BS852 Final Project: The association of grip strength with mortality

Overview: This 8-year follow-up study mainly aims to examine the association of weak grip strength with mortality in a sample of elders (>69 years). The dataset has 2038 subjects in total.

Methods: Descriptive statistics were computed using the proc means and proc freq to summarize subjects' baseline characteristics. The hazard ratios and 95% CI for the association between weak grip strength and mortality using both the unadjusted and adjusted cox proportional hazards model. For unadjusted analysis, obtain the Kaplan-Meier curves and log-rank test for time to mortality, for those with and those without weak grip strength. The association between weak grip strength and other covariates were assessed using several simple logistic regression models. We also assessed the association of weak grip strength with mortality between gender groups by adding an interaction item 'weak_grip*sex' and gender specific results. The confounding factors were examined using several cox proportional hazards models and 10% rules.

Data Overview: We fist recode the 'sex' variable let 1=Male and 0=Female, define 'Mortality' (based on 'Alive') coded by 1=not-alive and 0=alive at the end of the study, and create 'weak_grip' coded 1=weak grip strength and 0=not weak grip, where weak grip strength is defined by one standard deviation below its gender-specific mean grip strength. Considering data is time-to-event, we also create a 'time' variable refers to the follow-up time in years using two age-related variables. The number of missing values is shown:

	Mortality	weak grip	smoke	ed	BMI	gait_speed	fev1	DSST	sex	time	Age_la	Age_en
N miss	5	69	10	6	119	144	409	236	0	0	0	0

The summary of patients' characteristics are as follows. A total of 2038 elders were followed for 8 years. 267 (13.6%) have weak grip strength. (1) Compared with elders without weak grip, elders with weak grip were more likely to dead (61.28% vs 30.74%), higher age (93.20 vs 85.30), lower walk speed (0.57 vs 0.80), lower lung function (1.44 vs 1.89) and lower level of cognition (23.33 vs 32.79). Differences between the 2 groups in terms of smoke, education, and BMI were modest in comparison.

(2) Compared with different sex groups, females were more likely to smoke (69.69% vs 38.90%) and lower lung function (1.52 vs 2.18). Differences between the gender groups in terms of mortality, weak grip strength, education, age, BMI, walk speed, and level of cognition were modest in comparison.

Characteristic	No weak grip strength (n = 1702)	weak grip strength (n = 267)	Male (n = 948)	Female (n = 1090)
Mortality (Not alive)	522 (30.74)	163 (61.28)	365 (38.58)	357 (32.84)
weak grip strength	-	-	129 (14.01)	138 (13.17)
Sex (Male)	792 (46.53)	129 (48.31)	-	-
Smoke (smoker)	927 (54.75)	153 (57.52)	368 (38.90)	754 (69.69)
high_ed (> 12 yrs)	984 (57.92)	138 (52.08)	614 (65.11)	547 (50.23)
Age_enrollment	85.30 ± 8.99	93.20 ± 6.34	85.90 ± 8.88	86.89 ± 9.32
BMI	17.51 ± 2.91	16.76 ± 3.15	17.62 ± 2.54	17.23 ± 3.26
gait_speed	0.80 ± 0.27	0.57 ± 0.23	0.80 ± 0.26	0.74 ± 0.28
fev1	1.89 ± 0.67	1.44 ± 0.57	2.18 ± 0.67	1.52 ± 0.50
DSST	32.79 ± 13.62	23.33 ± 12.65	30.88 ± 13.09	32.12 ± 14.66

Analysis:
(1) Unadjusted analysis using Kaplan-Meier curves, log-rank test, and crude cox proportional regression.

