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4	Main results	#16c If relevant, consider translating estimates of relative risk into	
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12	Other analyses	#17 Report other analyses done—eg analyses of subgroups and	9
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14		interactions, and sensitivity analyses	
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17	Discussion		
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20	Key results	#18 Summarise key results with reference to study objectives	11
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23	Limitations	#19 Discuss limitations of the study, taking into account sources of	13
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25		potential bias or imprecision. Discuss both direction and	
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27		magnitude of any potential bias.	
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31	Interpretation	#20 Give a cautious overall interpretation considering objectives,	13
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33		limitations, multiplicity of analyses, results from similar studies,	
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35		and other relevant evidence.	
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39	Generalisability	#21 Discuss the generalisability (external validity) of the study	14
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41		results	
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44	Other Information		
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47	Funding	#22 Give the source of funding and the role of the funders for the	16
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49		present study and, if applicable, for the original study on which	
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51		the present article is based	
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BMJ Open

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

Journal:	<i>BMJ Open</i>
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, Institute of Population Sciences
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	GERIATRIC MEDICINE, PUBLIC HEALTH, EPIDEMIOLOGY

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1 **TITLE**

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

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32 **12 Word counts: 3087**

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1 ABSTRACT

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

6 **Design:** An 8-year retrospective cohort study.

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

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

10 **Primary and Secondary Outcome Measures:** Frailty was defined using the Fried criteria. The
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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.

14 **Results:** Four SRH trajectory classes were identified across the 8-year follow-up: 232 participants
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(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.

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

1 1 SRH in older adults should be recognized as a predictive tool for future frailty. Diet and exercise
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4 2 interventions may help to prevent frailty among high-risk older individuals with constantly low
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7 3 SRH.
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12 **Strengths and Limitation of study:**
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- 14
15 6 1. To the best of our knowledge, this is the first long-term study to investigate the relationship
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18 7 between SRH trajectory and frailty in an Asian population based on a nationally representative
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21 8 sample.
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24 9 2. Reporting bias could have occurred because all data were collected through self-reporting and
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26 10 not measured objectively.
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29 11 3. Frailty was defined according to a modified phenotype definition, and assessed using
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32 12 questionnaire data.
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37 14 **Key words:** self-rated health, frailty, trajectory, older adults
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1 BACKGROUND

2 Aging has become a serious challenge globally in both Western and developed Asian countries.
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4 The World Health Organization defines an aged society as a population in which people over 65
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6 years old comprise more than 14% of the total population. According to the Department of Health
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8 of Taiwan, the proportion of people over 65 in Taiwan increased from 8.6% to 10.7% between
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10 2000 and 2010 [1]. The Department of Development predicts this figure will rise to 20% by 2027
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12 [2], which would represent the fastest rate of aging in the world. Due to the rapidly aging
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14 population, the annual crude mortality rate for Taiwanese citizens over 65 increased from 46.9% to
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16 68.5% between 1981 and 2010 [1, 3].
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10 Many key indicators can be used to predict the future health of older adults, such as the self-rated
11 health (SRH) score. SRH refers to a single question, such as, “In general, would you say that your
12 health is excellent, very good, good, fair, or poor?” [4]. SRH is an assessment and predictor of
13 health based on an individual’s general condition and subjective feelings about their physical,
14 psychological, and social well-being, combined with objective measurements of health. Several
15 studies have demonstrated consistency between SRH and individual health status and have shown
16 SRH can predict future mortality, disability, and other adverse health outcomes [5-12]. Frailty has
17 been proven to be one of the most important key indicators of the health of older people in recent
18 decades. Frailty is a geriatric condition characterized by increased vulnerability and decreased
19 capacity to maintain homeostasis, and pre-frailty refers to a condition that meets one or two of the
20 criteria for the Fried frailty phenotype [13]. Frailty in later life has been proven to lead to a number
21 of adverse health outcomes and a poor quality of life [14-18]. As frailty can be addressed by
22 proper recognition and treatment, such as diet and exercise, it is important to identify risk factors

