

Falls in community-dwelling prefrail older adults

Hiroyuki Umegaki, MD, PhD^{1,*}, Taeko Makino, PhD², Kazuki Uemura, PhD³,
Hiroyuki Shimada, PhD⁴, Xian Wu Cheng PhD², Hiroko Dodge, PhD⁵, Masafumi
Kuzuya, MD, PhD^{1,2}

¹Department of Community Healthcare & Geriatrics, Nagoya University Graduate
School of Medicine, Aichi, Japan

²Institute of Innovation for Future Society, Nagoya University, Aichi, Japan

³Liberal Arts and Sciences, Faculty of Engineering, Toyama Prefectural University,
Toyama, Japan

⁴Department of Preventive Gerontology, Center for Gerontology and Social Science,
National Center for Geriatrics and Gerontology, Obu, Japan

⁵Department of Neurology, Michigan Alzheimer's Disease Center, University of
Michigan, Ann Arbor, Michigan, United States of America

***Corresponding author:** Dr. Hiroyuki Umegaki, Nagoya University Graduate School
of Medicine, Department of Community Healthcare and Geriatrics, 65 Tsuruma-cho,
Showa-ku, Nagoya, Aichi, 466-8550, Japan. Tel.: +81-52-744-2364; Fax:

This is the author manuscript accepted for publication and has undergone full peer review
but has not been through the copyediting, typesetting, pagination and proofreading
process, which may lead to differences between this version and the [Version of Record](#).
Please cite this article as [doi: 10.1111/HSC.12845](https://doi.org/10.1111/HSC.12845)

This article is protected by copyright. All rights reserved

+81-52-744-2371. Email: umegaki@med.nagoya-u.ac.jp

ORCID : 0000-0003-2504-4133

Running head: Falls in prefrailty

Author Manuscript

DR. HIROYUKI UMEGAKI (Orcid ID : 0000-0003-2504-4133)

Article type : Original Article

Falls in community-dwelling prefrail older adults

Abstract

Frailty has been established as a risk factor for falls, and prefrailty also seems a risk; however, few studies have focused on the association between falls and each of the five components of frailty proposed by Fried. In the present study, we sought to elucidate the association between prefrailty and falls, and moreover, the association of frailty component with falls. Participants were community-dwelling older people who had cognitive complaints but not dementia (N=447, male 54.6%). Prefrailty was defined as exhibiting one or two of the five Fried criteria. Frail individuals were excluded. Background characteristics were compared between the prefrail and robust groups, and multiple regression analysis was performed to investigate the associations between fall history within the past year and factors that were significantly different between the groups. We also performed logistic regression analysis with adjustment for age, education, and sex to assess associations with frailty components. We found that prefrailty was associated with fall history. Depressed mood was also significantly associated with fall history. Among the five frailty criteria, exhaustion was significantly associated with falls. Prefrailty, especially the criteria of exhaustion, and depressed mood were associated with fall history.

Key words: depression, exhaustion, fall, gait speed, prefrailty

Bullet points

What is known about this topic

Falls are frequent events that lead to serious consequences in older people.

Frailty is a risk factor for falls.

Prefrailty may be a risk for falls, however, it has not been determined which of the frailty component is associated with falls.

What this paper adds

Prefrailty was found to be associated with falls.

Depressed mood was significantly associated with fall history.

Among the five frailty criteria, exhaustion had a significant association with falls.

Introduction

Falls are a major problem in geriatric medicine. They can have serious consequences, such as hip fracture, which are often associated with poor prognosis (Cree et al., 2000). Past studies have indicated that up to 30-60% of community-dwelling older people experience falls (Rubenstein & Josephson, 2002).

Frailty is also a major issue in geriatric medicine. There is a growing body of research on the characteristics of frailty and its association with unfavorable outcomes including geriatric syndrome. Although frailty is a dynamic condition that includes reduced capacity in physical, social, and psychological aspects, the concept of physical frailty is the most widely accepted. There is a growing consensus that the markers of physical frailty include age-associated declines in lean body mass, strength, endurance, balance, and walking performance; that physical frailty is associated with low physical activity; and that multiple components must be present for a clinical diagnosis of frailty (Lang, Michel, & Zekry, 2009).