According to the survival curve, those with weak grip strength have significantly higher risk of mortality with those without weak grip strength. The Log-rank test chi-sq (1) = 118.1662 with p<0.0001, so we have enough evidence to reject H_0 and conclude that those two groups are statistically significantly different. Those with weak grip strength have 2.478 times the hazard of mortality as those without weak grip strength (95% CI 2.078, 2.956). This means those who with weak grip strength have significantly higher risk of mortality compared to those without weak grip strength. The 95% CI didn't overlap null value and P-value smaller than 0.05 both indicates the results are statistically significant.
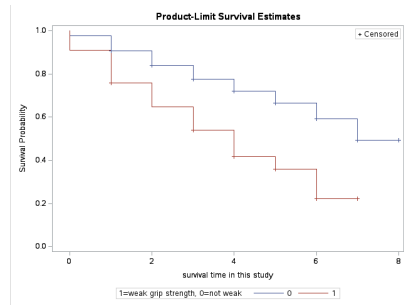
log-rank test			
Test	Chi-square	df	P-value
Log-Rank	118.1662	1	<.0001

simple cox proportional regression			
Variable	Hazard Ratio	95% CI for HR	P-value
weak_grip	2.478	(2.078, 2.956)	<.0001

(2) Adjusted multiple cox proportional hazards model.

Variable	crude HR	Adjust HR	95% CI for adjust HR	P-value
weak_grip	**2.478 (2.078, 2.956)**	**0.81**	(0.621, 1.055)	**0.1184** >0.05
sex	-	2.231	(1.724, 2.887)	<.0001
smoke	-	0.873	(0.707, 1.078)	**0.2075** >0.05
high_ed	-	1.067	(0.874, 1.301)	**0.5251** >0.05
Age_enrollment	-	1.061	(1.042, 1.08)	<.0001
BMI	-	0.924	(0.888, 0.961)	<.0001
gait_speed	-	0.219	(0.133, 0.363)	<.0001
fev1	-	0.675	(0.547, 0.833)	0.0002
DSST	-	0.977	(0.968, 0.986)	<.0001

According to the results of multiple cox proportional hazards model which include all possible covariates, those with weak grip strength have 0.81 times the hazard of mortality as those without weak grip strength after adjusting for other covariates. The results are not significant as the 95% CI overlap 1.0 and P > 0.05. Also, the 'smoke' and 'high_ed' are all have no associations with the hazard of mortality after adjusting for other variables. Since weak grip strength loses its significant association with mortality (adj-HR of 0.81 < crude HR of 2.478) when accounting for other 8 covariates, the potential confounding effect exists.

(3) Assess association between weak grip strength and other covariates.
We perform eight simple logistic regression model first, and then perform three chi-square tests to double check the associations for the three categorical variables 'sex', 'smoke', and 'high_ed'.

covariate	Logistic Model	OR	95% CI of OR	P-value
sex	weak_grip = sex	1.074	(0.830, 1.391)	**0.5877** >0.05
smoke	weak_grip = smoke	1.119	(0.862, 1.453)	**0.3996** >0.05
high_ed	weak_grip = high_ed	0.790	(0.609, 1.024)	**0.0744** >0.05
Age_enrollment	weak_grip = Age_enrollment	1.142	(1.118, 1.168)	<.0001
BMI	weak_grip = BMI	0.909	(0.864, 0.956)	0.0002
gait_speed	weak_grip = gait_speed	0.035	(0.019, 0.062)	<.0001
fev1	weak_grip = fev1	0.306	(0.233, 0.403)	<.0001
DSST	weak_grip = DSST	0.950	(0.939, 0.961)	<.0001

From the logistic regression result, we could notice that only for three categorical variables 'sex', 'smoke', and 'high_ed', the p-values are all larger than 0.05 and 95% CI of OR overlap the null value. Therefore, we could conclude that there is no significant association between 'sex', 'smoke', 'high_ed' and whether subjects with weak grip strength or not, whereas there is significant association between 'Age_enrollment', 'BMI', 'gait_speed', 'fev1', 'DSST' and whether subjects with weak grip strength or not. The results of chi-square tests (shown in Appendix) match the results of logistic regressions. Therefore, five continuous variables (age, BMI, gait_speed, fev1, and DSST) have statistically significant associations with weak grip strength, which might be the potential confounders for our study. And three categorical variables 'sex', 'smoke', and 'high_ed' are not associated with weak grip strength.

(4) Assess association of weak grip strength with mortality between gender groups.

