children, children-in-law and grand-children, compared to those who 'live and eat with others', most of whom live with their spouse.

#### DISCUSSION

The main aim of the present study wasto examine the association between social engagement and depressive symptoms in community-dwelling Japanese older adults, with a particular focus on eating alone and on the changes in the association along geriatric trajectories of aging and mental frailty.

The study was carried out on a population sample of Japanese older adults, of whom 14.7% showed depressive symptoms (GDS≥6). This is on the lower end compared to previous studies that usedthe same GDScut-off point, in which the prevalence ranged between 14% and 40%<sup>4</sup>.

The results highlighted a significant association between depressive symptoms and social engagement variables such as social ties, eating alone, social participation, social stressors and reciprocity of social support. Of particular interest was eating alone, which to our knowledge has not been assessed before in combination with different components of social engagement and in relation to the living arrangement. 'Living with others yet eating alone' was a significant predictor of depression for both age groups, with odds ratio reaching as high as 5 times for the young-old. Thissuggeststhat eating alone acts as stronger risk factor than living alone, and that theliving arrangement in which older adults eat alone can act as a critical determinant of depressive risks. Mealsare an important location of socialization whereby older adults enjoy intimate interactions, and when shared with others, they can provide valuable opportunities for companionship and social support<sup>18</sup>. A lack of communication during meals may result in feelings of loneliness anddepressedmoods<sup>19</sup>.

Table 5 suggests that those who eat alone despite living with their families tend to be the most socially withdrawn, with least awareness of their health conditions and the poorest physical, oral and cognitive functions as well as nutritional status. The fact that they do not share a single meal with their families despite living together suggests that they have distant relationships with them. Compared to those who eat with others, a greater proportion of those who eat alone live with their children, children-in-law or grandchildren, and less with their spouse. This suggests that they may be eating alone because they lead different life styles, suffer from emotional distance, concerns that they will addburdens on their families if they eat together, or from uncomfortable relationships with family members such as children-in-law. This is supported by the fact that they have the weakest social ties with family. This may result in lower interest in their health shown by their families, as well as in lower self-interest. The fact that they show the lowest health literacy also supports this hypothesis. They also exhibit the lowest mobility and social ties with friends, suggesting that they are the most socially isolated not only at home but also outside. The fact that their gait speeds and IADL are the lowest imply that their poor physical functions play a role in limiting their social activities. GOHAI scores, number of remaining teeth and occlusal force are lowest in this group, indicating the possibility that they eat alone because they eat too slowly, require different menus or because they have concerns about their oral appearance. The poor oral functions and nutritional/dietary status (low food variety and MNA-SF scores)may also be another manifestation of the lack of interest in their health shownby their families as well as by themselves.

In any case, the sentiments or perceptions that lead them to eat alone despite living with their families are likely to be negative in nature, and may be internally conceived by the older adults themselves, or externally imposed by families living together or the wider society. The functional declines which may cause as well as result from eating alone may also contribute to the depressive outcomes.

Stratification by age groups and multinomial regression analysis by different severities of depression revealed that fewer variables of social engagement were associated with depressive outcomes as the population ages or becomes more mentally frail. This suggests that social engagement is a more powerful predictor of mental health at earlier points along geriatric trajectories, and thus that effective social preventive measures require early interventions. Lower down the geriatric trajectories, social factors fall in their relative importance and the role of health and functional factors increase. This is suggested by the fact that the number of medications becomes a significant predictor for old-old, and the history of cerebrovascular diseases and MNA-SF scores become significant for severe depression.

Outside thedomain of social engagement, the independentrisk factors for depressive symptomsin both age groupsincluded GOHAI and health literacy, supporting the findings of previous studies<sup>36-38</sup>. Uniquely for young-old, mobility, MNA-SF and income wereassociated. For old-old only, the number of medicationsremained a predictor of depressive symptoms.

This study elucidates that reducing the risk of depression requires much more than medical care and that preventive measures need to be introduced early on in the geriatric trajectories, before frailty sets in. The present study shows that social factors such as eating alone pose substantial risk for mental health. Comprehensive assessment that covers a wide range of health-related domains including physicalhealth, oral functions, nutritional dietary status well as social relations will be necessary to identify those at risk effectively.

The limitations of our study are mainly four-fold. First, the cross-sectional nature of the study prevents it from making any conclusive comments about the causality between independent variables and the outcome. Second, data on household income were not available, and instead individual income was used. Given that the older adults in the present study grew up in a period when it was rare for women to work after marriage, household income would have been abetterindicator of the economic environment for women. Third, depressive symptoms were measured using self-administered GDS questionnaire rather than diagnosis by physicians. Fourth, the participants inevitably comprised those who had greater degrees of interest in health and lower barriers to participation in the study. This may have skewed the nature of participants, to those who were more socially active and interested in health, missing out those who were most socially disengaged.

## **CONCLUSION**

For community-dwelling Japanese older adults, depressive symptoms were significantly associated with social engagement, with greater associations in younger and less mentally frail populations. Eating alone wasidentified as a key risk factor for depressive symptoms, and those who live with their families yet eat their meals alone were at highest risk. Mental health management for older adults therefore requires comprehensive assessment of their social relations, taking into account their companionship during mealtimes. Social preventive measures need to involve early interventions in order to augment its effectiveness against mental frailty.

Given that depression can lay the ground for further frailty and various detrimental health outcomes, further study with alongitudinal design, with more detailed data collection on social predictors of depression, may play a pivotal role in identifying possible interventionopportunities to prevent not only mental but also physical frailties.

## **ACKKNOWLEDGEMENTS**

This work was supported by a Health and Labor Sciences Research Grant (H24-Choju-Ippan-002) from the MHLW. The authors thank the staff members and participants of the Kashiwa study and the following individuals for helping with the acquisition of data: Dr Takashi Higashiguchi, Fujita Health University School of Medicine; Dr Kazuko Ishikawa-Takata RD, National Institute of Health and Nutrition; Dr Yoshiya Oishi PhD DDS, Oishi Dental Clinic; Dr Noriaki Takahashi, The Nippon Dental University; Seigo Mitsutake, Tokyo Metropolitan Institute of Gerontology; and staff members of The Institute of Healthcare Innovation Project, The University of Tokyo.