1 for frailty in older adults [19]. Several studies have explored the relationship between SRH and
2 frailty[20-22]. A population-based study of more than 2,000 healthy participants conducted in
3
4 Finland by Huohvanainen et al. (2016) found that SRH in midlife could predict frailty, pre-frailty,
5
6 and mortality in later life [23]. However, most previous studies were conducted in Western
7
8 countries; evidence of the value of SRH for predicting frailty remains scarce for older Asian adults,
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10 especially from long-term observation. The problem with long-term observations of older adults is
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12 that rapid changes in biological function and psychosocial processes occur over time in this
13
14 population, and it is not possible to detect these changes using traditional statistical methods. Thus,
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16 the group-based trajectory model (GBTM) was developed, which provides a statistical standard for
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18 establishing the influence of life trajectory [24, 25]. The aim of this study was to explore the long-
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20 term relationships between SRH trajectories and future frailty in older Taiwanese adults using a
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22 national population cohort study.
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1 1 **METHODS**

2 2 *Data sources*

3 3 We retrieved data from the Taiwan Longitudinal Study in Aging (TLSA), a population-based,
4 4 national representative study initiated by Taiwan's Bureau of Health Promotion, and the
5 5 University of Michigan's Population Studies Center and Institute of Gerontology in the United
6 6 States. Data were collected from systematically selected representative samples of the Taiwanese
7 7 population, including institutionalized older people. In the TLSA, a three-stage systematic random
8 8 sampling design was used for the selection of an equal probability sample [26]. We believe that the
9 9 TLSA contains samples that are highly representative of the true population structure under this
10 10 kind of sampling method. Personal interviews were conducted by highly trained interviewers. To
11 11 ensure high data quality collection, careful supervision was provided during data collection and
12 12 data processing was conducted by a professional data entry company.

13 13 The TLSA was started in 1989 and six waves of data collection had been completed by 2007. For
14 14 this study, we used the 1999 sample, which included 2,130 subjects aged 53–69 years old in 1999.
15 15 We followed up this cohort for 8 years and used data from 2007 to analyze outcomes. The
16 16 Population Studies Center at the University of Michigan reviewed the representativeness of the
17 17 completed sample, and the analysis showed that the sample was highly representative, with a
18 18 90.6% response rate. Details of the study design have been described elsewhere [27-29].

19 19 *Study group identification*

20 20 We analyzed the 1999 sample, which included 2,130 subjects aged 53–69 years old in 1999.
21 21 Individuals who had developed frailty in 1999 or who had any functional disability in 1999 were
22 22

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

19 *Demographics*

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21 For each eligible subject, we gathered data in 1999 on age, gender, level of education, marital
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24 status, income level, social participation, employment status, smoking, alcohol consumption, and
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26
27 chronic diseases. We gathered SRH data in 1999, 2003, and 2007. Level of education was
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30 classified into four groups: illiterate (0 years), elementary school (1–6 years), junior to senior high
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33 school (7–12 years), and college or above (> 12 years). Income level was determined by asking
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36 individuals how they felt about their income level. The possible answers were *very satisfied*,
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39 *satisfied*, *fair*, *unsatisfied*, and *very unsatisfied*. We classified the income levels as “good ” (rated
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42 *very satisfied*, *satisfied*), “fair” (rated *fair*), or “poor” (*unsatisfied* or *very unsatisfied*).
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46 *Health factors*

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

1 Social participation was determined based on whether individuals performed either paid or
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4 2 voluntary work or participated in community activities. The individuals were classified into two
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7 3 groups based on job status in 1999: with a job and without job [31]. Participants were considered
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10 4 to be employed (“With a job”) if they chose the response “ I had a job whether it was fulltime or
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13 5 part-time job” or “I had a job but took a leave temporarily.” Participants were considered to be
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16 6 unemployed (“Without job”) if they chose the response, “I had no job and was looking for a job.”
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18 7 or “I did not do any job.” The number of chronic diseases suffered by each individual was
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21 8 recorded, including hypertension, diabetes, cardiovascular disease, stroke, cancer, chronic
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24 9 respiratory diseases, arthritis or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and
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27 10 kidney diseases. Information about chronic conditions was ascertained by a positive answer to the
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30 11 question, “Have you ever been told by a doctor that you suffer from...”.

