

1 **Age-Specific Risk Factors for Incident Disability in Activities of Daily**
2 **Living among Middle-Aged and Elderly Community-Dwelling**
3 **Japanese Women during an 8-9 Year Follow-up: The Hizen-Oshima**
4 **Study**

5

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29

30 **Short running title:** Age-Specific Risk Factors of Disability

31

32 **ABSTRACT**

33 **Aim:** The purposes of the present study were to investigate risk factors

34 for incident disability in activities of daily living (ADL) among

35 middle-aged and older women, and to determine whether there are

36 differences in risk factors according to age groups.

37 **Methods:** The participants were 264 Japanese women aged 40 and older.

38 A self-administered questionnaire was used to survey participants about

39 difficulty in performing selected basic and instrumental ADLs at baseline

40 and at follow-up. ADL disability was defined as difficulty performing 3

41 or more ADLs. Information on knee joint or back pain and comorbidities

42 (heart disease, lung disease, stroke, or diabetes mellitus) was obtained

43 using a self-administered questionnaire at baseline. Physical performance

44 measurements (grip strength, chair stand time, rapid walking speed, and

45 functional reach) were also conducted at baseline.

46 **Results:** Prevalence of incident ADL disability was 44 (27.5%) in women

47 aged 40-64 years and 57 (54.8%) in women aged 65 years and older

48 ($P<0.001$). Multiple logistic regression analysis revealed that decreased

49 grip strength and having pain were significantly associated with a higher

50 risk for incident ADL disability among women aged 40-64 years. For
51 women aged 65 years and older, decreased rapid walking speed, having a
52 comorbidity, and having pain were associated with incident ADL
53 disability.

54 **Conclusions:** This study revealed that a different set of risk factors was
55 associated with incident ADL disability among women aged 40-64 years
56 and women aged 65 years and older. Age-specific screening and
57 intervention strategies are necessary for effective prevention of incident
58 ADL disability.

59

60 **Key words:** activities of daily living, knee pain, back pain, comorbidity,
61 physical functioning

62 **Introduction**

63 The incidence of disability in activities of daily living (ADL) increases
64 with age ¹⁻³. The number of elderly people is increasing worldwide ⁴. In
65 Japan, 26.0% of the population was older than 65 years in 2014, and
66 36.1% of the population will be older than 65 years by 2040 ⁵.
67 Approximately 26% of the Japanese population aged 60 years and older

68 reported disability in ADL in 2014 ⁶. Among women, ADL disability can
69 especially be a critical issue since women are expected to spend a larger
70 proportion of life in poor health than men⁷.

71 Furthermore, the prevalence of ADL disability was shown to
72 increase with advancing age (60-64 years, 12.8%; 65-74 years, 17.7%; 75
73 years and older, 44.6%) ⁶. The ability to perform ADLs without assistance
74 largely determines whether an individual can live independently ⁸. ADL
75 disability results in greater use of medical care, more institutionalization,
76 and poorer physical and mental health ². Maintaining and restoring
77 independence in ADL is important for optimal quality of life ⁹. ADL
78 disability in elderly adults is thus an important and growing public health
79 concern.

80 Multiple risk factors appear to be responsible for ADL disability
81 ¹⁰. Identifying contributors to ADL disability is important in establishing
82 prevention strategies. Previous cross-sectional studies have demonstrated
83 associations of physical function ¹¹, pain ¹², and comorbid disorders ¹³
84 with ADL disability. Longitudinal studies have also reported that similar
85 risk factors (physical function ^{2, 3, 14-16}, pain ^{17, 18}, and comorbidities ^{1, 2})

86 may predict future incidence of ADL disability.

87 Most previous studies have assessed the factors associated with
88 incident ADL disability only in elderly people aged 65 years and older. To
89 the best of our knowledge, no studies have investigated ADL disability
90 and its risk factors considering possible differences between middle-aged
91 and elderly people. It is important to identify risk factors for the
92 incidence of ADL disability considering possible differences between
93 middle-aged and elderly people to prevent ADL disability at an earlier
94 age.

95 The objective of the present study was to investigate risk factors
96 for incident ADL disability during 8-9 years of follow-up among women
97 aged 40 years and older, and determine whether there are differences in
98 risk factors between women younger than 65 years and women aged 65
99 and older.