There are no conflicts of interest.

# REFERENCES

- [1] Djernes JK. Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatrica Scandinavica*. 2006;**113**: 372-387.
- [2] Schwarzbach M, Luppa M, Forstmeier S, et al. Social relations and depression in late life-A systematic review. *International Journal of Geriatric Psychiatry*. 2014;**29**: 1-21.
- [3] Muramatsu N, Akiyama H. Japan: Super-Aging Society Preparing for the Future. *Gerontologist*. 2011;**51**: 425-432.
- [4] Wada T, Ishine M, Sakagami T, et al. Depression in Japanese community-dwelling elderly prevalence and association with ADL and QOL. Archives of Gerontology and Geriatrics. 2004;39: 15-23.
- [5] Blazer DG, Hybels CF. Origins of depression in later life. *Psychological Medicine*. 2005;**35**: 1241-1252.
- [6] Park NS, Jang Y, Lee BS, et al. The Mediating Role of Loneliness in the Relation Between Social Engagement and Depressive Symptoms Among Older Korean Americans: Do Men and Women Differ? Journals of Gerontology Series B-Psychological Sciences and Social Sciences. 2013;68: 193-201.
- [7] Beekman ATF, Deeg DJH, vanTilburg T, et al. Major and minor depression in later life: A study of prevalence and risk factors. *Journal of Affective Disorders*. 1995;**36**: 65-75.
- [8] Fukunaga R, Abe Y, Nakagawa Y, et al. Living alone is associated with depression among the elderly in a rural community in Japan. *Psychogeriatrics*. 2012;**12**: 179-185.
- [9] Kawachi I, Berkman LF. Social ties and mental health. *Journal of Urban Health-Bulletin of the New York Academy of Medicine*. 2001;**78**: 458-467.
- [10] Heun R, Hein S. Risk factors of major depression in the elderly. *European Psychiatry*. 2005;**20**: 199-204.
- [11] Mendes de Leon CF. Social engagement and successful aging. *European Journal of Ageing*. 2005;**2**: 64-66.
- [12] Park NS. The Relationship of Social Engagement to Psychological Well-Being of Older Adults in Assisted Living Facilities. *Journal of Applied Gerontology*. 2009;**28**: 461-481.
- [13] Tilvis RS, Routasalo P, Karppinen H, et al. Social isolation, social activity and loneliness as survival indicators in old age; a nationwide survey with a 7-year follow-up. European Geriatric Medicine. 2012;3: 18-22.
- [14] Tomaka J, Thompson S, Palacios R. The relation of social isolation, loneliness, and social support to disease outcomes among the elderly. *Journal of Aging and Health*. 2006;**18**: 359-384.
- [15] Avlund K, Lund R, Holstein BE, Due P. Social relations as determinant of onset of disability in aging. *Archives of Gerontology and Geriatrics*. 2004;**38**: 85-99.
- [16] Bassuk SS, Glass TA, Berkman LF. Social disengagement and incident cognitive decline in community-dwelling elderly persons. *Annals of Internal Medicine*. 1999;**131**: 165-+.
- [17] Bath PA, Deeg D. Social engagement and health outcomes among older people: introduction

- to a special section. European Journal of Ageing. 2005;2: 24-30.
- [18] Vesnaver E, Keller HH. Social influences and eating behavior in later life: a review. *Journal of nutrition in gerontology and geriatrics*. 2011;**30**: 2-23.
- [19] Kimura Y, Wada T, Okumiya K, *et al.* Eating alone among community-dwelling Japanese elderly: Association with depression and food diversity. *Journal of Nutrition Health & Aging*. 2012;**16**: 728-731.
- [20] Markle-Reid M, Browne G. Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing*. 2003;**44**: 58-68.
- [21] Schreiner AS, Hayakawa H, Morimoto T, Kakuma T. Screening for late life depression: cut off scores for the Geriatric Depression Scale and the Cornell Scale for Depression in Dementia among Japanese subjects. *International journal of geriatric psychiatry*. 2003;**18**: 498-505.
- [22] Crooks VC, Lubben J, Petitti DB, et al. Social network, cognitive function, and dementia incidence among elderly women. *American Journal of Public Health*. 2008;**98**: 1221-1227.
- [23] Lubben J, Blozik E, Gillmann G, et al. Performance of an abbreviated version of the Lubben Social Network Scale among three European community-dwelling older adult populations. *Gerontologist*. 2006;**46**: 503-513.
- [24] Ishikawa H, Nomura K, Sato M, Yano E. Developing a measure of communicative and critical health literacy: a pilot study of Japanese office workers. *Health Promotion International*. 2008;**23**: 269-274.
- [25] Liu BC-p, Leung DS-y, Chi I. Social functioning, polypharmacy and depression in older Chinese primary care patients. *Aging & Mental Health*. 2011;**15**: 732-741.
- [26] Koyano W, Shibata H, Nakazato K, et al. MEASUREMENT OF COMPETENCE RELIABILITY AND VALIDITY OF THE TMIG INDEX OF COMPETENCE. Archives of Gerontology and Geriatrics. 1991;13: 103-116.
- [27] Baker PS, Bodner EV, Allman RM. Measuring life-space mobility in community-dwelling older adults. *Journal of the American Geriatrics Society*. 2003;**51**: 1610-1614.
- [28] Peel C, Baker PS, Roth DL, et al. Assessing mobility in older adults: The UAB Study of Aging Life-Space Assessment. *Physical Therapy*. 2005;**85**: 1008-1019.
- [29] Shimada H, Sawyer P, Harada K, *et al.* Predictive Validity of the Classification Schema for Functional Mobility Tests in Instrumental Activities of Daily Living Decline Among Older Adults. *Archives of Physical Medicine and Rehabilitation*. 2010;**91**: 241-246.
- [30] Shimada H, Ishizaki T, Kato M, et al. How often and how far do frail elderly people need to go outdoors to maintain functional capacity? Archives of Gerontology and Geriatrics. 2010;50: 140-146.
- [31] Ishii S, Tanaka T, Shibasaki K, et al. Development of a simple screening test for sarcopenia in older adults. *Geriatrics & Gerontology International*. 2014;**14**: 93-101.
- [32] Atchison KA, Dolan TA. Development of the geriatric oral health assessment index. *Journal of Dental Education*. 1990;**54**: 680-687.