Accordingly, Fried et al. (2001) proposed that a diagnosis of frailty requires three or more of the following five characteristics: unintended weight loss, exhaustion, weakness, slow gait speed, and low physical activity. Frailty is a syndrome that results from the accumulation of multiple types of age-related physical decline together with impairment of physiological

reserve, thus increasing vulnerability to adverse health outcomes including falls, hospitalization, institutionalization, and mortality (Vermeiren et al., 2016). Frailty has been reported to be associated with depressed mood (Vaughan, Corbin, & Goveas, 2015), and by definition, low endurance and physical performance, reduced muscle mass, and decreased physical activity.

Prefrailty is the state between robustness and frailty, in which one or two of the five criteria are met (Blaum, Xue, Michelon, Semba, & Fried, 2005). As a transitional status between robust and frailty, prefrailty has been reported to be associated with chronic comorbidity (Danon-Hersch, Rodondi, Spagnoli, & Santos-Eggimann, 2012) and functional decline (Acosta-Benito & Sevilla-Machuca, 2016). Frailty has been established to be a risk factor for falls (Kojima, 2015). Several systematic reviews have also suggested a possible association between falls and prefrailty (Cheng & Chang, 2017; Kojima, 2015; Fhonw et al., 2016). Because prefrailty is prevalent in older people (Kojima et al., 2017), the impact on older people would be rather large and intervention to prevent falls in prefrail older people would be warranted.

As described above, frailty has five components. However, few studies have focused on the association between falls and each component of frailty. For screening to identify individuals at high risk of falls, it would be useful to establish which components of frailty are associated with falls. Moreover, establishing such components could contribute to the development of interventions for fall prevention. Similarly, it is necessary to investigate which factors are associated with falls in both frail and prefrail older people from among various factors, including muscle mass, physical performance, physical activity, and depressed mood.

In this study, we utilized the baseline dataset of a randomized control trial conducted to investigate the effects of exercise on cognition and physical performance in community-dwelling older people. The aim of the study was to confirm that prefrailty was associated with fall history within the past one year, and explore which of the five components of frailty and which factors closely associated with prefrail status were most closely associated with fall history.

Materials and Methods

The TOYota Preventional Intervention for Cognitive decline and Sarcopenia [TOPICS] was a randomized controlled trial conducted to investigate the effects of various forms of exercise (aerobic, resistance, and aerobic + resistance) on cognition in older people who had a slight decline of memory function. The baseline data of TOPICS were analyzed in this cross-sectional study.

The Ethics Committee of the Graduate School of Medicine, Nagoya University approved the study protocol (approval no. 2014-0155-2), which was registered with the University Hospital Medical Information Network (UMIN) clinical trials registry (no. UMIN000014437). All participants provided written informed consent prior to inclusion in the study.

Participants

Participants were community-dwelling residents aged 65–85 years in selected areas of Toyota City, Aichi, Japan (22,790 residents), who were screened using the Kihon Checklist, a 25-item self-administered questionnaire for assessing frailty status (Arai & Satake, 2015). Respondents were regarded as being at high risk of cognitive decline if they answered “no” to Q19 (Do you make a call by looking up phone numbers?) or “yes” to the Q18 (Do your family or friends point out your memory loss? [e.g., Do they tell you that you ask the same question over and over again?]) or Q20 (Do you find yourself not knowing today’s date?) (Maki et al., 2012). A total of 4441 potential participants (2424 [men [54.6%]]) who met the criteria for high risk of cognitive decline were sent letters describing the interventional study of TOPICS. Written and oral explanations of the study were provided to those who were interested, and informed consent to take part in the study was ultimately obtained from 504 participants. Data of 447 participants without missing data were analyzed. The Mini-Mental State Examination (MMSE) was administered to all participants (Folstein, Folstein, & McHugh, 1975).