100

101 **Methods**

102 **Study participants**

103 The Hizen-Oshima Study is a prospective, population-based cohort

104 study of osteoporosis and osteoarthritis. Details of the Hizen-Oshima
105 study have been previously published ¹⁹. Briefly, all women aged 40 years
106 and older in Oshima, a town in Nagasaki Prefecture in Japan, were invited
107 to participate. The town of Oshima has a population of approximately
108 5800 (2850 men, 2950 women), including approximately 2000 women
109 aged 40 or older. Despite having a shipyard in the town, Oshima is mainly
110 a rural area. The baseline examination of each participant was performed
111 at the Oshima Health Center between 1998 and 1999. A total of 586
112 women (approximately 30% of eligible women) participated in the study.
113 All participants were noninstitutionalized, living independently at
114 baseline, and were able to ambulate independently (with or without a
115 cane). All participants provided written informed consent before
116 participation. In 2008, a follow-up mail survey on ADL was conducted.
117 Of the 586 participants in the baseline survey, 495 were alive, 46 were
118 dead, and 45 had moved to a different municipality. The questionnaire
119 was mailed to the women who were known to be alive, and 394 women
120 responded (Figure 1). This study was approved by the local and
121 institutional ethics committees.

122

123 **Main outcome measurement**

124 Our primary outcome was incident of difficulty in performing
125 selected basic and instrumental ADL at 8-9 years follow-up, measured by
126 a self-administered questionnaire. The ADL questionnaire survey was
127 conducted at baseline (in 1998-1999) and at follow-up (in 2008).
128 Participants were asked if they had any difficulty performing the
129 following 6 ADLs that included 14 activities (yes/no): (1) bending-related
130 activities (getting in or out of a car, bending over or picking up a
131 lightweight object, putting on socks or stockings, lifting a 5-kg object
132 from the floor), (2) spine-extension activity (reaching an object above
133 your head), (3) walking-related activities (walking 100m on a level
134 surface, climbing 10 steps without stopping, walking down 10 steps,
135 shopping for groceries or clothes), (4) standing endurance (standing on
136 your feet for 2 hours), (5) heavy activities (heavy housework or yard work,
137 lifting a heavy suitcase of about 15 kg or a 3- to 4-year-old child by
138 yourself), and (6) basic activities (feeding or dressing yourself, preparing
139 your own meals). ADL disability was defined as difficulty performing 3

140 or more ADLs; this definition was validated previously ²⁰.

141

142 **Measurements at baseline**

143 All participants were asked if they had knee joint and back pain on
144 most days during the previous month, and if they had comorbidities (heart
145 disease, lung disease, stroke, or diabetes mellitus). Height and weight
146 were measured with the participants in light clothing and without shoes.

147 Body mass index (BMI) was calculated as weight (kg)/height (m)².

148 Measures of physical performance included grip strength, chair stand time,
149 rapid walking speed, and functional reach. Grip strength of the dominant
150 hand was measured using a hydraulic dynamometer (Jamar Hydraulic

151 Hand Dynamometer Model J00105, Lafayette Instrument Company, Inc.,

152 Lafayette, IN, USA). Grip strength was calculated as the average of 2

153 trials. Chair stand time was measured as the time to stand up from a

154 standard chair 5 times; the participants were asked, if possible, to not use

155 their arms for assistance ²¹. Results were calculated as the average of 2

156 trials. Rapid walking speed was calculated from the time required for

157 participants to walk a 6-meter course at a rapid but safe pace (rapid

158 walking speed). Rapid walking speed was recorded as a single trial. To
159 determine functional reach, the subject first stood comfortably upright,
160 facing forward, hand in a fist, with the arm extended next to a yardstick
161 mounted on a wall. The participants then reached forward as far as
162 possible without stepping or losing balance, and the difference between
163 the 2 points on the yardstick was taken as functional reach, calculated as
164 the average of 3 trials.

