



## Mortality risk in older Japanese people based on self-reported dyslipidemia treatment and socioeconomic status: The JAGES cohort study

Yota Katsuyama<sup>a,\*</sup>, Katsunori Kondo<sup>b,c</sup>, Masayo Kojima<sup>b</sup>, Koto Kamiji<sup>b</sup>, Kazushige Ide<sup>c</sup>, Genmei Iizuka<sup>a</sup>, Go Muto<sup>c,d</sup>, Takanori Uehara<sup>e</sup>, Kazutaka Noda<sup>e</sup>, Masatomi Ikusaka<sup>e</sup>

<sup>a</sup> Chiba University, Graduate School of Medical and Pharmaceutical Sciences, Chiba, Japan

<sup>b</sup> National Center for Geriatrics and Gerontology, Aichi, Japan

<sup>c</sup> Chiba University, Center for Preventive Medical Sciences, Chiba, Japan

<sup>d</sup> Department of Hygiene, Kitasato University School of Medicine, Kanagawa, Japan

<sup>e</sup> Department of General Medicine, Chiba University Hospital, Chiba, Japan

### ARTICLE INFO

#### Keywords:

Socioeconomic status  
Dyslipidemia  
Older people  
Mortality

### ABSTRACT

Few studies consider socioeconomic status when assessing mortality risk in dyslipidemia cases. This study used cohort data from the 2010 Japan Gerontological Evaluation Study (JAGES), which contains data on older Japanese people, to associate socioeconomic status with mortality risk in patients treated for dyslipidemia. In this 6-year longitudinal study, we examined 47,275 older Japanese people aged  $\geq 65$  years who could independently perform activities of daily living. Patients' background characteristics were classified based on their dyslipidemia treatment status and were assessed using the chi-squared test. The mortality risk was assessed using the Cox proportional hazards model, wherein the objective and explanatory variables were total mortality and self-report of dyslipidemia treatment, respectively. The participants were stratified by sex and age into younger (aged 65–74 years) and older (aged  $\geq 75$  years) groups of men and women. The results were adjusted, with health condition, health behavior, and socioeconomic status as confounding factors. The adjusted hazard ratios of 5514 people who died during the follow-up who had self-reported dyslipidemia treatment were 0.49 [95% confidence interval (CI) 0.35–0.69] for younger men; 0.57 (95% CI 0.42–0.76) for older men; 0.52 (95% CI 0.34–0.80) for younger women; and 0.47 (95% CI 0.33–0.67) for older women. Older people undergoing treatment for dyslipidemia had factors beneficial for health, such as good socioeconomic status. Despite considering these factors, individuals undergoing dyslipidemia treatment had a negative association with mortality risk.

### 1. Introduction

Coronary artery disease and cerebrovascular disease are the predominant causes of death worldwide (World Health Organization, 2020) and also in the Japanese population (Ministry of Health Labor and Welfare, 2019). Therefore it is important for patients to manage dyslipidemia, which is also a major risk factor for arteriosclerotic disease. Globally, the recommended drug therapies for managing dyslipidemia are secondary prophylactics, which are aimed at preventing the recurrence of arteriosclerotic diseases, particularly coronary artery disease and cerebrovascular disease, and primary prophylactics for patients at high risk of developing arteriosclerotic diseases (Kinoshita et al., 2018; United States Preventive Services Task Force, 2016; Arnett et al., 2019;

Mach et al., 2019). According to the Japanese guidelines for managing dyslipidemia, primary prophylaxis against arteriosclerotic diseases is effective in younger people, but its benefits are not apparent in older people, for whom the decision is left to the primary care physician (Kinoshita et al., 2018). The effectiveness of primary prophylaxis against arteriosclerotic diseases among older individuals remains debatable because of the impact of aging on prognoses and the lack of evidence on primary prophylaxis (Kinoshita et al., 2018).

In Japan, the health insurance system (Ministry of Health Labor and Welfare. Health insurance) covers all Japanese individuals; in addition, a long-term care insurance system (Ministry of Health Labor and Welfare. Long-term care, health and welfare services for the elderly) covers people aged  $\geq 65$  years and those aged  $\geq 40$  years having a specific

Abbreviations: CI, Confidence interval; HR, Hazard ratio; JAGES, Japan Gerontological Evaluation Study; GDS, Geriatric depression scale.

\* Corresponding author at: Chiba University Graduate School of Medical and Pharmaceutical Sciences, 1-8-1, Inohana Chuo-ku, Chiba-shi, Chiba 260-8670, Japan.

E-mail address: [katsuyama-cib@umin.ac.jp](mailto:katsuyama-cib@umin.ac.jp) (Y. Katsuyama).

<https://doi.org/10.1016/j.pmedr.2022.101779>

Received 28 December 2021; Received in revised form 1 March 2022; Accepted 20 March 2022

Available online 21 March 2022

2211-3355/© 2022 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

disease. Patients must pay 10%–30% of the costs of treatment and long-term care based on their income. These insurance programs do not cover preventive care; however, the Japanese government supports the costs of specific health checkups, (Ministry of Health Labor and Welfare. [Specific health checkups and specific health guidance](#)) which include dyslipidemia and diabetes testing, and about 50% of this target population undergoes these health checkups for preventive care (Ministry of Health Labor and Welfare. [Implementation status of specific health checkups and specific health guidance on, 2019](#)). In Japan, patients can go to any hospital and choose their physician based on their symptoms; however, their income may limit which physician they choose (Murata et al., 2010).

Social factors have an impact on health and mortality (Schroeder, 2007); in particular, socioeconomic status has been reported to be a social determinant of health (World Health Organization, 2008; Ministry of Health Labor and Welfare, 2013). Socioeconomic status is also associated with hypertension and diabetes (Tedesco et al., 2001; Nagamine et al., 2019), which are lifestyle-related diseases. In studies assessing coronary artery disease and mortality risk that have been conducted to establish the Japanese guidelines for managing dyslipidemia, identified risk factors included health conditions (other diseases, such as hypertension, diabetes, cardiovascular disease, and stroke); body mass index (BMI); and behaviors such as smoking, alcohol consumption, and exercise (Imamura et al., 2009; Imano et al., 2011; Yokokawa et al., 2011). However, most previous studies did not consider socioeconomic status. It is therefore unclear whether socioeconomic status affects the onset of coronary artery disease or the risk of mortality in older individuals treated for dyslipidemia and whether it has an impact on the treatment of older people.