- [33] Naito M, Suzukamo Y, Nakayama T, et al. Linguistic adaptation and validation of the General Oral Health Assessment Index (GOHAI) in an elderly Japanese population. *Journal of Public Health Dentistry*. 2006;**66**: 273-275.
- [34] Kumagai S, Watanabe S, Shibata H, et al. EFFECTS OF DIETARY VARIETY ON DECLINES IN HIGH-LEVEL FUNCTIONAL CAPACITY IN ELDERLY PEOPLE LIVING IN A COMMUNITY. Japanese journal of public health. 2003;50: 1117-1124.
- [35] Rubenstein LZ, Harker JO, Salva A, *et al.* Screening for undernutrition in geriatric practice: Developing the Short-Form Mini-Nutritional Assessment (MNA-SF). *Journals of Gerontology Series a-Biological Sciences and Medical Sciences*. 2001;**56**: M366-M372.
- [36] Hassel AJ, Danner D, Schmitt M, et al. Oral health-related quality of life is linked with subjective well-being and depression in early old age. Clinical Oral Investigations. 2011;15: 691-697.
- [37] de Andrade FB, Lebrao ML, Santos JLF, et al. Relationship Between Oral Health-Related Quality of Life, Oral Health, Socioeconomic, and General Health Factors in Elderly Brazilians. *Journal of the American Geriatrics Society*. 2012;**60**: 1755-1760.
- [38] Gazmararian J, Baker D, Parker R, Blazer DG. A multivariate analysis of factors associated with depression: evaluating the role of health literacy as a potential contributor. *Archives of Internal Medicine*. 2000;**160**: 3307-3314.

# **GRAPHICS**

**Table 1:**Geriatric characteristics of normal (non-depressed) and depressed study subjects\* (n=1,856)

	Young-old (65-74 years old)		Old-old (≥75 years old)				l)			
variables	(n====	ormal 1,033)  mean±SD	syn (n:	pressive aptoms = 168)	p-value -	(n=	ormal =551)  mean±SD	sym (n=	ressive ptoms =104)	p-value -
Socio-demographic variables								<u> </u>		
Sex (male)	519	(50.2)	71	(42.3)	0.055	282	(51.2)	56	(53.8)	0.618
Age	69.6	$6 \pm 2.7$	69.	$6 \pm 2.6$	0.969	79.0	$0 \pm 3.7$	79.4	$\pm 4.0$	0.294
Education (years)	13.0	$0 \pm 2.5$	12.	$6 \pm 2.6$	0.089	12.4	$4 \pm 3.1$	11.7	$2 \pm 3.3$	0.056
Health literacy	4.03	± 0.61	3.71	± 0.67	<.001	4.07	$\pm 0.60$	3.64	± 0.70	<.001
Low income	598	(57.9)	126	(75.0)	<.001	293	(53.2)	62	(59.6)	0.227
Social engagement										
Living alone	77	(7.5)	20	(11.9)	0.050	84	(15.2)	15	(14.4)	0.830
Eating alone	91	(8.8)	42	(25.0)	<.001	104	(18.9)	34	(32.7)	0.002
Living & Eating with others	929	(89.9)	124	(73.8)	<.001	428	(77.7)	68	(65.4)	0.007
Living & Eating alone	64	(6.2)	18	(10.7)	0.031	65	(11.8)	13	(12.5)	0.839
Living alone yet Eating with others	13	(1.3)	2	(1.2)	1.000	19	(3.4)	2	(1.9)	0.555
Living with others yet Eating alone	27	(2.6)	24	(14.3)	<.001	39	(7.1)	21	(20.2)	<.001
Low reciprocal social support	45	(4.4)	29	(17.3)	<.001	34	(6.2)	18	(17.3)	<.001
Fewer frequency of going out	127	(12.3)	65	(38.7)	<.001	107	(19.4)	47	(45.2)	<.001
Major change in life	225	(21.8)	62	(36.9)	<.001	85	(15.4)	28	(26.9)	0.004
Social ties with family	8.33	$3 \pm 3.1$	6.5	$8 \pm 3.1$	<.001	8.2	$1 \pm 3.2$	6.91	± 3.0	<.001
Social ties with friends	8.43	$3 \pm 3.5$	6.2	$3 \pm 3.4$	<.001	8.43	$3 \pm 3.6$	6.30	$\pm 3.4$	<.001
Medical histories										
Hypertension	388	(37.6)	78	(46.4)	0.029	270	(49.0)	69	(66.3)	0.001
Cerebrovascular diseases	36	(3.5)	16	(9.5)	<.001	47	(8.5)	13	(12.5)	0.198
Diabetes	116	(11.2)	17	(10.1)	0.671	68	(12.3)	14	(13.5)	0.752
Osteoporosis	77	(7.5)	21	(12.5)	0.027	79	(14.3)	23	(22.1)	0.045
Heart diseases	151	(14.6)	28	(16.7)	0.489	111	(20.1)	32	(30.8)	0.016
Malignant neoplasm	152	(14.7)	16	(9.5)	0.072	92	(16.7)	23	(22.1)	0.183
Number of medications	2.21	$1 \pm 2.5$	2.8	$5 \pm 2.9$	0.008	3.8	$0 \pm 3.3$	5.72	$2 \pm 3.9$	<.001
Physical health & functions										
IADL	4.90	$\pm 0.36$	4.77	$7 \pm 0.63$	0.013	4.85	$5\pm0.50$	4.61	± 0.89	0.007
Mobility	25.8	$3 \pm 9.8$	21.	$1 \pm 10$	<.001	24.	$1 \pm 9.9$	20.9	9 ± 11	0.003