32 *Outcome*

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35 13 Data regarding frailty was collected in 2007 as the outcome measure. Frailty was defined
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38 14 according to the Fried criteria [13]. Individuals who exhibited at least three of five traits (i.e.,
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41 15 weight loss, exhaustion, low physical activity, slowness, and weakness) were considered frail.
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44 16 Individuals meeting only one or two of the five traits of the Fried frailty criteria were regarded as
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47 17 pre-frail. We used substitute evaluations for these five traits because we retrieved data from
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50 18 questionnaires, and this modified frailty definition has been widely used and previously published
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53 19 with validity [32-34]. The parameter “decreased appetite” was used instead of “body weight loss”
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56 20 to represent nutritional status. Hence, participants who reported poor appetite often in the previous
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59 21 week were classified as having the trait “shrinking”. For mobility, we used walking/moving in and
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22 around the house instead of gait speed. Participants who had difficulty or were unable to walk a

1 distance of 200 to 300 m were considered slow. For strength, we used the “lifting heavy groceries”
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4 2 parameter instead of “hand grip strength”. Participants who had difficulty or were unable to carry
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7 3 12 kg of groceries were considered weak. For physical activity, we used the duration of leisure
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10 4 time/physical activities per week instead of the level of physical activity. Participants who did not
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13 5 take a walk, hike or jog, do gardening, or participate in other outdoor activities at least once or
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16 6 twice a week were considered to have low activity. We used the questionnaire of the Center for
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18 7 Epidemiologic Studies Depression Scale (CES-D) to determine the level of energy. Participants
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21 8 who reported, “*I could not get going*” or “*I felt everything I did was an effort*” often or most of the
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24 9 time in the previous week were considered to be exhausted. As nearly all older people approaching
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27 10 end of life have functional disability and frailty, we regarded those who died during the study
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30 11 period as having frailty in our study [35]

31 32 33 34 35 13 *Statistical analysis*

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38 14 Group-based trajectory modelling (GBTM) was applied to determine the SRH trajectories. GBTM
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41 15 is a finite mixture model and also a semi-parametric model for longitudinal data. We chose this
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44 16 model because it postulates a discrete distribution of the population, which makes it possible to
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47 17 distinguish groups/classes of homogeneous individuals within the population [36]. We used the
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50 18 three groups based on SRH, good (rated *excellent* or *good*), fair (*fair*), or poor (*poor* or *very poor*),
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53 19 as indicators to generate the model and employed the Bayesian Information Criterion to identify
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56 20 the most appropriate model groups[37]. Previous geriatric research studies have used this model
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59 21 [27, 33, 34, 38, 39]. For the descriptive analysis, we used analysis of variance and the chi-square
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22 test to compare continuous and categorical variables, respectively. Logistic regression was used to

1 analyze the relationship between SRH trajectories and frailty, with adjustments for age, gender,
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4 2 level of education, income level, marital status, number of chronic diseases, social participation,
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7 3 smoking, alcohol consumption, and employment status. Statistical significance was set at $p < 0.05$.
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10 4 All data were analyzed using SPSS (version 22.0, IBM, Chicago, IL, USA).
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17 6 *Patient and Public Involvement*

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20 7 Patients or the public were not involved in the design, or conduct, or reporting of our research.
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23 8 However, the Taiwan Association of Gerontology and Geriatrics, who listens to and represents
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26 9 geriatric patients, will help to disseminate our plans, which are based on our research results.
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1 RESULTS