Exclusion criteria were (1) meeting clinical criteria for dementia; (2) any disability affecting basic and instrumental activities of daily living; (3) requiring support or care from the Japanese public long-term care insurance system; (4) MMSE score ≤ 19 ; (5) severe visual impairment; (6) diagnosis of a neurodegenerative disease (e.g., Parkinson’s disease); (7) medical contraindications to exercise; (8) psychiatric disease (e.g., major depressive disorder or schizophrenia); and (9) history of serious cardiovascular, musculoskeletal, respiratory, or cerebrovascular disease or another serious health issue.

Physical function

Grip strength in the dominant hand of each participant was measured using a portable grip strength dynamometer (GRIP-D; Takei Ltd., Niigata, Japan). Usual gait speed was assessed by timing the time required for the participant to walk between two markers spaced 5 m apart with a 1-m section in front of the start marker so that the participant could reach a comfortable pace before entering the timed path.

Body composition

Measurements were performed using a bioelectrical impedance analyzer (Inbody 430; Biospace Co., Seoul, Korea) with electrical current at three frequencies (5, 50, and 250 kHz) to directly measure extracellular and intracellular water in the body. Appendicular skeletal muscle mass was calculated based on segmental body composition and used in the subsequent analysis.

Skeletal muscle mass index (SMI) was calculated by dividing appendicular muscle mass by height squared (kg/m^2).

Physical activity

Daily physical activity data were collected with an activity monitor (Kenz Lifecorder; Suzuken Co., Ltd., Nagoya, Aichi, Japan), which was set up based on each participant's height and body mass. The activity monitor records duration and intensity of physical activity. Participants were instructed to wear the activity monitor on their waist all day with the exception of when they were bathing or sleeping. Activity monitoring was performed over 14 consecutive days, participants were asked to continue their normal daily activities during the measurement period. Participants were blinded to the measurement values.

The duration spent at particular activity intensity levels was detected (device records a signal of 0, 0.5, or 1–9 [in steps of 1] every 4 s). Intensity of physical activity was categorized into 11 levels (0, 0.5, 1–9) based on the acceleration pattern recorded. Metabolic equivalents (METs) is reported to be significantly correlated to activity intensity ($r^2 = 0.929$) (Kumahara et al., 2004). Physical activity was categorized as light physical activity (LPA; <3.0 METs), moderate physical activity (MPA; 3.0 – 6.0 METs), or vigorous physical activity (VPA; > 6.0 METs) (Kumahara et al., 2004). Mean duration of LPA and the sum of the mean durations of MPA and VPA (moderate + vigorous physical activity, MVPA) were calculated.

Fall assessment

Fall history within the previous year was assessed in the questionnaire, with fallers defined as participants who had fallen one or more times within the past year.

Frailty assessment

Frailty was defined using the Fried criteria. Specifically, participants who met three of the following five criteria were regarded as frail: unintended weight loss, exhaustion, weakness, slow gait speed, and low physical activity (Fried et al., 2001) Prefrailty was defined as meeting

one or two of these criteria (Blaum et al., 2005).

These criteria are defined as follows.

Weight loss: A decrease of > 5% in body mass in the previous 2 or 3 years by self-report.

Exhaustion: Answering “yes” to the question, “In the last two weeks, have you felt tired without a reason?” on the Kihon Checklist (Arai & Satake, 2015).

Weakness: Handgrip strength < 26 kg for men or < 18 kg for women (cutoffs defined by the Consensus Report of the Asian Working Group for Sarcopenia (Chen et al., 2014).

Slow gait speed: Usual walking speed < 1 m/s on a 5-m course.

Low physical activity: No regular exercise habits by self-report.

In this study, 9 frail participants were excluded because there were too few for statistical analysis; only robust and prefrail participants were included in the analysis.