Cognitive function: MMSE	$28.5\pm1.7$	$28.0 \pm 1.9$	0.002	$28.0\pm1.9$	$27.3 \pm 2.3$	0.006
Oral health & functions: GOHAI	$55.8 \pm 5.4$	$51.3 \pm 7.1$	<.001	$54.5 \pm 6.3$	$49.5 \pm 8.9$	<.001
Nutritional & dietary status						
BMI (kg/m²)	$23.0\pm2.9$	$22.6 \pm 3.0$	0.071	$22.7 \pm 3.1$	$22.6 \pm 3.0$	0.625
Food variety	$3.63\pm2.0$	$3.04\pm1.9$	<.001	$4.23\pm2.1$	$3.72\pm2.1$	0.021
MNA-SF	$12.7\pm1.3$	$12.1\pm1.8$	<.001	$12.4\pm1.5$	$11.8\pm1.8$	0.004

SD: standard deviation; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; GOHAI: General Oral Health Assessment Index; BMI: body mass index; MNA-SF: Mini Nutritional Assessment Short-Form \*Chi-square test or Fisher's Exact Test was used for categorical variables and non-paired t-test was used for continuous variables

**Table 2:** Association between depressive symptoms and risk factors by binomial multiple logistic regression

	Young-old (65-74 years old) (n=1,201)							
variables		Model 1	Model 2					
	OR	95%CI	p-value	OR	95%CI	p-value		
Social engagement								
Living & Eating with others (ref)		-			-			
Living & Eating alone	1.94	(1.1-3.6)	0.034	1.53	(0.79-2.9)	0.204		
Living alone yet Eating with others	1.59	(0.32-7.9)	0.569	1.14	(0.19-6.8)	0.885		
Living with others yet Eating alone	6.33	(3.3-12)	<.001	5.02	(2.5-9.9)	<.001		
Low reciprocal social support	2.57	(1.5-4.6)	0.001	2.41	(1.3-4.5)	0.006		
Fewer frequency of going out	3.79	(2.6-5.6)	<.001	2.57	(1.7-3.9)	<.001		
Major change in life	1.78	(1.2-2.6)	0.004	1.72	(1.1-2.6)	0.009		
Social ties with family	0.901	(0.84-0.96)	0.002	0.905	(0.84-0.97)	0.005		
Social ties with friends	0.911	(0.86-0.96)	0.001	0.940	(0.88-1.0)	0.049		
Socio-demographic variables								
Sex (male)				1.29	(0.77-2.2)	0.334		
Health literacy				0.691	(0.52-0.93)	0.013		
Low income				1.77	(1.0-3.0)	0.038		
Medical histories								
Hypertension				1.17	(0.75-1.8)	0.486		
Cerebrovascular diseases				1.99	(0.89-4.4)	0.094		
Osteoporosis				1.38	(0.74-2.6)	0.308		
Number of medications				1.03	(0.96-1.1)	0.402		
Physical health & functions								
IADL				0.824	(0.54-1.3)	0.369		
Mobility				0.973	(0.96-0.99)	0.007		
Cognitive function: MMSE				1.04	(0.92-1.2)	0.521		
Oral health & functions: GOHAI				0.944	(0.92-0.97)	<.001		
Nutritional & dietary status								
Food variety				0.929	(0.84-1.0)	0.163		
MNA-SF				0.870	(0.76-0.99)	0.038		
		O	ld-old (≥75 ye	ars old) (n=6	555)			
variables		Model 1			Model 2			
	OR	95%CI	p-value	OR	95%CI	p-value		

L'alas O Fatina alama	1.01	(0.51.2.0)	0.060	1.06	(0.40.0.4)	0.000
Living & Eating alone	1.01	(0.51-2.0)	0.968	1.06	(0.48-2.4)	0.889
Living alone yet Eating with others	0.753	(0.17-3.4)	0.712	0.979	(0.19-5.0)	0.980
Living with others yet Eating alone	2.45	(1.3-4.7)	0.006	2.41	(1.2-4.8)	0.014
Low reciprocal social support	1.91	(0.95-3.9)	0.071	1.04	(0.48-2.3)	0.917
Fewer frequency of going out	2.97	(1.9-4.7)	<.001	2.09	(1.2-3.6)	0.008
Major change in life	1.98	(1.2-3.4)	0.012	2.18	(1.2-3.9)	0.009
Social ties with family	0.981	(0.90-1.1)	0.651	0.972	(0.89-1.1)	0.548
Social ties with friends	0.880	(0.82-0.94)	<.001	0.895	(0.83-0.97)	0.006
Socio-demographic variables						
Sex (male)				1.56	(0.88-2.8)	0.126
Health literacy				0.499	(0.34-0.74)	<.001
Medical histories						
Hypertension				1.46	(0.83-2.6)	0.185
Osteoporosis				1.27	(0.63-2.5)	0.505
Heart diseases				1.21	(0.68-2.1)	0.525
Number of medications				1.10	(1.0-1.2)	0.010
Physical health & functions						
IADL				0.842	(0.59-1.2)	0.340
Mobility				1.00	(0.98-1.0)	0.990
Cognitive function: MMSE				0.919	(0.82-1.0)	0.160
Oral health & functions: GOHAI				0.935	(0.90-0.97)	<.001
Nutritional & dietary status						
Food variety				0.982	(0.87-1.1)	0.770
MNA-SF				0.929	(0.79-1.1)	0.365

OR: odds ratio; CI: confidence interval; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; GOHAI: General Oral Health Assessment Index; MNA-SF: Mini Nutritional Assessment Short-Form Model 1: social engagement

Model 2: social engagement, socio-demographic variables, medical histories, number of medications, physical health & functions, cognitive function, oral health & functions, nutritional & dietary status