2 Figure 1 shows the flow chart of this study, including data collection from 1999, 2003, and 2007.

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

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

15 Table 3 illustrates the results of the multivariate logistic regression analysis of the relationships
16 between SRH trajectories and frailty. After adjustments for relevant factors, including age, gender,
17 level of education, income level, social participation, alcohol consumption behavior, number of
18 chronic diseases, and job status, logistic regression analysis revealed age, poor income satisfaction,
19 without job, and constantly poor SRH was associated with an increased risk of frailty [OR 3.091,
20 95% CI (2.036-4.692) for constantly poor SRH], while constantly good SRH [OR 0.044, 95% CI
21 (0.006-0.323)] and good-to-fair SRH [OR 0.192, 95% CI (0.059-0.625)] were associated with a
22 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.

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

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12 However, some studies have suggested that in the relationship between SRH and frailty, the
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15 direction of causality may be different. Pinto et al. discovered that self-rated health is a mediator
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18 variable between physical and mental health and life satisfaction [42]. Possibly, low-level daily
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21 activities prevent older adults from participating in community activities, leading to poor
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24 subjective health and life satisfaction. Our study showed that constantly poor SRH would lead to
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27 increased incidence of frailty, and we believe that this causal relationship does exist, because
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30 several studies have identified mechanisms that potentially link SRH to frailty. Dysregulation of
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33 neuroendocrine processes and the immune system may lead to further vulnerability and lower
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36 resistance [43], and previous studies showed that inflammatory responses are related to SRH.
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39 Christian et al. (2011) found that poorer SRH was associated with elevated serum inflammatory
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42 markers, such as IL-6 and CRP, among generally healthy older adults [44]. These inflammatory
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45 markers have been associated with frailty. Low physical activity could also be a factor. Granger et
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48 al. (2017) reported that high levels of physical activity were positively associated with self-rated
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51 'good health' status in European adolescents [45]. Additionally, Savela et al. (2013) found that a
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54 higher level of physical activity from midlife onwards was strongly associated with a lower risk of
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57 frailty in old age [46]. Further investigation is warranted to explore this intervention for the
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60 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

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

1 **ABBREVIATIONS**
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4 SRH Self-rated Health
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7 TLSA Taiwan Longitudinal Study on Aging
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10 CES-D Center for Epidemiologic Studies Depression Scale
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13 ADL Activities of Daily Living
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For peer review only

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

1 This work was supported by the Ministry of Health and Welfare, Taiwan (Grant number:
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3
4 M06M2346 awarded to M.-C.L.).
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10 **Author Contributions**

11
12 The individual contributions of all authors: Meng-Chih Lee conceived of the study and supervised
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14 all aspects of its implementation. Wei-Min Chu completed the analyses and drafted the content.
15
16 Yu-han Hsiao, Shu-Hsin Lee, and Pi-Shan Hsu assisted with the study design and revised the
17
18 content. Hsin-En Ho and Chih-Jung Yeh assisted with the statistical analysis and revised the
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20 content. All authors helped to conceptualize ideas, interpret findings, and review drafts of the
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22 manuscript.
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32 **Acknowledgements**

33
34 We thank our colleagues from Chung Shan Medical University, Taichung, Taiwan for assisting
35
36 with the statistical analysis. The sponsor had no role in the design, methods, subject recruitment,
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38 data collection, analysis, or preparation of paper.
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TABLES

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

Characteristics	SRH Trajectory					P value
	Total n=1956	Group 1 n=232	Group 2 n=1123	Group 3 n=335	Group 4 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%)	