Statistical analysis

Student's t-test was used for comparing continuous variables. The frequency distributions of categorical variables were analyzed using the Chi-square (χ^2) test. Multiple logistic analysis was performed using factors that exhibited significant differences between the robust and prefrailty groups (age, gait speeds, grip, LPA, MVPA, and Geriatric Depression Scale 15 [GDS-15]) to examine their association with fall history. We also performed logistic regression analysis to examine the associations between fall history and the components of frailty, with adjustment for age, education, and sex. Each component of frailty was entered into the model separately.

Results

Background characteristics of the 447 participants are shown in Table 1, of whom 183 (40.9%) were prefrail. The ratio of the fallers was significantly higher in the prefrail group (33.3%) compared than in the robust group (22.0%). In terms of background characteristics, there were no statistically significant differences between prefrailty and robust groups in BMI, SMI, and MMSE. However, prefrail participants were significantly older and had significantly lower gait speed and grip strength. GDS-15 scores were significantly higher in the prefrail. Both LPA and MVPA were shorter in the prefrail.

To explore which characteristics of prefrailty were associated with falls we performed multiple logistic analysis using factors that were significantly different between the prefrail and robust groups. The analysis revealed that GDS-15 score was significantly associated with fall

history (Table 2).

To explore which components of prefrailty were associated with falls we further performed logistic regression analysis for each frailty component with adjustment for age, education, and sex. It showed that exhaustion was significantly associated with fall history (table 3).

Discussion

We confirmed that prefrailty was associated with fall history in the community-dwelling older people in this study. Among the frailty criteria, exhaustion was significantly associated with fall history. Among the factors associated with prefrailty, depressed mood assessed by GDS-15 was significantly associated with fall history.

The participants had mild objective or subjective cognitive decline; however, dementia was excluded. More than one-fourth of this population had a history of fall within the past year. In the general population, it has been reported that more than one-third of persons aged 65 years or older fall each year (Tinetti, 2003). Our previous study showed that 38% of community-dwelling older people at high risk of requiring care experienced a fall within the past year (Umegaki, Suzuki, Yanagawa, Nonogaki, & Endo, 2012). The prevalence of fall history within the past year in the current study was slightly lower than these figures. This study used baseline data from a randomized controlled trial of an exercise intervention, so participants who were able to perform exercise were selectively recruited. Therefore, preserved physical condition may be the reason for relative low fall rate, though recall bias is another possibility.

Depressed mood assessed by the GDS-15 and exhaustion were significantly associated with fall history. Past studies have found that depressed mood is a risk factor for falls (Kvelde et al., 2013, 2015) and that falls may induce depressed mood (Iaboni & Flint, 2013). The cross-sectional design of the present study precluded us from examining the cause-effect relationship. To investigate this, a prospective cohort study is needed. A previous study reported that depressed mood measured using the GDS-15 and falls were risk factors for incidence of frailty (Doi et al., 2018). Both depressed mood and falls are potentially modifiable risk factors (Van, Damme, Declercq, Lemey, Tandt, & Petrovic, 2018; Guirguis-Blake, Michael, Perdue, Coppola, & Beil, 2018). Elucidating the mechanism underlying depressed mood and falls in prefrail older people may lead to the development of preventive strategies for frailty, or clarify which condition should be preferentially targeted for intervention.

Exhaustion was found to be significantly associated with fall history in the present study. According to a recent report, exhaustion is associated with serious fall injury in older

people treated for hypertension (Bromfield et al., 2017). The reasons why exhaustion is associated with falls are unclear. Low endurance may induce loss of concentration or muscle strength during walking (Hamacher, Törpel, Hamacher, & Schega, 2016), and may ultimately lead to falls. Exhaustion may also be associated with psychological factors linked to depressed mood (Whitson et al., 2011). Indeed, our current results also showed depressed mood evaluated by GDS-15 was significantly associated with fall. Further studies are warranted to elucidate the possible association.