165

166 **Statistical analysis**

167 Women who had any missing variables (n=21) or with ADL
168 disability at baseline (n=109) were excluded from the analysis, leaving
169 264 women for the final analysis (Figure). The follow-up rate was 45.1%
170 (264/586). Student's *t*-test was used for continuous variables, and the
171 chi-square test was used for categorical variables to determine significant
172 differences between women with and without incident ADL disability at
173 follow-up. Multiple logistic regression analysis was used to evaluate the
174 simultaneous effects of variables on incident ADL disability. Odds ratios
175 and 95% confidence intervals were calculated. Starting with a model

176 including all variables with P values <0.20 in the univariate analysis, the
177 most appropriate model was selected based on Akaike's information
178 criteria. P values <0.05 were considered significant. Statistical analysis
179 was performed using SPSS software version 20 for Windows (SPSS Inc.,
180 Chicago, IL, USA).

181

182 **Results**

183 Table 1 summarizes some of the baseline characteristics of
184 participants according to age groups. Mean follow-up time was 9.1 ± 0.4
185 years (range, 8.3 - 9.7 years), and mean age at baseline was 61.1 ± 8.4
186 years. Women aged 65 years and older had significantly poorer physical
187 functioning (grip strength, chair stand time, rapid walking speed, and
188 functional reach test) than women aged 40-64 years. Prevalence of
189 comorbidity was 20 (12.5%) in women of aged 40-64 years and 28
190 (26.9%) in women aged 65 years and older ($P=0.005$). Prevalence of pain
191 was 65 (40.6%) in women aged 40-64 years and 38 (36.5%) in women
192 aged 65 years and older ($P=0.52$). Prevalence of incident ADL disability
193 was 44 (27.5%) in women aged 40-64 years and 57 (54.8%) in women

194 aged 65 years and older ($P < 0.001$).

195 Table 2 shows comparisons of baseline variables between women
196 with and without incident ADL disability at follow-up. In women aged
197 40-64 years, women with incident ADL disability had lower grip strength
198 ($P = 0.01$), poorer functional reach test ($P = 0.03$), and greater frequency of
199 pain ($P < 0.001$) compared with women without incident ADL disability.
200 For women aged 65 years and older, women with incident ADL disability
201 had significantly older age ($P = 0.005$), slower rapid walking speed
202 ($P = 0.002$), greater prevalence of comorbidity ($P = 0.004$), and greater
203 prevalence of pain ($P = 0.004$) compared with women without incident
204 ADL disability.

205 Multiple logistic regression analysis was used to evaluate the
206 simultaneous effects of baseline variables on incident ADL disability
207 (Table 3). In women aged 40-64 years, decreased grip strength and having
208 pain were significantly associated with higher risk of incident ADL
209 disability. For women aged 65 and older, decreased rapid walking speed,
210 comorbidity, and having pain were significantly associated with a higher
211 risk of incident ADL disability.

212

213 **Discussion**

214 This study assessed risk factors for incident ADL disability among
215 women aged 40-64 years and 65 years and older. To the best of our
216 knowledge, this is the first study that reported risk factors of ADL
217 disability considering differences between women younger than 65 years
218 and those aged 65 years and older.

219 Aging causes gradual changes in the organism, which leads to poor
220 physical conditions such as decline in physical function²²⁻²⁴ and increased
221 comorbidity²⁵. In our population, as expected, all examined physical
222 performance measures showed significant negative correlation with age
223 (data not shown), and the number of comorbidity significantly increased
224 with age (data not shown). On the other hand, level of age related changes
225 may vary according to factors. For example, decline in grip strength is
226 reported to start as early as ages 40 years²³, whereas rapid walking speed
227 decreases at a much later life²². Thus, predictive factors of incident ADL
228 disability might differ according to different age categories.

229 This study revealed that different sets of risk factors were

230 associated with incident ADL disability among women aged 40-64 years
231 and women aged 65 years and older. Previous studies have reported risk
232 factors of incident ADL disability among people aged 65 and older, such
233 as comorbidity, physical performance measurements, and pain ^{1, 2, 15, 17, 18}.
234 However, few studies have reported risk factors for ADL disability among
235 people younger than 65 years. Rantanen et al. reported that grip strength
236 was associated with an elevated risk of incident ADL disability in men
237 aged 45-68 years ¹⁶. Ouden et al. reported that, among a group of
238 participants including both middle-aged and elderly people, grip strength,
239 leg strength, and level of physical activity were associated with a high
240 risk of ADL disability ²⁶. However, no studies have assessed risk factors
241 for incident ADL disability in elderly and middle-aged people separately.
242 Our study demonstrated that risk factors for ADL disability might vary
243 depending on age. There would be a need for age-specific screening and
244 intervention strategies to prevent ADL disability.