1		>12 yrs	122(6.24%)	4(1.7%)	58(5.2%)	37(11%)	23(8.7%)	
2								
3								
4	Income							<0.0001*
5								
6		Poor	416(21.81%)	76(33.9%)	246(22.5%)	43(13.1%)	51(19.8%)	
7								
8		Fair	860(45.1%)	102(45.5%)	513(46.8%)	143(43.5%)	102(39.5%)	
9								
10		Good	631(33.09%)	46(20.5%)	337(30.8%)	143(43.5%)	105(40.7%)	
11								
12	Social participation							0.0003*
13								
14		No	475(24.28%)	61(26.3%)	305(27.2%)	56(16.7%)	53(19.9%)	
15								
16		Yes	1481(75.72%)	171(73.7%)	818(72.8%)	279(83.3%)	213(80.1%)	
17								
18	Marriage							0.0316*
19								
20		No	356(18.2%)	46(19.8%)	215(19.2%)	42(12.5%)	53(19.9%)	
21								
22		Yes	1600(81.8%)	186(80.2%)	908(80.9%)	293(87.5%)	213(80.1%)	
23								
24	Smoking							0.0876*
25								
26		No	1415(72.34%)	173(74.6%)	826(73.6%)	240(71.6%)	176(66.2%)	
27								
28		Yes	541(27.66%)	59(25.4%)	297(26.5%)	95(28.4%)	90(33.8%)	
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1	Alcohol						
2							
3							<0.0001*
4	consumption						
5							
6							
7	No	1361(69.62%)	181(78.4%)	817(72.8%)	204(60.9%)	159(59.8%)	
8							
9	Yes	594(30.38%)	50(21.7%)	306(27.3%)	131(39.1%)	107(40.2%)	
10							
11							
12	Without job						<0.0001*
13							
14							
15	No	816(41.82%)	75(32.6%)	431(38.5%)	178(53.1%)	132(49.6%)	
16							
17	Yes	1135(58.18%)	155(67.4%)	689(61.5%)	157(46.9%)	134(50.4%)	
18							
19							
20							
21	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*
22							
23							

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		

1		Fair	1.41	0.91-2.18	0.1259
2					
3					
4		Poor	2.32*	1.45-3.73	0.0005
5					
6					
7	Social participation				
8					
9		Yes	0.64*	0.44-0.93	<0.0001
10					
11		No	Ref		
12					
13					
14					
15	Marriage				
16					
17		Yes	Ref		
18					
19		No	1.28	0.83-1.96	0.2665
20					
21					
22					
23	Smoking				
24					
25		Yes	0.7	0.46-1.07	0.0991
26					
27		No	Ref		
28					
29					
30					
31	Alcohol consumption				
32					
33					
34		Yes	0.57*	0.37-0.86	0.0082
35					
36		No	Ref		
37					
38					
39					
40					

1 Without job

2
3
4 Yes 2.89* 1.91-4.36 <0.0001

5
6
7 No Ref

8
9 Self-Rated Health

10
11
12 Good 0.17* 0.17-0.27 <0.0001

13
14 Fair 0.43 0.29-0.64 <0.0001

15
16
17 Poor Ref

18
19
20 Number of diseases

21 1.41* 1.25-1.59 <.0001

22
23
24 * 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		

1		Fair	1.04	0.65-1.67	0.8746
2					
3					
4		Poor	1.73*	1.02-2.93	0.0413
5					
6					
7	Social Participation				
8					
9		Yes	1.30	0.83-2.02	0.2558
10					
11		No	Ref		
12					
13					
14					
15	Alcohol consumption				
16					
17		Yes	1.06	0.63-1.76	0.8382
18					
19		No	Ref		
20					
21					
22					
23	Without job				
24					
25		Yes	2.00*	1.22-3.27	0.0059
26					
27		No	Ref		
28					
29					
30					
31					
32	Self-Rated Health trajectory				
33					
34		Group 1	3.09*	2.04-4.69	<.0001
35					
36		Group 2	Ref		
37					
38					
39					
40					
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44					
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46					

1		Group 3	0.04*	0.01-0.32	0.0021
2					
3					
4		Group 4	0.19*	0.06-0.63	0.0061
5					
6					
7	Number of diseases		1.10	0.96-1.27	0.1645
8					
9					