In terms of the association between cholesterol level and socioeconomic status, a study conducted in the United Kingdom reported that a high socioeconomic status group had high total cholesterol levels and low triglyceride levels, total mortality, and risk of mortality from coronary artery disease (Stringhini et al., 2018). In a similar report from Japan, low-income men had a high prevalence of high total cholesterol levels; however, there were no associations observed with other socioeconomic statuses or between socioeconomic status and women's health conditions (Fujiyoshi et al., 2018). Although these studies assessed the association between total cholesterol levels and socioeconomic status, total cholesterol levels are not appropriate for assessing this risk because they also include high-density lipoprotein cholesterol levels; therefore, they have been excluded from the diagnostic criteria for dyslipidemia since 2007. It is therefore unclear whether the individuals in groups with high total cholesterol levels included in the above studies experienced dyslipidemia. In another study that focused on self-reported questionnaires from 5759 Japanese people from 10 municipalities aged  $\geq 50$  years, 12% of the participants were diagnosed with dyslipidemia and 6% were undergoing dyslipidemia treatment at that time, and disposable household income, high education level, and health checkup in the past year were found to have positive associations with the diagnosis of dyslipidemia (Ibuka et al., 2020); however, mortality risk was not assessed.

In the present study, therefore, longitudinal data on older Japanese people were used to investigate the socioeconomic status of older patients undergoing treatment for dyslipidemia to evaluate the association between mortality risk and socioeconomic status.

## 2. Methods

### 2.1. Study population

The present study was a longitudinal cohort study that used data from the Japan Gerontological Evaluation Study (JAGES) cohort (Kondo, 2016; Kondo and Rosenberg, 2018). The JAGES is an epidemiological survey conducted with an emphasis on studying the social determinants of health in older Japanese people.

Between August 2010 and January 2012, a self-administered survey was distributed via mail to 95,827 older individuals aged  $\geq 65$  years who were living in 13 municipalities and who had not been certified as requiring long-term care. A total of 62,418 responses were obtained (response rate: 65.1%). The follow-up period was approximately 6 years (shortest: 5.2 years; longest: 6.6 years). Data from long-term care insurance provided a basis for tracking mortality in 54,537 (87.4%) people. The included participants were older individuals who independently performed activities of daily living and in whom it was possible to determine whether they were reportedly undergoing treatment for dyslipidemia; the excluded participants were those whose status of disease treatment during the survey was unclear ( $n = 5373$ ), those who had been receiving treatment for an unknown disease ( $n = 301$ ), and those who lacked independence in activities of daily living ( $n = 869$ ) or whose independence was unclear ( $n = 719$ ). Those who had indicated that they were not undergoing treatment for any disease but whose responses to subsequent questions indicated that they were undergoing treatment for certain diseases were deemed to be undergoing treatment for those diseases. Ultimately, 47,275 participants were included in the analysis (Fig. 1). During the follow-up period, 791 participants dropped out for reasons other than death.

### 2.2. Mortality outcome

The objective variable was total mortality during the follow-up period. Total mortality was tracked from each municipality's database for long-term care insurance, similar to other JAGES studies (Tani et al., 2018; Nagamine et al., 2020; Tani et al., 2018). Of the participants under examination, 5514 (11.7%) deaths were reported.

### 2.3. Status of dyslipidemia treatment

The explanatory variable was dyslipidemia treatment. We checked the dyslipidemia treatment status of each participant included in the JAGES cohort study, which was a self-administered survey. If the participants chose the survey option that indicated that they were undergoing treatment for dyslipidemia (regarded as "dyslipidemia" hereinafter due to changes in medical terminology) among the diseases listed in the survey, then they were considered to be undergoing treatment for dyslipidemia.

### 2.4. Covariates

Based on prior studies (Kinoshita et al., 2018; United States Preventive Services Task Force, 2016; Arnett et al., 2019; Mach et al., 2019; Stringhini et al., 2018; Fujiyoshi et al., 2018; Ibuka et al., 2020) the

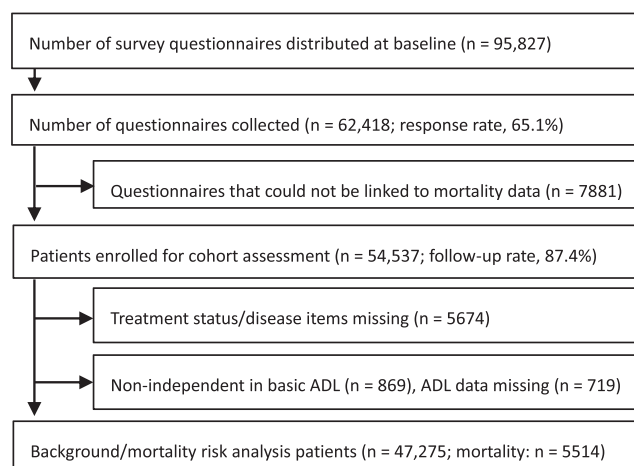


Fig. 1. Flowchart showing the selection of patients for the study cohort.

adjusted confounding factors for dyslipidemia and mortality were age, sex, self-report of receiving disease treatment (hypertension, diabetes, heart disease, stroke, cancer, or liver disease), depressive tendency, BMI, alcohol consumption, and smoking status. Because of the differences between younger (age 65–74 years) and older (age  $\geq 75$  years) participants (Kinoshita et al., 2018) and between male and female participants in terms of the outcomes of dyslipidemia treatment, (Kinoshita et al., 2018; United States Preventive Services Task Force, 2016; Arnett, 2019; Mach et al., 2019) the participants were stratified based on age and sex. The depressive tendency was defined as a score of  $\geq 5$  or  $\leq 4$  on the geriatric depression scale (Nyunt et al., 2009), and BMI was stratified as  $\geq 25$  or  $< 25$  kg/m<sup>2</sup>.

The health behaviors surveyed included a history of health checkups (visits within the past year or more), walking time ( $\geq 30$  min or  $< 30$  min daily), frequency of consuming meat/fish ( $\geq 1$  time or  $< 1$  time daily), and frequency of consuming fruits/vegetables ( $\geq 1$  time or  $< 1$  time daily). Questions regarding socioeconomic status included those on equivalized income [ $\geq 2$  million Japanese Yen (JPY) or  $< 2$  million JPY],

educational level ( $\geq 10$  years or  $< 10$  years), employment status (working or not), and marital status (married or not) as social determinants of health.

