THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2018, Vol. 73, No. 2, 261–266
doi:10.1093/gerona/glx097
Advance Access publication June 2, 2017

OXFORD

Research Article

Adverse Childhood Experiences and Higher-Level Functional Limitations Among Older Japanese People: Results From the JAGES Study

Airi Amemiya,[1,2] Takeo Fujiwara,[3] Hiroshi Murayama,[4] Yukako Tani,[3,5] and Katsunori Kondo[6,7]

[1]Department of Social Medicine, National Research Institute for Child Health and Development, Tokyo, Japan. [2]Department of Health Education and Health Sociology, School of Public Health, The University of Tokyo, Japan. [3]Department of Global Health Promotion, Tokyo Medical and Dental University (TMDU), Japan. [4]Institute of Gerontology, The University of Tokyo, Japan. [5]Japan Society for the Promotion of Science, Tokyo, Japan. [6]Center for Preventive Medical Sciences, Chiba University, Japan. [7]Department of Gerontological Evaluation, Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Aichi, Japan.

Address correspondence to: Takeo Fujiwara, MD, PhD, MPH, Department of Global Health Promotion, Tokyo Medical and Dental University (TMDU), 1-5-45 Yushima, Bunkyo-ku, Tokyo 113 - 8510, Japan. E-mail: fujiwara.hlth@tmd.ac.jp

Received: September 11, 2016; Editorial Decision Date: May 13, 2017

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: A life-course perspective is essential in understanding the determinants of higher-level functional limitations. We examine the impact of adverse childhood experiences (ACEs) on higher-level functional limitations in older people.

Methods: Data were from the Japan Gerontological Evaluation Study 2013, a population-based cohort of independent people aged 65 years or older across Japan (n = 19,220). ACEs before the age of 18 were assessed in terms of seven adversities: parental death, parental divorce, parental mental illness, family violence, physical abuse, psychological neglect, and psychological abuse. Associations between the cumulative number of ACEs and higher-level functional limitations were investigated by multivariate Poisson regression with robust error variances, adjusted for age, gender, childhood disadvantage, adult sociodemographics, adult health behaviors, and health status.

Results: Of the older people, 36.3% reported at least one ACE. Older people who had experienced two or more ACEs showed significantly greater higher-level functional limitations than those with no ACE in a crude model (prevalence ratio, PR = 1.61, 95% confidence interval, CI = 1.51–1.71). After adjusting the covariates, this association remained (PR = 1.19, 95% CI = 1.12–1.27).

Conclusions: ACEs showed robust independent effects on higher-level functional limitations among older Japanese without disabilities, even after adjusting for potential covariates in childhood and adulthood. The current findings may help in understanding the impact of the latent effects of ACEs on functional limitations in older people.

Keywords: Childhood disadvantage—Latent effect—Life-course epidemiology

Recently, a life-course perspective, including exposure to major events at an early life stage, has been proposed as an important determinant of disability or higher-level functional limitations, such as socializing and activities that require higher cognitive functions (1–3). Previous studies suggested that low childhood socioeconomic status (SES), assessed by parental education or parental occupation (2), was also a risk factor for disability later in middle life. However, the mechanism(s) by which low childhood SES induces higher-level functional limitations later in life remain(s) unknown.

Adverse childhood experiences (ACEs), including interpersonal loss, family psychopathology, abuse, and neglect (4), are more likely to be observed among children in poverty. Several studies have reported that ACEs are linked with health risk behaviors and diseases, such as cardiovascular disease (5), cancer (6), chronic obstructive pulmonary disease (7), depression (8), obesity (9), and alcohol abuse (8), which are associated with disabilities. ACEs have been suggested as having enduring emotional, immune, and metabolic effects, which may ultimately increase the risks of associated diseases

(10). ACEs have also been associated with poorer verbal retrieval and visual space memory among people aged more than 65 years (11). In terms of disability, Rose et al. reported a dose–response relationship between ACEs and disability (self-reported activity limitations and/or assistive device use) in middle-age adulthood (mean age, 48 years) with adjustment for potentially mediating health conditions (12). These results indicated that ACEs may lead directly to disabilities in later life (a latent effect model (13)). In addition, more recent research has pointed out the importance of investigating factors in young adults that could mitigate the influence of ACEs on older people (14). Thus, increasing awareness of the potential long-term impact of ACEs could be an essential and potentially cost-effective target for avoiding at least some disabilities in older people. However, to our knowledge, the impact of ACEs on higher-level functional limitations in older people has not been reported before.