10 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;

11
12 Group 4 refers to good-to-fair SRH group

13
14
15 * P<0.05

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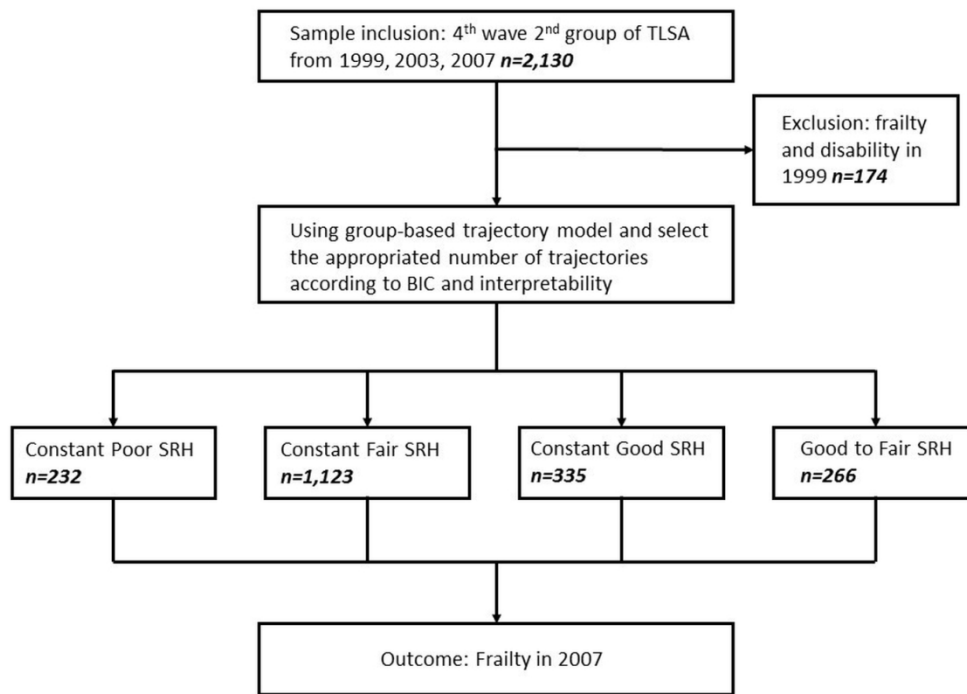


Figure 1. Flow chart of the study design

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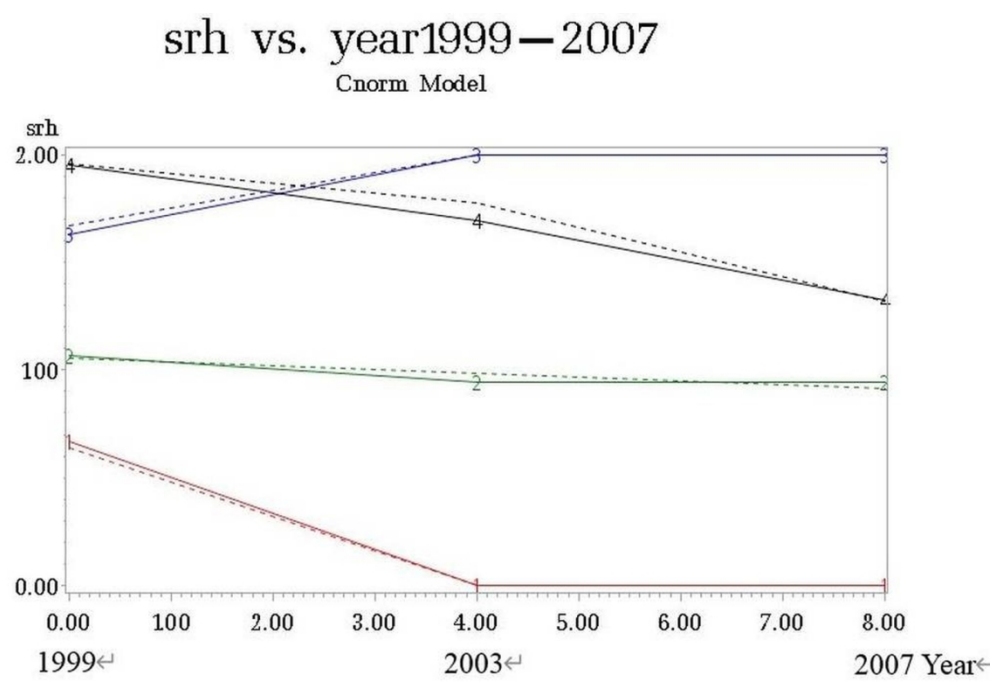