## 2.5. Statistical analysis

First, we used the chi-squared test to assess the background characteristics of the patients undergoing treatment for dyslipidemia. Next, we employed a Cox proportional hazards model to assess the hazard ratio (HR) and 95% confidence interval (CI) for the 6-year mortality risk based on whether the participants were treated for dyslipidemia. In the regression analysis, we used self-reported treatment of diseases (hypertension, diabetes, heart disease, stroke, cancer, and liver disease), depressive tendency, BMI, alcohol consumption, and smoking status as confounding factors based on prior research conducted on dyslipidemia (Model 1). A history of health checkup visits, walking time, frequency of consuming meat/fish, and frequency of consuming fruits/vegetables, as health behaviors, were also considered confounding factors (Model 2).

**Table 1**

Participants' background characteristics based on data from the 2010 Japan Gerontological Evaluation Study.

Self-reported dyslipidemia treatment		Men (n = 22,219)			Women (n = 25,056)		
		Yes (n = 1,609) n (%)	No (n = 20,610) n (%)	P values	Yes (n = 3,218) n (%)	No (n = 21,838) n (%)	P values
Age (years)	65–69	520 (32.3)	5969 (29.0)	< 0.001	1078 (33.5)	5932 (27.2)	<0.001
	70–74	520 (32.2)	6240 (30.3)		1027 (31.9)	6568 (30.1)	
	75–79	344 (21.4)	4611 (22.4)		693 (21.5)	4963 (22.7)	
	80–84	177 (11.0)	2666 (12.9)		314 (9.8)	2861 (13.1)	
	$\geq 85$	48 (3.0)	1124 (5.5)		106 (3.3)	1514 (6.9)	
Depressive tendency (GDS $\geq 5$ )	Yes	395 (24.6)	4985 (24.2)	0.006	732 (22.8)	4731 (21.7)	<0.001
	No	1047 (65.1)	13049 (63.3)		1975 (61.4)	12854 (58.9)	
	Missing data	167 (10.4)	2576 (12.5)		511 (15.9)	4253 (19.5)	
BMI (kg/m <sup>2</sup> )	<18.5	31 (1.9)	1184 (5.8)	< 0.001	142 (4.4)	2006 (9.2)	<0.001
	$\geq 18.5$ to $< 25$	1058 (65.8)	14436 (70.0)		2218 (68.9)	14448 (66.2)	
	$\geq 25$	496 (30.8)	4320 (21.0)		769 (23.9)	4260 (19.5)	
	Missing data	24 (1.5)	670 (3.3)		89 (2.8)	1124 (5.2)	
Smoking status	Yes	220 (13.7)	3876 (18.8)	< 0.001	60 (1.9)	706 (3.2)	<0.001
	No	1285 (79.9)	15243 (74.0)		2849 (88.5)	18418 (84.3)	
	Missing data	104 (6.5)	1491 (7.2)		309 (9.6)	2714 (12.4)	
Drinking status	Yes	901 (56.0)	10955 (53.2)	0.038	469 (14.6)	3055 (14.0)	0.040
	No	615 (38.2)	8453 (41.0)		2583 (80.3)	17475 (80.0)	
	Missing data	93 (5.8)	1202 (5.8)		166 (5.2)	1308 (6.0)	
Equivalized income (million JPY)	<2	562 (34.9)	8523 (41.4)	< 0.001	1204 (37.4)	8766 (40.1)	<0.001
	$\geq 2$ to $< 4$	678 (42.1)	7505 (36.4)		1157 (36.0)	6102 (27.9)	
	$\geq 4$	220 (13.7)	2136 (10.4)		347 (10.8)	1879 (8.6)	
	No response	149 (9.3)	2446 (11.9)		510 (15.9)	5091 (23.3)	
Employed	Yes	463 (28.8)	5777 (28.0)	< 0.001	456 (14.2)	3471 (15.9)	<0.001
	No	1089 (67.7)	13279 (64.4)		2353 (73.1)	14405 (66.0)	
	Missing data	57 (3.5)	1534 (7.4)		409 (12.7)	3962 (18.1)	
Educational attainment (years)	<6	15 (0.9)	294 (1.4)	< 0.001	42 (1.3)	677 (3.1)	<0.001
	6–9	526 (32.7)	8927 (43.3)		1312 (40.8)	10719 (49.1)	
	$\geq 10$	553 (34.4)	6498 (31.5)		1335 (41.5)	7191 (32.9)	
	$\geq 13$	496 (30.8)	4525 (22.0)		472 (14.7)	2644 (12.1)	
	Missing data	19 (1.2)	366 (1.8)		57 (1.8)	607 (2.8)	
Marital status	Has a spouse	1417 (88.1)	17622 (85.0)	0.004	2012 (62.5)	12555 (57.5)	<0.001
	No spouse	185 (11.5)	2726 (13.2)		1179 (36.6)	8830 (40.4)	
	Missing data	7 (0.4)	262 (1.3)		27 (0.8)	453 (2.1)	
History of health checkup visits	Within past year	1100 (68.4)	11633 (56.4)	< 0.001	2275 (70.7)	12057 (55.2)	<0.001
	More than 1 year	335 (20.8)	5218 (25.3)		526 (16.4)	4863 (22.3)	
	No	137 (8.5)	3143 (15.3)		309 (9.6)	3898 (17.9)	
	Missing data	37 (2.3)	616 (3.0)		108 (3.4)	1020 (4.7)	
Meat/fish consumption	$\leq 3$ times weekly	508 (31.6)	7283 (35.3)	0.009	872 (27.1)	7093 (32.5)	<0.001
	4–6 times weekly	354 (22.0)	4678 (22.7)		706 (21.9)	4778 (21.9)	
	Once daily or more	647 (40.2)	7354 (35.7)		1486 (46.2)	8731 (40.0)	
	Missing data	100 (6.2)	1295 (6.3)		154 (4.8)	1236 (5.7)	
Fruit/vegetable consumption	$\leq 3$ times weekly	119 (7.4)	2007 (9.7)	0.077	97 (3.0)	1252 (5.7)	<0.001
	4–6 times weekly	206 (12.8)	2831 (13.7)		279 (8.7)	2028 (9.3)	
	Once daily or more	1191 (74.0)	14600 (70.8)		2692 (83.7)	17455 (79.9)	
	Missing data	93 (5.8)	1172 (5.7)		150 (4.7)	1103 (5.1)	
Walking time	$\geq 30$ min	1045 (65.0)	13371 (64.9)	0.336	992 (30.8)	7062 (32.3)	<0.001
	$< 30$ min	488 (30.0)	6233 (30.2)		2050 (63.7)	13238 (60.6)	
	Missing data	76 (4.7)	1006 (4.9)		176 (5.5)	1538 (7.1)	

BMI, body mass index; GDS, geriatric depression scale.