**Table 3:**Geriatric characteristics of normal, mildly depressed and severely depressed subjects\* (n=1,856)

variables		rmal 1,584)	dep	Mild ression =193)	depre	vere ession =79)	p-value
		· · · · · · · · · · · · · · · · · · ·	mean±SI	O or n (%)	***************************************		-
Socio-demographic variables							
Sex (male)	801	(50.6)	84	(43.5)	43	(54.4)	0.601
Age	72.8	$3 \pm 5.4$	72.	$7 \pm 5.6$	74.8	± 6.0	0.201
Education (years)	12.8	$\pm 2.7$	12.3	$3 \pm 2.9$	12.2	± 3.1	0.007
Health literacy	4.04	± 0.61	3.75	$5 \pm 0.67$	3.52	± 0.70	<.001
Low income	891	(56.3)	137	(71.0)	51	(64.6)	0.001
Social engagement							
Living alone	161	(10.2)	19	(9.8)	16	(20.3)	0.031
Eating alone	195	(12.3)	47	(24.4)	29	(36.7)	<.001
Living& Eating with others (ref)	1357	(85.7)	146	(75.6)	46	(58.2)	<.001
Living & Eating alone	129	(8.1)	19	(9.8)	12	(15.2)	0.031
Living alone yet Eating with others	32	(2.0)	0	(0.0)	4	(5.1)	0.681
Living with others yet Eating alone	66	(4.2)	28	(14.5)	17	(21.5)	<.001
Low reciprocal social support	79	(5.0)	30	(15.5)	17	(21.5)	<.001
Fewer frequency of going out	234	(14.8)	75	(38.9)	37	(46.8)	<.001
Major change in life	310	(19.6)	66	(34.2)	24	(30.4)	<.001
Social ties with family	8.29	± 3.1	6.82	$2 \pm 3.1$	6.42	± 3.0	<.001
Social ties with friends	8.43	$\pm 3.5$	6.42	$2 \pm 3.4$	5.86	± 3.4	<.001
Medical histories							
Hypertension	658	(41.5)	107	(55.4)	40	(50.6)	0.001
Cerebrovascular diseases	83	(5.2)	17	(8.8)	12	(15.2)	<.001
Diabetes	184	(11.6)	23	(11.9)	8	(10.1)	0.805
Osteoporosis	156	(9.8)	31	(16.1)	13	(16.5)	0.003
Heart diseases	262	(16.5)	43	(22.3)	17	(21.5)	0.043
Malignant neoplasm	244	(15.4)	27	(14.0)	12	(15.2)	0.739
Number of medications	2.77	$\pm 2.9$	3.84	$4 \pm 3.4$	4.20	± 3.9	<.001
Physical health & functions							
IADL	4.88	± 0.42	4.73	$3 \pm 0.70$	4.66	± 0.83	<.001
Mobility	25.2	$\pm 9.8$	21.	$0 \pm 10$	20.9	± 11	<.001
Cognitive function: MMSE	28.3	± 1.8	27.	$7 \pm 2.0$	27.7	± 2.2	<.001
Oral health & functions: GOHAI	55.4	± 5.8	51.	$1 \pm 7.4$	49.2	± 8.7	<.001
Nutritional & dietary status							

BMI (kg/m²)	$22.9 \pm 3.0$	$22.7\pm3.1$	$22.3 \pm 2.9$	0.163
Food variety	$3.84 \pm 2.0$	$3.34 \pm 2.0$	$3.20 \pm 2.1$	<.001
MNA-SF	$12.6 \pm 1.4$	$12.1 \pm 1.7$	$11.7 \pm 1.9$	<.001

SD: standard deviation; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; GOHAI: General Oral Health Assessment Index; BMI: body mass index; MNA-SF: Mini Nutritional Assessment Short-Form \*Cochran-Armitage trend test was used for categorical variables and Jonckheere-Terpstra trend test was used for continuous variables

**Table 4:**Association between mild and severe depression and their risk factors by multinomial multiple logistic regression (n=1,856)

		Mild depression	Severe depression			
variables		(n=193)		(n=79)		
	OR	95%CI	p-value	OR	95%CI	p-value
Social engagement						
Living alone	0.374	(0.19-0.74)	0.005	0.777	(0.33-1.8)	0.566
Eating alone	2.96	(1.8-5.0)	<.001	3.33	(1.6-6.8)	0.001
Low reciprocal social support	1.73	(1.0-2.9)	0.045	1.66	(0.80-3.4)	0.172
Fewer frequency of going out	2.21	(1.5-3.2)	<.001	2.79	(1.6-4.8)	<.001
Major change in life	1.78	(1.2-2.6)	0.002	1.63	(0.93-2.9)	0.091
Social ties with family	0.940	(0.88-1.0)	0.046	0.935	(0.85-1.0)	0.162
Social ties with friends	0.929	(0.88-0.98)	0.007	0.895	(0.82-0.97)	0.009
Socio-demographic variables						
Sex (male)	1.27	(0.78-2.1)	0.335	2.46	(1.2-5.0)	0.013
Age	0.950	(0.92-0.98)	0.005	0.998	(0.95-1.0)	0.943
Education (years)	1.05	(0.98-1.1)	0.190	1.03	(0.93-1.1)	0.582
Health literacy	0.670	(0.52-0.87)	0.003	0.440	(0.31-0.63)	<.001
Low income	1.72	(1.1-2.8)	0.024	1.65	(0.84-3.3)	0.145
Medical histories						
Hypertension	0.743	(0.51-1.1)	0.118	1.14	(0.64-2.0)	0.655
Cerebrovascular diseases	1.38	(0.74-2.6)	0.312	2.36	(1.1-5.2)	0.033
Osteoporosis	0.712	(0.43-1.2)	0.184	0.839	(0.39-1.8)	0.652
Heart diseases	1.00	(0.65-1.5)	0.994	1.28	(0.67-2.5)	0.461
Number of medications	1.08	(1.0-1.1)	0.017	1.10	(1.0-1.2)	0.027
Physical health & functions						
IADL	0.834	(0.63-1.1)	0.215	0.862	(0.59-1.3)	0.446
Mobility	0.983	(0.97-1.0)	0.044	0.988	(0.96-1.0)	0.327
Cognitive function: MMSE	0.927	(0.85-1.0)	0.103	0.994	(0.87-1.1)	0.930
Oral health & functions: GOHAI	0.943	(0.92-0.97)	<.001	0.928	(0.90-0.96)	<.001
Nutritional & dietary status						
Food variety	0.959	(0.88-1.0)	0.344	0.960	(0.84-1.1)	0.531
MNA-SF	0.936	(0.84-1.0)	0.251	0.839	(0.72-0.98)	0.029

OR: odds ratio; CI: confidence interval; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; GOHAI: General Oral Health Assessment Index; MNA-SF: Mini Nutritional Assessment Short-Form