Older people with exhaustion are good candidates for non-pharmacological interventions to prevent falls. Several studies demonstrated that endurance training or multicomponent training including endurance training reduced falls (Lord et al., 2003; Cadore, Rodríguez-Mañas, Sinclair, & Izquierdo, 2013). Frailty and even prefrailty are associated with cognitive dysfunction (Umegaki et al., 2018) and risk of falls (Tom et al., 2013; Zaslavsky et al., 2016), and older people who complain of exhaustion could be at high risk of falling and should be screened for interventions. The simple and subjective nature of the complaint of exhaustion might be suitable for screening high risk individuals in populations. Older people with depressed mood may also be considered to be at high risk of falls. Depressed mood is potentially treatable, and the intervention may lead to the prevention of falls and/or progression to frailty. Moreover, falls are at least partially preventable, and fall prevention could be an effective way to prevent incidence of frailty in older people.

A major limitation of this study is its retrospective design, which made it necessary to speculate on the cause-effect relationship. Fear of falls is reported to be associated with fall history and depression (Aibar-Almazán et al., 2018). Within the limitations of its retrospective design, the present study suggests that general fatigue may reflect depressed mood and fear of falls. A second limitation was that fall history within the past year was assessed by self-report, which depends on the memory of the participants. Although dementia was excluded, even mild memory impairment could affect the accuracy of the information. A third limitation was that this study used baseline data of an interventional trial, not a random sample, which could limit the generalizability of the results and their interpretation. A sub-analysis of the prospective TOPICS study and other future prospective studies are warranted to confirm the association of exhaustion with falls. Another potential limitation of the current study was the participants were all Japanese, and it is unclear that the results can be generalized to other population. A strength of the present study was that it measured a wide variety of physical and cognitive parameters.

In conclusion, depressed mood evaluated by GDS-Q15 was significantly associated with falls independently from age, gait speed, grip and physical activity. Prefrailty was

associated with fall history, and among five components of frailty, only exhaustion was significantly associated with falls.

Disclosure statement

No potential conflicts of interest were disclosed.

References

- Acosta-Benito, M.A., & Sevilla-Machuca, I. (2016). Using prefrailty to detect early disability. *Journal of family & community medicine*, 23(3), 140-4. doi: 10.4103/2230-8229.189106.
- Aibar-Almazán, A., Martínez-Amat, A., Cruz-Díaz, D., Jiménez-García, J.D., Achalandabaso, A., Sánchez-Montesinos, I., de la Torre-Cruz, M., & Hita-Contreras, F. (2018). Sarcopenia and sarcopenic obesity in Spanish community-dwelling middle-aged and older women: Association with balance confidence, fear of falling and fall risk. *Maturitas*, 107, 26-32. doi: 10.1016/j.maturitas.2017.10.001.
- Arai, H., & Satake, S. (2015). English translation of the Kihon Checklist. *Geriatrics & gerontology international*, 15(4), 518-9. doi: 10.1111/ggi.12397.
- Blaum, C.S., Xue, Q.L., Michelon, E., Semba, R.D., & Fried, L.P. (2005). The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. *Journal of the American Geriatrics Society*, 53, 927-34.
- Bromfield, S.G., Ngameni, C.A., Colantonio, L.D., Bowling, C.B., Shimbo, D., Reynolds, K., Safford, M.M., Banach, M., Toth, P.P., & Muntner, P. (2017). Blood Pressure, Antihypertensive Polypharmacy, Frailty, and Risk for Serious Fall Injuries Among Older Treated Adults With Hypertension. *Hypertension*, 70(2), 259-266. doi: 10.1161/HYPERTENSIONAHA.116.09390.
- Cadore, E.L., Rodríguez-Mañas, L., Sinclair, A., & Izquierdo, M. (2013). Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. *Rejuvenation research*, 16(2), 105-14. doi: 10.1089/rej.2012.1397.
- Chen, L.K., Liu, L.K., Woo, J., Assantachai, P., Auyeung, T.W., Bahyah, K.S., Chou, M.Y., Chen, L.Y., Hsu, P.S., Krairit, O., Lee, J.S., Lee, W.J., Lee, Y., Liang, C.K., Limpawattana, P., Lin, C.S., Peng, L.N., Satake, S., Suzuki, T., Won, C.W., Wu, C.H., Wu, S.N., Zhang, T.,