Finally, we also considered socioeconomic status, including equivalized income, educational level, employment status, and marital status, which are social determinants of health, as confounding factors (Model 3).

STATA/SE V.16 (Stata Corp, College Station, TX, USA) was used for the statistical analysis, with the level of significance set at 5%.

### 2.6. Ethical considerations

The study protocol for the JAGES project was approved by the ethics committees of the Nihon Fukushi University (10–05) and the National Center for Geriatrics and Gerontology (992–2).

### 3. Results

Table 1 shows the participants' descriptive statistics. Of 47,275 participants, 22,219 were men and 25,056 were women. A total of 1609 (7.2%) men and 3218 (12.8%) women were reported to be treated for dyslipidemia.

The mean age of those being treated for dyslipidemia was 72.9 (standard deviation [SD] 5.5) years, which is younger than that of those not undergoing treatment (74.0 [SD 6.1] years). We observed that some 55% of those being treated for dyslipidemia were obese. On comparing the health-related behaviors of those undergoing dyslipidemia treatment versus those who were not, we found that more patients undergoing treatment consumed alcohol (men, 56.0% vs. 53.2%; women, 14.6% vs. 14.0%), few smoked (men, 13.7% vs. 18.8%; women, 1.9% vs. 3.2%), many had a history of visits for health/wellness checkups in the past year (men, 68.4% vs. 56.4%; women, 70.7% vs. 55.2%), many consumed meat/fish at least once daily (men, 40.2% vs. 35.7%; women, 46.2% vs. 40.0%), many consumed fruits/vegetables at least once daily (men, 74.0% vs. 70.8%; women, 83.7% vs. 79.9%), and more women walked for at least 30 min daily (30.8% vs. 32.3%). In terms of socioeconomic status in those undergoing dyslipidemia treatment compared with those who were not, many had high equivalized income ( $\geq 4$  million JPY: men, 13.7% and 10.4%, respectively; women, 10.8% and 8.6%, respectively), attained a high level of education ( $\geq 13$  years: men, 30.8% and 22.0%, respectively; women, 14.7% and 12.1%, respectively), and were not working (men, 67.7% and 64.4%, respectively; women, 73.1% and 66.0%, respectively). In terms of marital status, many patients who were undergoing dyslipidemia treatment had a spouse (men, 88.1%; women, 62.5%) compared with those who were not under treatment (men, 85.0%; women, 57.5%).

Table 2 shows the results of the Cox proportional hazards models assessing mortality risk in individuals treated for dyslipidemia. The adjusted HRs for 5514 patients undergoing self-reported dyslipidemia treatment who died during follow-up were 0.49 (95% CI 0.35–0.69) for younger men; 0.57 (95% CI 0.42–0.76) for older men; 0.52 (95% CI 0.34–0.80) for younger women; and 0.47 (95% CI 0.33–0.67) for older women. Regardless of age and sex, self-reported dyslipidemia treatment exhibited a negative association with mortality risk in all models: a crude model, Model 1 adjusted for health conditions, Model 2 adjusted

for health behaviors in addition to Model 1, and Model 3 adjusted for socioeconomic status and marital status in addition to Model 2. Even when participants who died within 2 years were excluded, the results were the same in all models. In Model 3, the adjusted HRs were 0.53 (95% CI 0.36–0.78) for younger men, 0.44 (95% CI 0.30–0.64) for older men, 0.61 (95% CI 0.39–0.97) for younger women, and 0.42 (95% CI 0.28–0.64) for older women.

Table 3 shows the HRs for moderator variables, excluding dyslipidemia treatment. Although self-reported cancer and liver disease treatment, along with depressive tendency, had a negative association with mortality risk, treatment for hypertension or diabetes had either a slight or no association with mortality risk. For socioeconomic status, equivalized income had a negative association with mortality risk in younger people; however, education level, employment status, and marital status were unrelated to mortality risk.

### 4. Discussion

The present study reveals that individuals being treated for dyslipidemia have certain factors related to health behaviors and socioeconomic status, such as not smoking, a history of health checkups, and educational attainment, which are beneficial for their health. Considering health conditions, health behaviors, and socioeconomic status, treatment for dyslipidemia was confirmed to have a negative relationship with mortality risk.

Regarding health-related behaviors of those undergoing dyslipidemia treatment versus those who were not, many individuals had undergone health or wellness checkups in the past year (men 68.4% vs. 56.4%; women 70.7% vs. 55.2%). Moreover, in terms of socioeconomic status, many individuals had high equivalized incomes ( $\geq 4$  million JPY: men, 13.7% vs. 10.4%; women, 10.8% vs. 8.6%) and attained high levels of education ( $\geq 13$  years: men, 30.8% vs. 22.0%; women, 14.7% vs. 12.1%). The estimated number of dyslipidemia patients in Japan was 2.25 million in 2017, (Ministry of Health Labor and Welfare, 2017) i.e., approximately 1.8% of the population, (Ministry of Health Labor and Welfare, 2017) and 33.6% of people were found to have hypercholesterolemia during wellness visits (Sasamori et al., 2015). Dyslipidemia has few subjective symptoms unless there are complications, and Japanese people have a low incidence of coronary artery disease and cerebrovascular disease (Ueshima et al., 2008); therefore, it is likely that many cases are identified by chance during health checkups. Our results are consistent with findings of reports stating that disposable household income, high levels of education, and health checkups within the past year have positive relationships with the diagnosis of dyslipidemia (Ibuka et al., 2020). Therefore, individuals who engage in health behaviors such as visiting clinics for health checkups, and those who are socioeconomically privileged to afford health checkup visits, are more likely to be diagnosed with dyslipidemia.