**Table 5:** Characteristics by living and eating arrangement (n=1,856)

variables	Living & Eating alone (n=160)	Living alone yet Eating with others (n=36)	Living with others yet Eating alone (n=111)	Living & Eating with others (n=1,549)	p-value*
		mean±SD	or n (%)		
Social engagement					
Live with spouse	- -	-	61 (55.0)	1393 (89.9)	<.001
Live with children	-	-	74 (66.7)	627 (40.5)	<.001
Live with children-in-law	-	-	21 (18.9)	117 (7.6)	<.001
Live with grand-children	-	-	29 (26.1)	171 (11.0)	<.001
Social ties with family	$7.24 \pm 3.4$	$8.83 \pm 3.5$	$7.19 \pm 3.2$	$8.19 \pm 3.1$	<.001*
Social ties with friends	$8.08 \pm 3.4$	$8.86\pm2.9$	$6.86 \pm 4.0$	$8.19 \pm 3.6$	0.003*
Socio-demographic variables					
Sex (male)	42 (26.3)	11 (30.6)	63 (56.8)	812 (52.4)	<.001
Age	$74.6 \pm 6.0$	$75.4 \pm 5.2$	$75.3 \pm 5.7$	$72.5 \pm 5.3$	<.001*
Education (years)	$11.9 \pm 2.7$	$12.0\pm2.7$	$11.8\pm3.2$	$12.9\pm2.7$	<.001*
Health literacy	$3.87 \pm 0.71$	$4.13 \pm 0.71$	$3.86\pm0.66$	$4.01 \pm 0.62$	0.015
Number of medications	$3.50 \pm 3.5$	$4.17 \pm 4.3$	$3.76\pm3.7$	$2.79 \pm 2.9$	0.004
Physical health & functions					
Usual gait speed (m/s)	$1.43\pm0.25$	$1.44\pm0.26$	$1.41 \pm 0.27$	$1.48\pm0.25$	0.026
Max gait speed (m/s)	$2.05 \pm 0.38$	$2.03 \pm 0.46$	$2.01\pm0.36$	$2.17 \pm 0.39$	<.001*
IADL	$4.94\pm0.30$	$4.94 \pm 0.23$	$4.69 \pm 0.84$	$4.86 \pm 0.46$	0.007
Mobility	$23.9 \pm 10$	$27.3 \pm 11$	$21.0 \pm 11$	$24.9 \pm 9.9$	<.001*
Mental health					
GDS	$3.18 \pm 3.4$	$2.86 \pm 3.2$	$4.83 \pm 4.1$	$2.39\pm2.7$	<.001*
Depressive symptoms: GDS≥6	31 (19.4)	4 (11.1)	45 (40.5)	192 (12.4)	<.001
Severe depression: GDS≥10	12 (7.5)	4 (11.1)	17 (15.3)	46 (3.0)	<.001
Cognitive function: MMSE	$28.3 \pm 1.8$	$28.0 \pm 1.6$	$27.8 \pm 1.9$	$28.2 \pm 1.8$	0.029
Oral health & functions					
GOHAI	$53.8 \pm 7.3$	$53.3 \pm 7.8$	$53.1 \pm 6.6$	$54.9 \pm 6.2$	<.001*
Number of remaining teeth	$20.5\pm8.0$	$19.2 \pm 8.4$	$17.8 \pm 9.7$	$21.0 \pm 8.3$	0.003*
Occlusal force (N)	$496 \pm 333$	$522 \pm 365$	$478 \pm 345$	$585 \pm 361$	<.001*
Nutritional& dietary status					
BMI (kg/m²)	$22.3 \pm 3.3$	$24.3 \pm 3.6$	$22.8 \pm 3.3$	$22.9 \pm 2.9$	0.002
Food variety	$3.74 \pm 2.0$	$3.89 \pm 2.0$	$3.26 \pm 2.1$	$3.79\pm2.0$	0.037
MNA-SF	$12.2 \pm 1.6$	$12.4 \pm 1.6$	$12.1 \pm 1.7$	$12.5 \pm 1.4$	0.007

<sup>\*</sup>Kruskal-Wallis test for continuous variables and Chi-squared test for categorical vairables.

Those continuous variables that showed significant difference between "Living with others yet Eating alone" and "Living & Eating with others" in the multiple comparison test (Dunnett T3) are highlighted with '\*'.



# Metabolic Syndrome, Sarcopenia and Role of Sex and Age: Cross-Sectional Analysis of Kashiwa Cohort Study



Shinya Ishii<sup>1</sup>, Tomoki Tanaka<sup>2</sup>, Masahiro Akishita<sup>1</sup>, Yasuyoshi Ouchi<sup>3</sup>, Tetsuo Tuji<sup>2</sup>, Katsuya Iijima<sup>2\*</sup>, for the Kashiwa study investigators<sup>1</sup>

1 Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655 Japan, 2 Institute of Gerontology, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan, 3 Federation of National Public Service Personnel Mutual Aid Associations, Toranomon Hospital, 2-2-2, Toranomon, Minato-ku, Tokyo 105-8470, Japan

#### **Abstract**

Recent epidemiological evidence suggests that effects of cardiovascular risk factors may vary depending on sex and age. In this study, we assessed the associations of metabolic syndrome (MetS) with sarcopenia and its components in older adults, and examined whether the associations vary by sex and age. We also tested if any one of the MetS components could explain the associations. We conducted a cross-sectional analysis of the baseline data from the cohort study conducted in Kashiwa city, Chiba, Japan in 2012 which included 1971 functionally-independent, community-dwelling Japanese adults aged 65 years or older (977 men, 994 women). Sarcopenia was defined based on appendicular skeletal muscle mass, grip strength and usual gait speed. MetS was defined based on the National Cholesterol Education Program's Adult Treatment Panel-III criteria. The prevalence of sarcopenia was 14.2% in men and 22.1% in women, while the prevalence of MetS was 43.6% in men and 28.9% in women. After adjustment for potential confounders, MetS was positively associated with sarcopenia in men aged 65 to 74 years (odds ratio 5.5; 95% confidence interval 1.9–15.9) but not in older men or women. Among the sarcopenia components, MetS was associated with lower muscle mass and grip strength, particularly in men aged 65 to 74 years. The associations of MetS with sarcopenia and its components were mainly driven by abdominal obesity regardless of sex or age. In conclusion, MetS is positively associated with sarcopenia in older men. The association is modified by sex and age, but abdominal obesity is the main contributor to the association across sex and age.