- Zeng, P., Akishita, M., & Arai, H. (2014). Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *Journal of the American Medical Directors Association*, 15(2), 95-101. doi: 10.1016/j.jamda.2013.11.025.
- Cheng, M.H., & Chang, S.F. (2017). Frailty as a Risk Factor for Falls Among Community Dwelling People: Evidence From a Meta-Analysis. *Journal of nursing scholarship*, 49(5), 529-536. doi: 10.1111/jnu.12322.
- Cree, M., Soskolne, C. L., Belseck, E., Hornig, J., McElhaney, J. E., Brant, R., & Suarez-Almazor, M. (2000). Mortality and institutionalization following hip fracture. *Journal of the American Geriatrics Society*, 48, 283-8.
- Danon-Hersch, N., Rodondi, N., Spagnoli, J., & Santos-Eggimann, B. (2012). Prefrailty and chronic morbidity in the youngest old: an insight from the Lausanne cohort Lc65+. *Journal of the American Geriatrics Society*, 60, 1687-94. doi: 10.1111/j.1532-5415.2012.04113.x.
- Doi, T., Makizako, H., Tsutsumimoto, K., Nakakubo, S., Kim, M.J., Kurita, S., Hotta, R., & Shimada, H. (2018). Transitional status and modifiable risk of frailty in Japanese older adults: A prospective cohort study. *Geriatrics & gerontology international*, 18(11), 1562-1566. doi: 10.1111/ggi.13525.
- Fhon, J.R., Rodrigues, R.A., Neira, W.F., Huayta, V.M., & Robazzi, M.L. (2016). Fall and its association with the frailty syndrome in the elderly: systematic review with meta-analysis. *Revista da Escola de Enfermagem da U S P*, 50(6), 1005-1013. doi: 10.1590/S0080-623420160000700018.
- Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, 12(3), 189-98.
- Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W.J., Burke, G., & McBurnie, M.A.; Cardiovascular Health Study Collaborative Research Group. (2001). Frailty in older adults: evidence for a phenotype. *The journals of gerontology. Series A, Biological sciences and medical sciences*, 56, M146-56.
- Guirguis-Blake, J.M., Michael, Y.L., Perdue, L.A., Coppola, E.L., & Beil, T.L. (2018). Interventions to Prevent Falls in Older Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *Journal of the American Medical Association*, 319(16), 1705-1716. doi: 10.1001/jama.2017.21962.
- Hamacher, D., Törpel, A., Hamacher, D., & Schega, L. (2016). The effect of physical exhaustion on gait stability in young and older individuals. *Gait & posture*, 48, 137-139. doi:

10.1016/j.gaitpost.2016.05.007.