The present study reveals that, despite considering factors such as health condition, health behaviors, and socioeconomic status, self-reported dyslipidemia treatment showed a negative association with

**Table 2**  
Hazard ratios for mortality risk in individuals treated for dyslipidemia: results of Cox proportional hazards models.

	Men (age 65–74)		Men (age $\geq 75$ )		Women (age 65–74)		Women (age $\geq 75$ )	
	HR (95% CI)	P values	HR (95% CI)	P values	HR (95% CI)	P values	HR (95% CI)	P values
Crude	0.54 (0.41–0.71)	<0.001	0.67 (0.55–0.82)	<0.001	0.39 (0.28–0.56)	<0.001	0.67 (0.55–0.82)	<0.001
Model 1	0.51 (0.38–0.69)	<0.001	0.60 (0.47–0.77)	<0.001	0.49 (0.33–0.72)	<0.001	0.59 (0.46–0.76)	<0.001
Model 2	0.49 (0.36–0.68)	<0.001	0.58 (0.45–0.76)	<0.001	0.47 (0.32–0.71)	<0.001	0.56 (0.42–0.74)	<0.001
Model 3	0.49 (0.35–0.69)	<0.001	0.57 (0.42–0.76)	<0.001	0.52 (0.34–0.80)	0.002	0.47 (0.33–0.67)	<0.001

BMI, body mass index; CI, confidence interval; HR, hazard ratio.

<sup>a</sup>Model 1: Crude model + self-reported as being treated for different diseases (hypertension, diabetes, stroke, heart disease, cancer, liver disease), depressive tendency, BMI, drinking, and smoking.

Model 2: Model 1 + history of health checkup visits, walking time, and frequency of meat/fish and fruit/vegetable consumption.

Model 3: Model 2 + equivalized income, educational attainment, employment status, and marital status.

**Table 3**  
Hazard ratios of moderator variables for mortality risk: results of Cox proportional hazards models.

	Men (age 65–74)		Men (age ≥ 75)		Women (age 65–74)		Women (age ≥ 75)	
	HR (95% CI)	P values	HR (95% CI)	P values	HR (95% CI)	P values	HR (95% CI)	P values
Hypertension	0.93 (0.80–1.08)	0.345	0.89 (0.79–1.01)	0.065	1.06 (0.82–1.37)	0.640	0.87 (0.73–1.03)	0.107
Diabetes	1.24 (1.03–1.50)	0.021	1.13 (0.97–1.32)	0.122	0.93 (0.62–1.38)	0.718	1.10 (0.85–1.44)	0.464
Heart disease	1.32 (1.08–1.61)	0.006	1.35 (1.18–1.55)	<0.001	2.09 (1.45–3.02)	<0.001	1.21 (0.95–1.54)	0.123
Stroke	1.24 (0.77–2.02)	0.378	1.46 (1.04–2.05)	0.027	1.38 (0.34–5.63)	0.650	0.99 (0.32–3.10)	0.993
Cancer	3.94 (3.22–4.81)	<0.001	1.74 (1.45–2.08)	<0.001	6.27 (4.46–8.80)	<0.001	2.74 (1.96–3.82)	<0.001
Liver disease	2.47 (1.86–3.28)	<0.001	1.39 (1.01–1.92)	0.040	4.63 (2.96–7.26)	<0.001	1.43 (0.86–2.35)	0.164
Depressive tendency (GDS ≥ 5)	1.56 (1.34–1.82)	<0.001	1.37 (1.21–1.55)	<0.001	1.21 (0.93–1.58)	0.148	1.85 (1.55–2.21)	<0.001
BMI (≥25Kg/m <sup>2</sup> )	0.85 (0.71–1.02)	0.073	0.68 (0.58–0.80)	<0.001	0.91 (0.67–1.23)	0.526	0.83 (0.66–1.05)	0.272
Drinking	1.00 (1.00–1.00)	0.674	1.00 (1.00–1.00)	0.231	1.01 (0.87–1.17)	0.918	1.00 (1.00–1.00)	0.623
Smoking	1.39 (1.18–1.62)	<0.001	1.00 (1.00–1.00)	0.166	2.95 (1.99–4.36)	<0.001	1.51 (0.94–2.42)	0.091
Health checkup within past 1 year	1.00 (1.00–1.00)	0.743	1.00 (1.00–1.00)	0.622	1.00 (1.00–1.00)	0.802	1.00 (1.00–1.00)	0.774
Walking ≥ 30 min	1.00 (1.00–1.00)	0.744	1.00 (1.00–1.00)	0.651	1.00 (1.00–1.00)	0.842	1.00 (1.00–1.00)	0.001
Meat/fish daily	1.00 (1.00–1.00)	0.446	1.00 (1.00–1.00)	0.470	1.00 (1.00–1.00)	0.205	1.00 (1.00–1.00)	0.026
Fruits/vegetables daily	1.00 (1.00–1.01)	0.798	1.00 (1.00–1.00)	0.888	1.00 (1.00–1.00)	0.696	1.00 (1.00–1.00)	0.945
Equivalized income ≥2 million JPY	0.82 (0.71–0.95)	0.009	1.02 (0.91–1.15)	0.747	0.61 (0.48–0.78)	<0.001	1.19 (1.00–1.42)	0.051
Educational attainment ≥ 10 years	1.00 (1.00–1.00)	0.864	1.00 (1.00–1.00)	0.764	1.00 (0.99–1.01)	0.834	1.00 (1.00–1.00)	0.970
Employed	1.00 (1.00–1.00)	0.213	1.00 (1.00–1.00)	0.931	1.00 (1.00–1.01)	0.876	1.00 (1.00–1.01)	0.809
Have a spouse	1.00 (1.00–1.01)	0.842	1.00 (1.00–1.00)	0.037	1.00 (0.99–1.01)	0.901	1.00 (1.00–1.00)	0.730

BMI, body mass index; CI, confidence interval; GDS, geriatric depression scale; HR, hazard ratio; JPY, Japanese Yen.

mortality risk. In the present study, a high proportion of the participants being treated for dyslipidemia were obese, and only 1.9% of men and 4.4% of women were slim, a finding that is consistent with leanness being a mortality risk for older people (Nagai et al., 2010; Murayama et al., 2015); older men with BMI ≥ 25 kg/m<sup>2</sup> as a moderator variable showed a negative relationship with mortality risk, with an HR of 0.68 (95% CI 0.58–0.80,  $p < 0.001$ ). Liver disease could be another relevant factor for the increase in total mortality risk due to the low total cholesterol levels in Japanese people (Okamura et al., 2007). In the present study, however, individuals being treated for dyslipidemia had a low mortality risk even when health behaviors and health conditions such as BMI, liver disease, and cancer were considered. Despite adjusting for health conditions, health behaviors, and socioeconomic status based on prior research, those who self-reported receiving dyslipidemia treatment had a low mortality risk, suggesting the presence of unexplained factors that lower the mortality risk.