To explore any associations between ACEs and higher-level functional limitations in older people, we used data from the Japan Gerontological Evaluation Study (JAGES), which evaluated both ACEs and higher-level functional limitations in community-dwelling independent older people, aged 65 years or older, in Japan, some of whom survived World War II (1937–1945) during their early childhoods. Because the period of WWII was associated with ACEs, including severe poverty and parental death (15,16), these data provide a unique opportunity to investigate the impact of ACEs on higher-level functional limitations in older people. Thus, the purpose of this study was to investigate the independent effects of ACEs and higher-level functional limitations; and to explore potential mediation paths, including sociodemographics, adult health behavior, and health status as mediators and childhood disadvantage as a confounder of ACE effects in Japanese older people (Figure 1), referring to the recent life-course model on aging (14).

Methods

Sample

We used data from the JAGES 2013 Project, which was designed to investigate the social determinants of health among noninstitutionalized, functionally independent individuals aged 65 or older. The survey was initially conducted to elucidate the determinants of disability in older people; therefore, older adults with disabilities were not included in the survey. The survey data used were sampled in 2013 from 30 municipalities in 15 prefectures in Japan. Among the 30 municipalities, we sampled the entire population of residents in 14 municipalities, whereas in the remaining 16 municipalities, we mailed questionnaires to a random sample based on public long-term care insurance data acquired from municipal authorities. In total, 193,694 residents were targeted for the questionnaire. Of the eligible participants, 137,736 people responded (response rate = 71.1%). ACEs were investigated in one-fifth of the sample (n = 25,928). We excluded those who did not respond to questions on gender or age. We also excluded those with limitations in activities of daily living, meaning those who could not walk, take a bath, and use the toilet without assistance. Furthermore, to focus on associations between ACEs and higher-level functional limitations, we excluded those who did not respond fully to the 13 questions on functional limitations and ACEs (n = 4,606); thus, our analytic sample consisted of 19,220 individuals.

The JAGES protocol was approved by the Ethics Committee on Research of Human Subjects at Nihon Fukushi University.

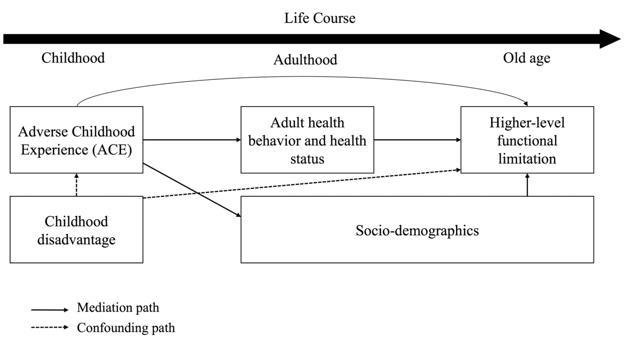

Figure 1. Conceptual model on the association between adverse childhood experience and higher-level functional limitation in life-course model.

Assessing Higher-Level Functional Limitations

Higher-level functional limitations were evaluated using the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC) (17), based on the Lawton instrumental activities of daily living scale (18). This is a 13-item index consisting of three sublevels of competence with yes/no responses (1): instrumental self-maintenance (five items: ability to use public transport, shop for daily necessities, prepare meals, pay bills, and handle a bank account) (2); intellectual activities (four items: ability to fill out forms, read newspapers, read books or magazines, and interest in television programs or news articles dealing with health); and (3) social role (four items: ability to visit the home of friends, give advice to relatives and friends, visit someone in hospital, and initiate conversation with younger people). This scale is used widely to assess higher-level functional capacity in older people in Japan (19). Although a higher TMIG-IC score denotes a higher capacity, we reversed the score so that a higher score denotes a higher functional limitation in our analysis.

Assessing ACEs

The ACE questionnaire was developed based on previous ACE studies (4), modified to suit older Japanese people (20). The respondents were asked whether they had experienced the following adversities before the age of 18 (yes/no responses): interpersonal loss (parental loss, parental divorce), family psychopathology (parental mental illness, family violence), and abuse and neglect (physical abuse, psychological neglect, psychological abuse). The sum of the number of ACEs was categorized as 0, 1, and 2 or more, because the percentage of people who experienced three or more ACE was only 2.0%, which needed to be collapsed.