Figure 2. Trajectories of Self-Rated Health score between 1999 and 2007

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 cohort reporting guidelines, and cite them as:

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

			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

1	Bias	#9	Describe any efforts to address potential sources of bias	7
2				
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4	Study size	#10	Explain how the study size was arrived at	7
5				
6				
7	Quantitative	#11	Explain how quantitative variables were handled in the	7
8	variables		analyses. If applicable, describe which groupings were chosen,	
9			and why	
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15	Statistical	#12a	Describe all statistical methods, including those used to control	
16	methods		for confounding	
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23	Statistical	#12b	Describe any methods used to examine subgroups and	8
24	methods		interactions	
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29	Statistical	#12c	Explain how missing data were addressed	8
30	methods			
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34	Statistical	#12d	If applicable, explain how loss to follow-up was addressed	8
35	methods			
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38				
39	Statistical	#12e	Describe any sensitivity analyses	
40	methods			
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48	Results			
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51	Participants	#13a	Report numbers of individuals at each stage of study—eg	9
52			numbers potentially eligible, examined for eligibility, confirmed	
53			eligible, included in the study, completing follow-up, and	
54			analysed. Give information separately for for exposed and	
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unexposed groups if applicable.

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4	Participants	#13b	Give reasons for non-participation at each stage 9
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6	Participants	#13c	Consider use of a flow diagram
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13	Descriptive data	#14a	Give characteristics of study participants (eg demographic, 9
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15			clinical, social) and information on exposures and potential
16			confounders. Give information separately for exposed and
17			unexposed groups if applicable.
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22	Descriptive data	#14b	Indicate number of participants with missing data for each
23			variable of interest
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31	Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)
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37	Outcome data	#15	Report numbers of outcome events or summary measures
38			over time. Give information separately for exposed and
39			unexposed groups if applicable.
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48	Main results	#16a	Give unadjusted estimates and, if applicable, confounder- 9
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50			adjusted estimates and their precision (eg, 95% confidence
51			interval). Make clear which confounders were adjusted for and
52			why they were included
53			
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58	Main results	#16b	Report category boundaries when continuous variables were 9
59			
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4	Main results	#16c If relevant, consider translating estimates of relative risk into	
5			
6		absolute risk for a meaningful time period	
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12	Other analyses	#17 Report other analyses done—eg analyses of subgroups and	9
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14		interactions, and sensitivity analyses	
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17	Discussion		
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20	Key results	#18 Summarise key results with reference to study objectives	11
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23	Limitations	#19 Discuss limitations of the study, taking into account sources of	13
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25		potential bias or imprecision. Discuss both direction and	
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27		magnitude of any potential bias.	
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31	Interpretation	#20 Give a cautious overall interpretation considering objectives,	13
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33		limitations, multiplicity of analyses, results from similar studies,	
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35		and other relevant evidence.	
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39	Generalisability	#21 Discuss the generalisability (external validity) of the study	14
40			
41		results	
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44	Other Information		
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47	Funding	#22 Give the source of funding and the role of the funders for the	16
48			
49		present study and, if applicable, for the original study on which	
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51		the present article is based	
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