Low-density lipoprotein cholesterol and triglycerides are risk factors for coronary artery disease and cerebrovascular disease (Imamura et al., 2009; Sarwar et al., 2007); therefore, the presence of atherosclerosis does not lower mortality risk. Dyslipidemia drugs might have therapeutic effects and could explain the results. Individuals treated for hypertension and diabetes, however, did not show a decrease in mortality risk in the present study; therefore, there might be certain dyslipidemia-specific factors other than drug therapy. The preventive effects of dyslipidemia drug therapy against arteriosclerotic disease in older people remain unclear, (Kinoshita et al., 2018) and there are other possibilities beyond the effects of drug therapy. Dyslipidemia has few subjective symptoms unless there are complications and adherence to statin therapy is poor compared with that to other cardiovascular disease medications (Chowdhury et al., 2013). Therefore, the participants receiving dyslipidemia treatment may have higher health consciousness than those not treating their dyslipidemia just because they do not know that they have a chronic disease, such as dyslipidemia. Many participants in the present study had a low risk of arteriosclerotic disease, and because Japan's universal health coverage makes it relatively inexpensive to access medical care, receiving medical care could have had a negative association with mortality risk in these individuals. However, this information was not clarified in the present study; therefore, further research is needed to highlight unknown factors that could contribute to

the negative relationship between treatment for dyslipidemia and mortality risk.

#### 4.1. Limitations

First, given that the present study investigated whether participants were treated for diseases based on a self-administered questionnaire, their cholesterol levels and severity of diseases were unknown, and it could not be confirmed whether they truly had dyslipidemia. In a prior study, self-reported responses regarding various diseases matched medical records to a certain extent, with the specificity for hypercholesterolemia reportedly being 93% for all age groups and 84% for the ≥ 65-year age group (Koller et al., 2014); these results largely match those in the present study. Second, even when participants reported receiving dyslipidemia treatment, the extent of their treatment was unknown. It is possible that they were not receiving drug therapy and were only following diet or exercise therapy, or that they were not actually being treated. For those who were receiving drug therapy, the drug contents were unknown, and it was unclear whether the therapy was primary or secondary prophylaxis. In the present study, heart disease and stroke were included as moderator variables to reduce the aforementioned effects. Third, we did not investigate the presence of chronic kidney disease or peripheral artery disease, which are high-risk factors for coronary artery disease with an impact on mortality; therefore, it was not possible to adjust for this variable. Fourth, the response rate of the self-administered questionnaire in the present study was 65.1%. A lower educational level entails fewer responses to self-administered questionnaires, (Korkeila et al., 2001) and the participants in the present study could potentially be biased as belonging to a higher socioeconomic status. Those with a disadvantaged socioeconomic status would less frequently engage in health checkups and therefore have fewer opportunities to be diagnosed with hyperlipidemia. Although dyslipidemia was noted during checkups, lower health awareness did not lead to further consultations. Therefore, the socioeconomic status of patients with dyslipidemia could have had an outsized impact on the results of the present study. The mortality risk of latent dyslipidemia in individuals who have not been examined needs further investigation.

## 5. Conclusions

This longitudinal cohort study, with a follow-up period of approximately 6 years, consisted of older Japanese participants who independently performed their activities of daily living. The study investigated the association between socioeconomic status and mortality risk in patients undergoing treatment for dyslipidemia. The socioeconomic status of individuals who were treated for dyslipidemia was beneficial for their health; however, despite considering health condition, health behaviors, and socioeconomic status, self-report of dyslipidemia treatment was confirmed to have a negative association with mortality risk.

### CRedit authorship contribution statement

**Yota Katsuyama:** Conceptualization, Methodology, Formal analysis, Writing – original draft. **Katsunori Kondo:** Investigation, Writing – review & editing, Project administration, Funding acquisition. **Masayo Kojima:** Conceptualization, Writing – review & editing, Supervision. **Koto Kamiji:** Conceptualization, Methodology, Formal analysis, Writing – review & editing. **Kazushige Ide:** Writing – review & editing, Supervision. **Genmei Iizuka:** Writing – review & editing. **Go Muto:** Writing – review & editing. **Takanori Uehara:** Writing – review & editing. **Kazutaka Noda:** Writing – review & editing. **Masatomi Iku-saka:** Writing – review & editing, Supervision.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgment

This study used data from the JAGES.

### Funding

This study was supported by Grant-in-Aid for Scientific Research [grant numbers 15H01972, 15H04781, 15H05059, 15K03417, 15K03982, 15K16181, 15K17232, 15K18174, 15K19241, 15K21266, 15KT0007, 15KT0097, 16H05556, 16K09122, 16K00913, 16K02025, 16K12964, 16K13443, 16K16295, 16K16595, 16K16633, 16K17256, 16K17281, 16K19247, 16K19267, 16K21461, 16K21465, 16KT0014, 17K04305, 17K34567, 17K04306, 25253052, 25713027, 26285138, 26460828, 26780328, 18H03018, 18H04071, 18H03047, 18H00953, 18H00955, 18KK0057, 19H03901, 19H03915, 19H03860, 19K04785, 19K10641, 19K11657, 19K19818, 19K19455, 19K24060, 19K20909, 20H00557] from JSPS (Japan Society for the Promotion of Science); Health Labour Sciences Research Grants [grant numbers H26-Choju-Ippan-006, H27-Ninchisyou-Ippan-001 H28- Choju-Ippan-002, H28-Ninchisyou-Ippan-002, H29-Chikyukibo-Ippan-001, H30-Jyunkankinado-Ippan-004, 18H04071, 19FA1012, 19FA2001] 209 from the Ministry of Health, Labour and Welfare, Japan; the Research and Development Grants for Longevity Science from Japan Agency for Medical Research and development (AMED) [grant numbers JP17dk0110027, JP18dk0110027, JP18ls0110002, JP18le0110009, JP20dk0110034, JP20dk0110037]; the Research Funding for Longevity Sciences from National Center for Geriatrics and Gerontology [grant numbers 24–17, 24–23, 29–42, 30–30, 30–22, 20–19]; Open Innovation Platform with Enterprises, Research Institute and Academia (OPERA) [grant number JPMJOP1831] from the Japan Science and Technology (JST); a grant from the Japan Foundation For Aging And Health [grant number J09KF00804]; a grant from Innovative Research Program on Suicide Countermeasures (1–4); a grant from Sasakawa Sports Foundation; a grant from Japan Health Promotion & Fitness Foundation; a grant from Chiba Foundation for Health Promotion & Disease Prevention; the