Covariates

Potential covariates were also assessed with the questionnaire, including age, gender, childhood disadvantage, sociodemographics, and adult health behaviors and health status. Childhood disadvantages were childhood economic hardship (a proxy measure of childhood SES) and adulthood height (a marker of cumulative nutritional and unhygienic exposure during early childhood (21)). Childhood economic hardship was assessed with a question about whether the financial condition during childhood provided difficulties to thriving (yes/no response). Self-reported height was obtained from the questionnaire. People reporting heights above 3 SDs from the mean height (from the 2010 Japanese National Health and Nutrition Survey (22)) were eliminated because they were assumed to be outliers. Furthermore, height was categorized into five groups in 5-cm intervals for men (<155, 155–159.9, 160–164.9, 165–169.9, and ≥170 cm) and women (<145, 145–149.9, 150–154.9, 155–159.9, and ≥160 cm) (3). In terms of adult sociodemographics, SES was assessed by educational attainment (<10 years, 10–12 years, ≥13 years), annual household income (<1.5, 1.5–2.9, 3.0–4.9, ≥5 million yen: 1 million yen is equivalent to 10,000 US$), and employment status (currently working, retired, or never worked). Marital status (married, widowed, divorced/never married/other) and living status (living alone, living with wife/husband, living with other) were also obtained. Health behaviors included smoking (current, quit, never) and drinking (current, quit, never) were investigated. Body mass index was determined from the self-reported height and weight (kg/m^2), then categorized as underweight (<18.5), normal weight (18.5–24.9), and overweight (≥25). Depression was assessed with the Geriatric Depression Scale (GDS) (23), then categorized as no depression (score 0–4), mild depression (score 5–9), and severe depression (score 10–15). The respondents were also questioned as to whether they were currently under medical care. Missing values were treated as dummy variables (24).

Analysis

Multiple Poisson regression analysis with robust error variances was used to examine any associations between ACEs and higher-level functional limitations, treated as count data. In addition to a crude model, Model 1 was adjusted for age and gender and Model 2 was additionally adjusted for childhood disadvantage. Model 3 was adjusted for adult sociodemographics beyond Model 2. Model 4, the final model, was also adjusted for adulthood health behaviors and health status. Further, we conducted mediation analysis to convert higher-level functional limitations into dichotomous (0–1 vs 2 or more) limitations, using a Stata program called "binary_mediation", which allows for multiple mediator variables (25). All statistical analyses were conducted using Stata (ver. 13.1; StataCorp, College Station, TX). The level of statistical significance was set at p <0.05 (two-tailed).

Results

The mean age was 73.2 (standard deviation [*SD*] = 5.9) years old, and 52.9% were women (Table 1). Approximately three quarters (73.5%) were married, and 13.0% were living alone. Regarding adult SES, 36.4% had less than 10 years of education, 12.4% earned less than 1.5 million yen, and 60.8% were retired. Approximately one-third were currently drinking and one-tenth were currently smoking. Most of the participants were receiving medical treatment (78.5%). Regarding the prevalence of each ACE, parental death was the highest (22.1%), followed by psychological neglect (11.6%), and psychological abuse (5.1%). In total, 36.3% reported at least one ACE and 7.4% reported two or more ACEs. Prevalence of ACEs by age cohort showed that the rates of parental death were higher in the age group of 70+ years, who were 2+ years old when World War II ended, compared to the age group of 65–69 years (Supplementary Table S1). On the other hand, the rates of parental divorce and family violence were higher in the 65–69 age group than in the 70+ age group.

Comorbidity of ACEs was also confirmed. For example, 21.2% of those who experienced physical abuse reported any one more additional ACE and 64.4% experienced any two or more additional ACEs (Supplementary Table S2).

Table 2 shows the prevalence ratio (PR) of higher-level functional limitations, according to cumulative numbers of ACEs, using multiple Poisson regression analysis with robust error variance. Regarding higher-level functional limitations, the mean reversed TMIG-IC score was 1.38 (*SD* = 1.82) and the median was 1, similar to other studies (26–28). Overall, the cumulative number of ACEs showed a positive association with higher-level functional limitations; that is, the "dose–response" relationship was statistically significant. For example, the PR of one ACE for higher-level functional limitation was 1.21 (95% confidence interval [CI] = 1.16–1.26) in comparison with no ACE, and the PR of two or more ACEs was 1.61 (95% CI = 1.51–1.71), showing a significant dose–response association (p for trend < 0.001). For two or more ACEs, the significant association remained even after correction for possible confounders. Association of other covariates and higher-level functional limitations can be found in Supplementary Table S3. Childhood economic hardship was also associated with higher-level functional limitations, after adjusting for age and gender (PR = 1.23, 95% CI = 1.18–1.27), and the point estimate was attenuated after adjusting for ACE and adulthood height (PR = 1.16, 95% CI = 1.11–1.20), suggesting that ACE and adulthood height (as a marker of cumulative nutritional and unhygienic exposure during early childhood) mediated the association between childhood economic hardship and higher-level functional limitations in older people.

Mediation analysis revealed that adult sociodemographics (marital status, living status, education, annual income, employment status), adult health behaviors (drinking, smoking), and health status (body mass index, depression, and disease status) mediated the association between ACEs and higher-level functional limitations by 66.1% (95% CI: 54.8%–77.5%), after adjustment of confounders (i.e., age, gender, childhood economic hardship, adult height). Thus, a significant portion of the association between ACEs and higher-level functional limitations was mediated by adult sociodemographics, health behaviors, and health status; however, independent effects exist, as hypothesized in Figure 1.