245 Walking ability plays an important role in ADL independence of the
246 elderly. Walking speed is a common physical performance measurement
247 used in clinical practice and is a good predictor of ADL dependence ¹⁴.

248 Several studies reported that slower walking speed was significantly
249 associated with the risk for incident ADL disability ^{2, 3, 15}. In our study,
250 women aged 65 years and older with slower baseline rapid walking speed
251 had a higher risk of incident ADL disability, which is in line with
252 previous studies. Rapid walking speed decreases with advancing age,
253 especially after 70 years ²². Suzuki et al. confirmed that decreased rapid
254 walking speed increases the risk for falls and therefore increases ADL
255 disability either from fracture itself or post-fall syndrome in the
256 community-dwelling elderly ³. Thus an age-related decline in walking
257 speed might lead to lower physical activity, a higher risk for falls, and
258 ADL disability. In the elderly, walking ability should be targeted in
259 interventions aimed at preventing ADL disability.

260 In our study, among women aged 65 years and older, having a
261 comorbidity was significantly associated with a higher risk of incident
262 ADL disability. Several studies reported that elderly people with a
263 comorbidity have a higher risk of developing incident ADL disability ^{1, 2,}
264 ^{11, 13} and mortality ¹. Our study is consistent with these previous studies.
265 Prevalence of comorbidity increases with age, and number of

266 comorbidities is reported to increase with age ²⁵, which might lead to
267 ADL disability in older age. Proper screening and management of medical
268 conditions is thus important.

269 Our study showed that having knee joint or back pain was
270 significantly associated with a higher risk of incident ADL disability both
271 among women aged 40-64 years and women aged 65 years and older.
272 Several studies reported that elderly people with pain have a higher risk
273 of developing incident ADL disability ^{17, 18}. Knee joint pain and back pain
274 are major symptoms that occur in middle-aged and elderly people ^{27, 28},
275 and these symptoms often become chronic. Covinsky et al. reported that
276 people with pain also commonly have functional limitations and
277 speculated that mutual feedback loops in which pain and functional
278 limitations are mutually reinforcing, with pain exacerbating functional
279 limitations and functional limitations exacerbating pain ²⁴. Having pain
280 might cause functional limitations, which might lead to difficulties in
281 various ADLs.

282 We showed that poorer grip strength was significantly associated
283 with incident ADL disability only in middle-aged women. Two studies

284 have shown significant associations between weaker grip strength and
285 higher risk of incident ADL disability among populations that include
286 middle-aged people ^{16, 26}. Grip strength decreases with advancing age ²⁹.

287 In a study of Japanese women, grip strength was reported to be at
288 the highest among women in their early 40s and then decrease with age ²³.
289 Strength training should be started at an earlier age, before a decline in
290 muscular strength becomes evident.

291 As for elderly women, previous studies reported that grip strength
292 was not significantly associated with the incidence of ADL disability ^{3, 14,}
293 ³⁰. Our study showed no association between grip strength and risk for
294 incident ADL disability, which is consistent with previous studies. On the
295 other hand, several studies conducted in elderly populations, including
296 both genders, reported significant associations between weaker grip
297 strength and a higher risk of incident ADL disability ^{2, 31}. Further studies
298 are needed to determine the effect of grip strength on incident ADL
299 disability.

300 This study has several limitations. First, physical performance
301 measurements and information on comorbidity and pain were not

302 available at follow-up. Therefore, changes in these parameters over time
303 could not be considered. Second, non-responders were older than
304 responders. Some women may have not responded because they were
305 functionally limited by their age-related medical conditions, which might
306 weaken the association of incident ADL disability with baseline variables.
307 Third, we did not assess severity of pain; thus the influence of pain
308 severity on incident ADL disability could not be assessed. Fourth,
309 because the present study included only women, these results cannot be
310 generalized to men.