- Iaboni, A., & Flint, A.J. (2013). The complex interplay of depression and falls in older adults: a clinical review. *The American journal of geriatric psychiatry*, 21(5), 484-92. doi: 10.1016/j.jagp.2013.01.008.
- Kojima, G. (2015). Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. *Journal of the American Medical Directors Association*, 16(12), 1027-33. doi: 10.1016/j.jamda.2015.06.018.
- Kojima, G., Iliffe, S., Taniguchi, Y., Shimada, H., Rakugi, H., & Walters, K. (2017). Prevalence of frailty in Japan: A systematic review and meta-analysis. *Journal of epidemiology*, 27(8), 347-353. doi: 10.1016/j.je.2016.09.008.
- Kumahara, H., Schutz, Y., Ayabe, M., Yoshioka, M., Yoshitake, Y., Shindo, M., Ishii, K., & Tanaka, H. (2004). The use of uniaxial accelerometry for the assessment of physical-activity-related energy expenditure: a validation study against whole-body indirect calorimetry. *The British journal of nutrition*, 91(2), 235-43.
- Kvelde, T., Lord, S.R., Close, J.C., Reppermund, S., Kochan, N.A., Sachdev, P., Brodaty, H., & Delbaere, K. (2015). Depressive symptoms increase fall risk in older people, independent of antidepressant use, and reduced executive and physical functioning. *Archives of gerontology and geriatrics*, 60(1):190-5. doi: 10.1016/j.archger.2014.09.003.
- Kvelde, T., McVeigh, C., Toson, B., Greenaway, M., Lord, S.R., Delbaere, K., & Close, J.C. (2013). Depressive symptomatology as a risk factor for falls in older people: systematic review and meta-analysis. *Journal of the American Geriatrics Society*, 61(5), 694-706. doi: 10.1111/jgs.12209.
- Lang, P.O., Michel, J.P., & Zekry, D. (2009). Frailty syndrome: a transitional state in a dynamic process. *Gerontology*, 55(5), 539-49. doi: 10.1159/000211949.
- Lord, S.R., Castell, S., Corcoran, J., Dayhew, J., Matters, B., Shan, A., & Williams, P. (2003). The effect of group exercise on physical functioning and falls in frail older people living in retirement villages: a randomized, controlled trial. *Journal of the American Geriatrics Society*, 51(12), 1685-92.
- Maki, Y., Ura, C., Yamaguchi, T., Murai, T., Isahai, M., Kaiho, A., Yamagami, T., Tanaka, S., Miyamae, F., Sugiyama, M., Awata, S., Takahashi, R., & Yamaguchi, H. (2012). Effects of intervention using a community-based walking program for prevention of mental decline: a randomized controlled trial. *Journal of the American Geriatrics Society*, 60(3), 505-10. doi: 10.1111/j.1532-5415.2011.03838.x.
- Rubenstein, L.Z., & Josephson, K.R. (2002). The epidemiology of falls and syncope. *Clinics in*

geriatric medicine, 18, 141-58.

Tinetti, M.E. (2003). Clinical practice. Preventing falls in elderly persons. *The New England journal of medicine*, 348(1), 42-9.

Umegaki, H., Makino, T., Shimada, H., Hayashi, T., Wu Cheng, X., & Kuzuya, M. (2018). Cognitive Dysfunction in Urban-Community Dwelling Prefrail Older Subjects. *The journal of nutrition, health & aging*, 22(4), 549-554. doi: 10.1007/s12603-018-1017-5.

Umegaki, H., Suzuki, Y., Yanagawa, M., Nonogaki, Z., & Endo, H. (2012). Falls in elderly at high risk of requiring care. *Geriatrics & gerontology international*, 12(1), 147-8. doi: 10.1111/j.1447-0594.2011.00708.x.

Van Damme, A., Declercq, T., Lemey, L., Tandt, H., & Petrovic, M. (2018). Late-life depression: issues for the general practitioner. *International journal of general medicine*, 11, 113-120. doi: 10.2147/IJGM.S154876.

Vaughan, L., Corbin, A.L., & Goveas, J.S. (2015). Depression and frailty in later life: a systematic review. *Clinical interventions in aging*, 10, 1947-58. doi: 10.2147/CIA.S69632

Vermeiren, S., Vella-Azzopardi, R., Beckwée, D., Habbig, A.K., Scafoglieri, A., Jansen, B., & Bautmans, I.; Gerontopole Brussels Study group. (2016). Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *Journal of the American Medical Directors Association*, 17, 1163.e1-1163.e17. doi: 10.1016/j.jamda.2016.09.010.

Whitson, H.E., Thielke, S., Diehr, P., O'Hare, A.M., Chaves, P.H., Zakai, N.A., Arnold, A., Chaudhry, S., Ives, D., & Newman, A.B. (2011). Patterns and predictors of recovery from exhaustion in older adults: the cardiovascular health study. *Journal of the American Geriatrics Society*, 59(2), 207-13. doi: 10.1111/j.1532-5415.2010.03238.x.