8020 Research Grant for fiscal 2019 from the 8020 Promotion Foundation (adopted number: 19-2-06); a grant from Niimi University [grant number 1915010]; and grants from Meiji Yasuda Life Foundation of Health and Welfare. The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the respective funding organizations.

## References

- Arnett, D.K., Blumenthal, R.S., Albert, M.A., Buroker, A.B., Goldberger, Z.D., Hahn, E.J., Himmelfarb, C.D., Khera, A., Lloyd-Jones, D., McEvoy, J.W., Michos, E.D., Miedema, M.D., Muñoz, D., Smith Jr., S.C., Virani, S.S., Williams Sr., K.A., Yeboah, J., Ziaeian, B., 2019. ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. *Circulation* 2019 (140), e596–e646.
- Chowdhury, R., Khan, H., Heydon, E., Shroufi, A., Fahimi, S., Moore, C., Stricker, B., Mendis, S., Hofman, A., Mant, J., Franco, O.H., 2013. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. *Eur. Heart J.* 34 (38), 2940–2948.
- Fujiyoshi, N., Arima, H., Satoh, A., Ojima, T., Nishi, N., Okuda, N., Kadota, A., Ohkubo, T., Hozawa, A., Nakaya, N., Fujiyoshi, A., Okamura, T., Ueshima, H., Okayama, A., Miura, K., 2018. Associations between socioeconomic status and the prevalence and treatment of hypercholesterolemia in a general Japanese population: NIPPON DATA2010. *J. Atheroscler. Thromb.* 25 (7), 606–620.
- Ibuka, Y., Matsuda, Y., Shoji, K., Ishigaki, T., 2020. Evaluation of regional variations in healthcare utilization. *Jpn. J. Stat. Data Sci.* 3 (1), 349–365.
- Imamura, T., Doi, Y., Arima, H., Yonemoto, K., Hata, J., Kubo, M., Tanizaki, Y., Ibayashi, S., Iida, M., Kiyohara, Y., 2009. LDL cholesterol and the development of stroke subtypes and coronary heart disease in a general Japanese population: the Hisayama study. *Stroke* 40 (2), 382–388.
- Imano, H., Noda, H., Kitamura, A., Sato, S., Kiyama, M., Sankai, T., Ohira, T., Nakamura, M., Yamagishi, K., Ikeda, A.I., Shimamoto, T., Iso, H., 2011. Low-density lipoprotein cholesterol and risk of coronary heart disease among Japanese men and women: the circulatory risk in communities study (CIRCS). *Prev. Med.* 52 (5), 381–386.
- Kinoshita, M., Yokote, K., Arai, H., Iida, M., Ishigaki, Y., Ishibashi, S., Umamoto, S., Egusa, G., Ohmura, H., Okamura, T., Kihara, S., Koba, S., Saito, I., Shoji, T., Daida, H., Tsukamoto, K., Deguchi, J., Dohi, S., Dobashi, K., Hamaguchi, H., Hara, M., Hiro, T., Biro, S., Fujioka, Y., Maruyama, C., Miyamoto, Y., Murakami, Y., Yokode, M., Yoshida, H., Rakugi, H., Wakatsuki, A., Yamashita, S., 2018. Japan atherosclerosis society (JAS) Guidelines for prevention of atherosclerotic cardiovascular diseases 2017. *J. Atheroscler. Thromb.* 25 (9), 846–984.
- Koller, K.R., Wilson, A.S., Asay, E.D., Metzger, J.S., Neal, D.E., 2014. Agreement between self-report and medical record prevalence of 16 chronic conditions in the Alaska EARTH study. *J. Prim Care Commun. Health* 5 (3), 160–165.
- Kondo, K., 2016. Progress in aging epidemiology in Japan: the JAGES project. *J. Epidemiol.* 26 (7), 331–336.
- Kondo, K., Rosenberg, M., 2018. Advancing universal health coverage through knowledge translation for healthy ageing: lessons learnt from the Japan Gerontological Evaluation Study. World Health Organization, Geneva.
- Korkeila, K., Suominen, S., Ahvenainen, J., Ojanlatva, A., Rautava, P., Helenius, H., Koskenvuo, M., 2001. Non-response and related factors in a nation-wide health survey. *Eur. J. Epidemiol.* 17, 991–999.
- Mach F, Baigent C, Catapano A.L., Koskinas K.C., Casula M., Badimon L., Chapman M.J., de Backer G.G., Delgado V., Ference B.A., Graham I.M., Halliday A., Landmesser U., Mihaylova B., Pedersen T.R., Riccardi G., Richter D.J., Sabatine M.S., Taskinen M., Tokgozoglu L., Wiklund O. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). *Eur Heart J.* 2020;41:111-188.
- Ministry of Health Labor and Welfare. A basic direction for comprehensive implementation of National Health Promotion. <https://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000047330.pdf>; 2013 Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Vital statistics 2017. [https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei17/dl/00\\_all.pdf](https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei17/dl/00_all.pdf); 2018 Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Implementation status of specific health checkups and specific health guidance on 2019. <https://www.mhlw.go.jp/content/12400000/000757911.pdf> Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Vital statistics. <https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/geppo/nengai19/dl/gaikyouR1.pdf>; 2019 Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Health insurance. <https://www.mhlw.go.jp/english/policy/health-medical/health-insurance/index.html> Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Long-term care, health and welfare services for the elderly. <https://www.mhlw.go.jp/english/policy/care-welfare/care-welfare-elderly/index.html> Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Patient survey 2017. <https://www.mhlw.go.jp/toukei/saikin/hw/kanja/17/dl/01.pdf>; 2019 Accessed 13.02.2022.
- Ministry of Health Labor and Welfare. Specific health checkups and specific health guidance. <https://www.mhlw.go.jp/english/wp/wp-hw3/dl/2-007.pdf> Accessed 13.02.2022.