311 In conclusion, this study revealed that a different set of risk factors
312 were associated with incident ADL disability among women aged 40-64
313 years and women aged 65 years and older. Age-specific screening and
314 intervention strategies may be necessary for effective prevention of
315 incident ADL disability among elderly women.

316

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321

322 **Disclosure statement**

323 We declare that there is no financial support or relationship that may pose

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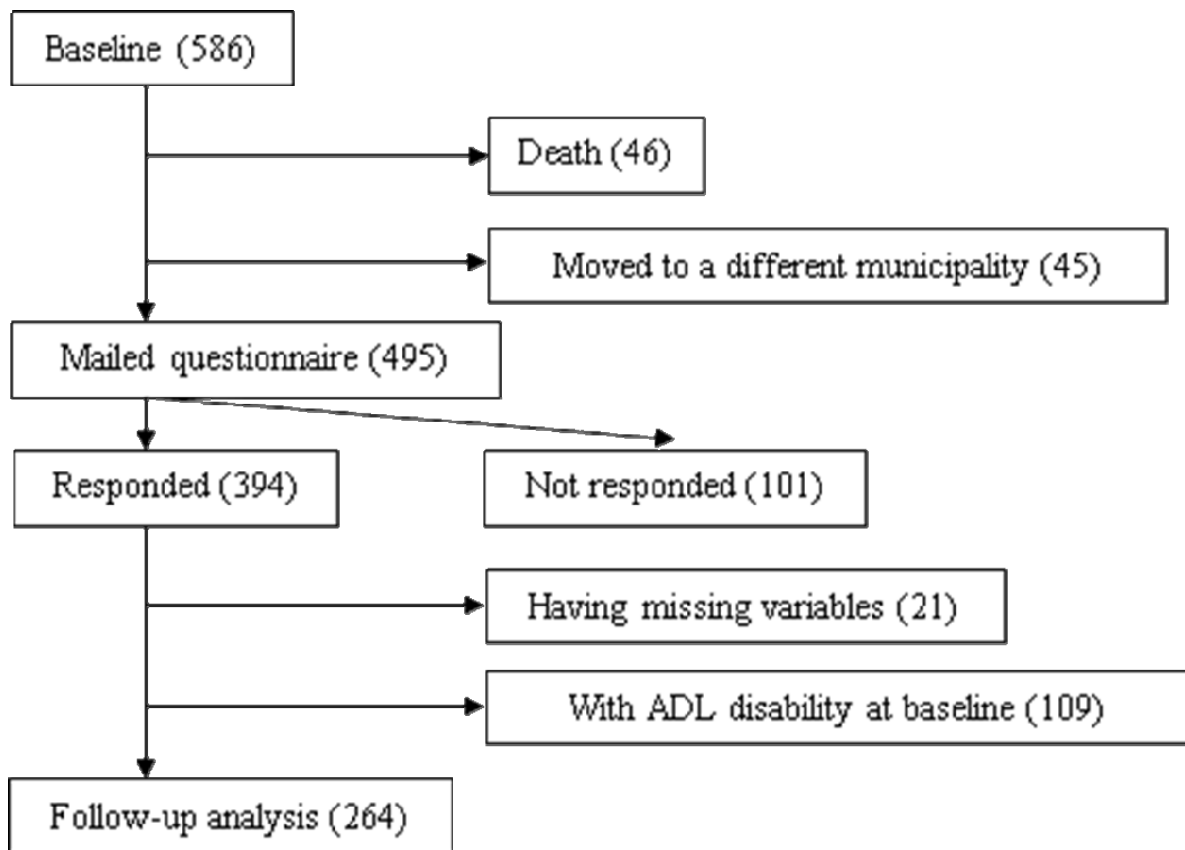
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414



415

416 **Figure 1**

417 Participants from baseline to follow up. Of the 586 participants in the baseline
 418 survey, 495 were alive, 46 were dead, and 45 had moved to a different
 419 municipality at follow-up. The questionnaire was mailed to the women who
 420 were known to be alive, and 394 women responded. Women who had any
 421 missing variables (n=21) or with ADL disability at baseline (n=109) were
 422 excluded from the analysis, leaving 264 women for data analysis.