Citation: Ishii S, Tanaka T, Akishita M, Ouchi Y, Tuji T, et al. (2014) Metabolic Syndrome, Sarcopenia and Role of Sex and Age: Cross-Sectional Analysis of Kashiwa Cohort Study. PLoS ONE 9(11): e112718. doi:10.1371/journal.pone.0112718

Editor: Stephen E. Alway, West Virginia University School of Medicine, United States of America

Received July 10, 2014; Accepted October 14, 2014; Published November 18, 2014

**Copyright:** © 2014 Ishii et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability: The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. All relevant data are within the paper and its Supporting Information files.

**Funding:** This work was supported by a Health and Labor Sciences Research Grant (H24-Choju-Ippan-002 to KI) from the Ministry of Health, Labor, and Welfare of Japan (http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/hokabunya/kenkyujigyou/). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

- \* Email: iijima@iog.u-tokyo.ac.jp
- ¶ Membership of the Kashiwa study investigators is provided in the Acknowledgments.

#### Introduction

Metabolic syndrome (MetS) is a constellation of cardiovascular risk factors which include abdominal obesity, dyslipidemia, hypertension and elevated glucose [1]. Insulin resistance and chronic inflammation are considered central mechanisms responsible for MetS [2] and inextricably correlate with each other to exert detrimental metabolic effects and lead to cardiovascular morbidity and mortality [3-5]. Accumulating epidemiological evidence suggests that both insulin resistance and chronic inflammation cause adverse effects on skeletal muscle. Diabetes, or even insulin resistance without diabetes, is associated with greater declines in skeletal muscle mass and strength [6,7]. A link between inflammation and muscle weakness has been reported in several studies [8,9]. Therefore, we postulate that MetS can accelerate age-related loss of muscle mass and strength, leading to the development of sarcopenia, a syndrome characterized by loss of skeletal muscle mass and function with a risk of physical disability [10]. Indeed, recent studies showed that MetS is associated with physical capacity impairment and increased risk of developing physical and functional disabilities [11-13].

Several recent studies have suggested that the effects of MetS may vary depending on age and sex. Cardiovascular risk factors, whose adverse effects have been established in younger people, may have different impacts in the elderly or frail population. Obesity did not seem to be a risk factor for increased mortality in elderly hospitalized patients with or without diabetes [14,15]. Elevated blood pressure was associated with lower mortality risk in physically frail elderly adults who could not walk 20 feet [16]. MetS was associated with lower probability of prevalent and incident functional disability in older adults [17]. The association between MetS and cardiovascular events was observed only in patients younger than 75, but not in patients aged 75 or over [18]. With regard to sex-related differences in the effects of MetS, MetS was associated with lower muscle strength in elderly men but not in elderly women [19]. However, data on sex- or age-related differences in the effect of MetS on sarcopenia are still scarce.

In the present study, we assessed the associations of MetS with sarcopenia and its components in functionally-independent community-dwelling Japanese older adults, and examined whether the associations were modified by sex or age. We hypothesized that MetS is positively associated with sarcopenia and its components, and that the associations are more pronounced in relatively young men. We also examined whether any of the individual MetS components could explain the associations and if the same MetS components contributed to the associations across sex and age.

#### **Methods**

#### Subjects

The Kashiwa study is a prospective cohort study designed to characterize the biological, psychosocial and functional changes associated with aging in a community-based cohort of 2044 older adults (1013 men, 1031 women). Those aged 75 and older accounted for 36.3% of men and 35.0% of women. The sampling and data collection process has been described in detail elsewhere [20]. Briefly, the inclusion criteria were age equal to or older than 65 years and functional independence (i.e., not requiring nursing care provided by long-term care insurance). The subjects were randomly selected from the resident register of Kashiwa city, Chiba, Japan, enrolled in 2012, and followed annually. The current study is a cross-sectional analysis of the Kashiwa study baseline data. Seventy three subjects who did not undergo bioimpedance analysis (BIA), usual gait speed or hand grip strength measurements were excluded, leaving an analytic sample of 1971 older adults (977 men, 994 women). Those excluded from the analysis were older compared to those included in the analysis (mean age 75.9 years vs. 72.9 years, p = 0.001), but did not significantly differ with respect to other characteristics including sex, height, weight, and prevalence of MetS.

The study was approved by the ethics committee of the Graduate School of Medicine, The University of Tokyo. All subjects provided written informed consent.

#### Definition of Sarcopenia

We followed the recommendations of the European Working Group on Sarcopenia in Older People (EWGSOP) for the diagnostic definition of sarcopenia [10]. The proposed diagnostic criteria required the presence of low muscle mass plus the presence of either low muscle strength or low physical performance. Muscle mass was measured by BIA using an Inbody 430 machine (Biospace, Seoul, Korea). Appendicular skeletal muscle mass (ASM) was derived as the sum of the muscle mass of the four limbs [10]. ASM was then normalized by height in meters squared to yield skeletal muscle mass index (SMI) (kg/m²). SMI values lower than two standard deviations below the mean values of young male and female reference groups were classified as low muscle mass (SMI <7.0 kg/m<sup>2</sup> in men, <5.8 kg/m<sup>2</sup> in women) [21]. Muscle strength was assessed by hand grip strength, which was measured using a digital grip strength dynamometer (Takei Scientific Instruments, Niigata, Japan). Hand grip strength values in the lowest quintile were classified as low muscle strength in this study (cutoff values: 30 kg for men, 20 kg for women). Physical performance was assessed by usual gait speed. Subjects were instructed to walk over an 11-meter straight course at their usual speed. Usual gait speed was derived from 5 meters divided by the time in seconds spent in the middle 5 meters (from the 3-meter line to the 8-meter line) [22]. Usual gait speed values in the lowest quintile were classified as low physical performance in the current study (cutoff values: 1.26 m/s for each sex).