- Murata, C., Yamada, T., Chen, C., Ojima, T., Hirai, H., Kondo, K., 2010. Barriers to health care among the elderly in Japan. *Int. J. Environ. Res. Public Health* 7, 1330–1341.
- Murayama, H., Liang, J., Bennett, J.M., Shaw, B.A., Botosaneanu, A., Kobayashi, E., Fukaya, T., Shinkai, S., 2015. Trajectories of body mass index and their associations with mortality among older Japanese: do they differ from those of western populations? *Am. J. Epidemiol.* 182, 597–605.
- Nagai, M., Kuriyama, S., Kakizaki, M., Ohmori-Matsuda, K., Sugawara, Y., Sone, T., Hozawa, A., Tsuji, L., 2010. Effect of age on the association between body mass index and all-cause mortality: the Ohsaki cohort study. *J. Epidemiol.* 20 (5), 398–407.
- Nagamine, Y., Kondo, N., Yokobayashi, K., Ota, A., Miyaguni, Y., Sasaki, Y., Tani, Y., Kondo, K., 2019. Socioeconomic disparity in the prevalence of objectively evaluated diabetes among older Japanese adults: JAGES cross-sectional data in 2010. *J. Epidemiol.* 29 (8), 295–301.
- Nagamine, Y., Fujiwara, T., Tani, Y., Murayama, H., Tabuchi, T., Kondo, K., Kawachi, I., 2020. Gender difference in the association between subjective socioeconomic mobility across life course and mortality at older ages: results from the JAGES longitudinal study. *J. Epidemiol.* 30 (11), 497–502.
- Nyunt, M.S.Z., Fones, C., Niti, M., Ng, T.-P., 2009. Criterion-based validity and reliability of the geriatric depression screening scale (GDS-15) in a large validation sample of community-living Asian older adults. *Aging Ment Health* 13 (3), 376–382.
- Okamura, T., Tanaka, H., Miyamatsu, N., Hayakawa, T., Kadowaki, T., Kita, Y., Nakamura, Y., Okayama, A., Ueshima, H., 2007. The relationship between serum total cholesterol and all-cause or cause-specific mortality in a 17.3-year study of a Japanese cohort. *Atherosclerosis* 190 (1), 216–223.
- Sarwar, N., Danesh, J., Eiriksdottir, G., Sigurdsson, G., Wareham, N., Bingham, S., Boekholdt, S.M., Khaw, K., Gudnason, V., 2007. Triglycerides and risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. *Circulation* 115, 450–458.
- Sasamori, H., Takahashi, E., Nakagawa, T., Matsuki, T., 2015. Review of comprehensive medical checkup in Japan 2014. *Ningen Dock* 30, 750–762.
- Schroeder, S.A., 2007. We can do better — Improving the health of the American people. *N Engl J Med.* 357 (12), 1221–1228.
- Stringhini, S., Zaninotto, P., Kumari, M., Kivimäki, M., Lassale, C., Batty, G.D., 2018. Socio-economic trajectories and cardiovascular disease mortality in older people: the English longitudinal study of ageing. *Int. J. Epidemiol.* 47, 36–46.
- Tani, Y., Suzuki, N., Fujiwara, T., Hanazato, M., Kondo, N., Miyaguni, Y., Kondo, K., 2018. Neighborhood food environment and mortality among older Japanese adults: results from the JAGES cohort study. *Int. J. Behav. Nutr. Phys. Act.* 15, 101.
- Tani, Y., Kondo, N., Noma, H., Miyaguni, Y., Saito, M., Kondo, K., 2018. Eating alone yet living with others is associated with mortality in older men: the JAGES cohort survey. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 73, 1330–1334.
- Tedesco, M.A., Di Salvo, G., Caputo, S., Natale, F., Ratti, G., Iarussi, D., Iacono, A., 2001. Educational level and hypertension: how socioeconomic differences condition health care. *J. Hum. Hypertens.* 15 (10), 727–731.
- Ueshima, H., Sekikawa, A., Miura, K., Turin, T.C., Takashima, N., Kita, Y., Watanabe, M., Kadota, A., Okuda, N., Kadowaki, T., Nakamura, Y., Okamura, T., 2008. Cardiovascular disease and risk factors in Asia: a selected review. *Circulation* 118 (25), 2702–2709.
- United States Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: preventive medication. <https://www.uspreventiveservicestaskforce.org/uspstf/document/ClinicalSummaryFinal/statin-use-in-adults-preventive-medication#:~:text=Statin%20Use%20for%20the%20Primary%20Prevention%20of%20Cardiovascular,and%20LDL-C%20and,%20to%20a%20less%20extent,%20triglycerides>; 2016 Accessed 13.02.2022.
- World Health Organization. Social determinants of health: the solid facts - second edition. <https://apps.who.int/iris/handle/10665/108082>; 2003 Accessed 13.02.2022.
- World Health Organization. Closing the gap in a generation. [https://www.who.int/social\\_determinants/final\\_report/csdh\\_finalreport\\_2008.pdf](https://www.who.int/social_determinants/final_report/csdh_finalreport_2008.pdf); 2008 Accessed 13.02.2022.
- World Health Organization. The top 10 cause of death. <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>; 2020 Accessed 13.02.2022.
- Yokokawa, H., Yasumura, S., Tanno, K., Ohsawa, M., Onoda, T., Itai, K., Sakata, K., Kawamura, K., Tanaka, F., Yoshida, Y., Nakamura, M., Terayama, Y., Ogawa, A., Okayama, A., 2011. Serum low-density lipoprotein to high-density lipoprotein ratio as a predictor of future acute myocardial infarction among men in a 2.7-year cohort study of a Japanese northern rural population. *J. Atheroscler. Thromb.* 18 (2), 89–98.