Table 1. Characteristics of participants (N=264)

	total n=264	40-64 years n=160	65 + years n=104	p-value [§]
	Mean ± SD, n (%)	Mean ± SD, n (%)	Mean ± SD, n (%)	
follow-up time (years)	9.1 ± 0.4	9.1 ± 0.4	9.2 ± 0.4	0.78
Age (years)	61.1 ± 8.4	55.8 ± 6.4	69.3 ± 3.0	<0.001
Body mass index (kg/m ²)	23.1 ± 3.0	23.3 ± 3.0	22.9 ± 3.1	0.35
Grip strength (kg)	25.8 ± 5.0	27.5 ± 4.8	23.2 ± 4.1	<0.001
Chair stand time (sec)	8.2 ± 1.8	7.6 ± 1.5	9.1 ± 1.9	<0.001
Rapid walking speed (m/s)	1.79 ± 0.24	1.87 ± 0.23	1.66 ± 0.21	<0.001
Functional reach test (cm)	27.0 ± 6.8	28.6 ± 6.6	24.5 ± 6.2	<0.001
Comorbidity [†]	48 (18.2)	20 (12.5)	28 (26.9)	0.005
Pain [‡]	103 (39.0)	65 (40.6)	38 (36.5)	0.52
Incident ADL disability	101 (38.3)	44 (27.5)	57 (54.8)	<0.001

[†] Presence of heart disease, lung disease, stroke, or diabetes mellitus.

[‡] Presence of knee or back pain.

[§] Comparison of variables between women aged 40-64 years and aged 65 + years.

Table 2. Comparison of baseline variables between women with and without incident ADL disability at follow-up

Variables	40-64 years (n=160)		p-value	65 + years (n=104)		p-value
	incident ADL disability			incident ADL disability		
	with	without		with	without	
	n=44	n=116		n=57	n=47	
	Mean \pm SD, n (%)			Mean \pm SD, n (%)		
Age (years)	57.2 \pm 5.1	55.3 \pm 6.7	0.06	70.0 \pm 3.2	68.4 \pm 2.6	0.005
Body mass index (kg/m ²)	23.4 \pm 3.1	23.2 \pm 3.0	0.67	22.9 \pm 3.0	22.9 \pm 3.2	0.92
Grip strength (kg)	26.0 \pm 3.8	28.0 \pm 5.0	0.014	23.5 \pm 4.2	22.9 \pm 4.0	0.40
Chair stand time (sec)	7.9 \pm 1.7	7.6 \pm 1.5	0.21	9.3 \pm 2.1	8.8 \pm 1.7	0.17
Rapid walking speed (m/s)	1.86 \pm 0.21	1.87 \pm 0.23	0.69	1.61 \pm 0.18	1.74 \pm 0.22	0.002
Functional reach test (cm)	26.8 \pm 6.7	29.3 \pm 6.5	0.03	23.9 \pm 6.5	25.1 \pm 5.7	0.32
Comorbidity [†]	8 (18.2)	12 (10.3)	0.19	22 (38.6)	6 (12.8)	0.004
Pain [‡]	29 (65.9)	36 (31.0)	<0.001	28 (49.1)	10 (21.3)	0.004

[†] Presence of heart disease, lung disease, stroke, or diabetes mellitus.

[‡] Presence of knee or back pain.

Table 3. Multiple logistic regression models for incident ADL disability at follow-up

Age	Variables	Units	Odds ratios (95%CI)
40-64 years (n=160)	Grip strength (kg)	-5	1.82 (1.17 – 2.83)
	Pain ‡	Yes/No	4.87 (2.25 – 10.54)
65 + years (n=104)	Rapid walking speed (m/s)	- 1 SD §	2.19 (1.24 – 3.87)
	Comorbidity †	Yes/No	4.40 (1.47 – 13.16)
	Pain ‡	Yes/No	4.72 (1.77 – 12.60)

† Presence of heart disease, lung disease, stroke, or diabetes mellitus.

‡ Presence of knee or back pain.

§ Rapid walking speed : 1SD=0.24 m/s