First, we perform two cox proportional hazards model: a) cox regression only include weak_grip, sex, and the interaction item if weak_grip and sex 'weak_grip*sex'; b) multiple cox regression include all possible covariates and the interaction item 'weak_grip*sex'. Based on the results of two models, the interaction between weak grip strength and sex is not significant (with p > 0.05) in both models. This indicates that the association between weak grip strength and mortality does not differ significantly between males and females, regardless of whether controlling for other 7 covariates.

Model	Variable	Chi-Square	Pr > ChiSq
time*Mortality(0) = weak_grip sex weak_grip*sex	weak_grip*sex	3.2722	**0.0705** >0.05
time*Mortality(0) = weak_grip sex weak_grip*sex smoke high_ed Age_enrollment BMI gait_speed fev1 DSST	weak_grip*sex	0.1765	**0.6744** >0.05

Then, separate dataset based on gender into 2 dataset and perform the adjusted cox proportional regression twice. The results show that weak grip strength is associated with low risk of mortality in both males and females, but the result is not significant. So, we could conclude the association between weak grip strength and mortality does not differ significantly between males and females.

	aHR for weak_grip	aHR for smoke	aHR for high_ed	aHR for age_enr	aHR for BMI	aHR for gait_s	aHR for fev1	aHR for DSST
male	0.776 (0.543, 1.108)	0.877	1.018	1.046	0.924	0.173	0.664	0.975
female	0.862 (0.575, 1.292)	0.817	1.097	1.086	0.923	0.296	0.686	0.980

(5) Assess potential confounders.
To assess potential confounders which would confounding the association between weak grip strength and mortality, we use the crude cox regression model in (1) as baseline (crude HR = 2.478 with 95% CI = 2.078, 2.956), then perform several cox regression models by adding 8 potential covariates respectively to compare if they have significant impact on the hazard ratio for weak grip strength.

Model	aHR for weak_grip	95% CI	P	|aHR - HR|/HR
outcome = weak_grip + sex	2.462	(2.064, 2.937)	<.0001	0.65%
outcome = weak_grip + smoke	2.464	(2.065, 2.940)	<.0001	0.56%
outcome = weak_grip + high_ed	2.450	(2.052, 2.924)	<.0001	1.13%
outcome = weak_grip + Age_enrollment	1.315	(1.094, 1.580)	0.0035	**46.93% > 10%**
outcome = weak_grip + BMI	2.247	(1.861, 2.713)	<.0001	9.32%
outcome = weak_grip + gait_speed	1.399	(1.146, 1.707)	0.0010	**43.54% > 10%**
outcome = weak_grip + fev1	1.788	(1.437, 2.224)	<.0001	**27.85% > 10%**
outcome = weak_grip + DSST	1.512	(1.225, 1.867)	0.0001	**38.98% > 10%**

Based on the results and the 10% rule, after adding 'Age_enrollment', 'gait_speed', 'fev1', and 'DSST' as potential confounders in separate models, there will be more than a 10% difference in the unadjusted and adjusted HR for weak grip strength. So, 'Age_enrollment', 'gait_speed', 'fev1', and 'DSST' does confound the association between weak grip strength and mortality. And other variables may not be confounders.

Conclusion: The results from the unadjusted analysis showed that those with weak grip strength have a significantly higher risk of mortality compared to those without. However, after adjusting for potential confounders, weak grip strength will have no significant association with mortality. The weak grip strength is not significantly associated with the three categorical variables - sex, smoke, and high_ed, while there is a significant association between weak grip strength and five continuous variables - age, BMI, gait_speed, fev1, and DSST. The interaction between weak grip strength and sex is not significant, as well as the sex-specific analysis results, both indicating that the association between weak grip strength and mortality does not differ significantly between gender groups. In terms of potential confounders, age at enrollment, gait speed, fev1, and DSST were found that does confound the association between weak grip strength and mortality. To sum up, in this study, weak grip strength is significantly associated with increased mortality risk in elders in the crude regression, but this association will not exist (non-significant) after adjusting for other covariates. And the association between weak grip strength and mortality does not differ significantly between genders.