#### Definition of metabolic syndrome

MetS was defined based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria [1]. The presence of any three of the following five abnormalities constitutes a diagnosis of MetS: (i) abdominal obesity; (ii) elevated triglycerides (TG) with fasting plasma triglycerides ≥150 mg/dL; (iii) low high density lipoprotein cholesterol (HDL-C) with fasting HDL-C <40 mg/dL in men and <50 mg/dL in women; (iv) elevated blood pressure with systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg; (v) elevated fasting plasma glucose with fasting plasma glucose ≥100 mg/dL. Abdominal obesity was defined by waist circumference using the thresholds recommended by the Japanese Obesity Society (≥85 cm in men and ≥90 cm in women) [1].

Waist circumference was measured at the umbilical level using a measuring tape with the subject in an upright position. Blood pressure was measured using a standard technique with an HEM-7080IT automated measuring device (Omron Co., Tokyo, Japan). Blood samples were obtained after an overnight fast. Total cholesterol, HDL-C and TG were analyzed by enzymatic methods using a JCA-BM8060 automated analyzer (Japan Electron Optics Laboratory Ltd., Tokyo, Japan). Fasting plasma glucose level was measured using a JCA-BM9030 automated analyzer (Japan Electron Optics Laboratory Ltd.).

#### Other measurements

Demographic information, medical history of doctor-diagnosed chronic conditions, use of medication, and food intake were obtained using a standardized self-reported questionnaire. Physical activity was assessed using the Global Physical Activity Questionnaire, and metabolic equivalents (METs)-minute per week was computed [23]. Height and weight were measured with the subject wearing light clothing and no shoes using a fixed stadiometer and a digital scale, and used to compute body mass index (BMI).

#### Statistical Analysis

Differences in subject characteristics between those with and without sarcopenia were examined using Student's t-test or Wilcoxon rank-sum test (for continuous variables) and chi-square test (for categorical variables).

First, we employed logistic regression analysis to evaluate the association of MetS with sarcopenia. Our preliminary analysis suggested that the association of metabolic syndrome with sarcopenia was modified by sex (p < 0.01), and therefore the following analyses were stratified by sex.

The model was initially adjusted for age only (model 1). We added height and weight to remove the confounding effect of body size (model 2). We then further adjusted for life-style risk factors for both sarcopenia and MetS, including physical activity and food intake (model 3). In the fully-adjusted model, the interaction between MetS and age was examined to test the hypothesis that the effect of MetS on sarcopenia varies by age.

To test if any MetS component could explain the MetS-sarcopenia association, we initially fitted a fully-adjusted logistic regression model to examine the association between each component of MetS and sarcopenia, followed by other logistic regression models between MetS and sarcopenia adjusted for MetS components.

Second, to examine the association of MetS with each component of sarcopenia (i.e., muscle mass, grip strength and usual gait speed), we employed multiple linear regression models. If the association between MetS and any one of the sarcopenia components was statistically significant, another multiple linear regression model with MetS components as independent variables

November 2014 | Volume 9 | Issue 11 | e112718

 Table 1. Characteristics of all subjects and according to sarcopenia status in men and women.

	All	Sarcopenia	No sarcopenia	р	
Men	977	139 (14.2%)	838 (85.8%)		
Age (years)	73.1±5.5	78.4±5.5	72.2±5.0	< 0.001	
Height (cm)	164.2±5.8	$160.0 \pm 5.6$	164.9±5.5	< 0.001	
Weight (kg)	62.8±8.6	54.1 ± 7.2	64.3±8.0	< 0.001	
BMI (kg/m²)	23.3±2.8	21.1 ± 2.5	23.6±2.6	< 0.001	
SMI (kg/m²)	7.28±0.68	$6.34 \pm 0.48$	7.44±0.58	< 0.001	
Hand grip strength (kg)	34.8±6.0	27.5±4.3	36.0±5.3	< 0.001	
Jsual gait speed (m/s)	1.47±0.26	$1.28 \pm 0.24$	$1.51 \pm 0.24$	< 0.001	
MetS	43.6%	36.0%	44.9%	0.048	
MetS components					
Abdominal obesity	55.5%	36.0%	58.7%	< 0.001	
High TG	22.7%	21.6%	22.9%	0.73	
Low HDL-C	21.4%	20.9%	21.5%	0.87	
High BP	90.4%	88.5%	90.7%	0.41	
High FPG	51.0%	53.2%	50.6%	0.56	
Food intake					
Very large	2.9%	1.4%	3.1%	< 0.001	
Large	15.3%	5.8%	16.8%		
Normal	65.4%	58.3%	66.6%		
Small	14.4%	30.2%	11.8%		
Very small	2.1%	4.3%	1.7%		
Physical activity (Mets)	3962.9±3981.0	3191.7±3612.2	4090.8±4026.7	0.01	
Medical history					
Hypertension	47.2%	51.1%	46.5%	0.32	
Diabetes	15.4%	18.0%	14.9%	0.36	
Dyslipidemia	29.8%	31.7%	29.5%	0.60	
Stroke	7.2%	12.2%	6.4%	0.01	
CAD	8.0%	11.5%	7.4%	0.10	
Cancer	19.0%	26.6%	17.8%	0.01	
Medication use					
Statin	17.6%	18.7%	17.4%	0.71	
<i>N</i> omen	994	220 (22.1%)	774 (77.9%)		
Age (years)	72.8±5.4	76.2±5.8	71.8±4.9	< 0.001	
Height (cm)	151.4±5.5	148.2±5.6	152.3±5.1	< 0.001	
Weight (kg)	51.5±7.7	46.4±5.7	52.9±7.6	< 0.001	
BMI (kg/m²)	22.5±3.2	21.1±2.6	22.8±3.2	< 0.001	
5MI (kg/m²)	5.84±0.65	5.25±0.41	6.02±0.60	< 0.001	
Hand grip strength (kg)	22.4±3.9	18.4±3.2	23.6±3.3	< 0.001	
Jsual gait speed (kg)	1.46±0.26	1.26±0.26	1.51±0.23	< 0.001	
MetS	28.9%	23.6%	30.4%	0.052	
MetS components					
Abdominal obesity	24.0%	14.6%	26.7%	< 0.001	
High TG	17.9%	16.4%	18.4%	0.50	
Low HDL-C	36.6%	33.2%	37.6%	0.23	
High BP	84.2%	87.3%	83.3%	0.23	
=	33.7%	34.1%	33.6%	0.16	
		JT. 1 /U	JJ.U /U	0.09	
High FPG Food intake					