Regarding the three sublevels of competence (instrumental-self maintenance, intellectual activities, social role), the "dose–response" relationship between the cumulative number of ACEs was also statistically significant with all three sublevels of competence of the TMIG-IC (Supplementary Table S4).

The PR for higher-level functional limitations according to cumulative numbers of ACE stratified by age group and stratified by sex are shown in Supplementary Tables S5 and S6, respectively. There was no statistically significant interaction between the cumulative number of ACEs and age or between ACEs and gender.

Discussion

In this large population-based study, the cumulative number of ACEs was significantly associated with higher-level functional limitations in older people without ADL limitations. Childhood disadvantage, adult sociodemographics, and adult health behaviors and health status attenuated the impact of ACEs on higher-level functional limitations. Generally, significant associations remained after adjustment for confounders and mediators, suggesting an independent effect of ACEs in older age (13).

Possible pathways include the following. First, ACE may harmfully affect the development of cognitive function during childhood, known to be a sensitive period. Danese and McEwen reported that those who with a history of ACEs showed smaller volumes of the prefrontal cortex and hippocampus in adulthood, suggesting that ACEs caused enduring changes in the nervous system (29). The prefrontal cortex plays important roles in cognitive control and the hippocampus has a specific role in the storage and recall of memory

Table 1. Characteristics of Sample (*n* = 19,220)

Characteristics	Total *N*	%
Demographics		
Age		
65–69 years old	6,138	31.9
70–74 years old	6,063	31.6
75–79 years old	3,959	20.6
80+ years old	3,060	15.9
Gender		
Men	9,060	47.1
Childhood disadvantage		
Economic hardship	8,617	44.8
Adulthood height		
Short	1,536	8.0
Middle-short	4,009	20.9
Middle	6,508	33.9
Middle-tall	4,760	24.8
Tall	2,407	12.5
Adult sociodemographics		
Education		
<10 years	7,000	36.4
10–12 years	7,638	39.7
13+ years	4,348	22.6
Missing	234	1.2
Annual income		
<1.5 million	2,382	12.4
1.5–2.9 million	6,078	31.6
3.0–4.9 million	4,705	24.5
5.0+ million	3,934	20.5
Missing	2,121	11.0
Employment status		
Current	4,624	24.1
Retirement	11,684	60.8
Never	2,037	10.6
Missing	875	4.6
Marital status		
Married	14,135	73.5
Widow	3,683	19.2
Divorce/never married/other	1,191	6.2
Missing	211	1.1
Living status		
Living alone	2,497	13.0
Living with wife/husband	15,805	82.2
Living with other	238	1.2
Missing	680	3.5
Health behaviors		
Drinking		
Current	6,969	36.3
Quit	896	4.7
Never	11,261	58.6
Missing	94	0.5
Smoking		
Current	1,973	10.3
Quit	3,077	16.0
Never	14,055	73.1
Missing	115	0.6
Health status		
BMI		
<18.5	1,338	7.0
18.5–24.9	13,703	71.3
25.0+	4,179	21.7
GDS		
0–4	12,918	67.2
5–9	3,073	16.0
10+	852	4.4
Missing	2,377	12.4
Disease status, currently in treatment	15,086	78.5
Retrospectively reported adverse childhood experience (ACE)		
Interpersonal loss		
Parental death	4,245	22.1
Parental divorce	378	2.0
Family psychopathology		
Parental mental illness	138	0.7
Family violence	717	3.7
Abuse and neglect		
Physical abuse	222	1.2
Psychological neglect	2,233	11.6
Psychological abuse	980	5.1
ACE total score		
0	12,248	63.7
1	5,556	28.9
2+	1,416	7.4

Note: ACE = adverse childhood experience; BMI = body mass index; GDS = Geriatric Depression Scale.

sequences in context. These cognitive functions are important for higher-level functional limitations; thus, ACEs may lead to higher-level functional limitations in older people.

Alternatively, a pathway effect may explain the association (13,30). That is, ACEs may increase the risk of a low adult SES, which is associated with poor health behavior (such as smoking and heavy drinking) and disease status (such as cardiovascular disease), which may all be associated with higher-level functional limitations (a pathway model). In our study, the effects of ACEs on higher-level functional limitations were attenuated by adding adult sociodemographics, health behaviors, and health status, suggesting that low adult SES, poor health behaviors, and health status are possible leading causes of higher-level functional limitations in older people.

Consistent with results of previous studies investigating associations between childhood SES and disabilities in older people (1–3), we found that childhood economic hardship and adulthood height (as a marker of cumulative social and environmental exposures during early childhood) were important factors for higher-level functional limitations. A reason may be that poverty exposes children to the risk of low birthweight (31) and poor nutrition (32), and more harmful health risks, such as environmental pollutants and second hand smoke (33), which are all associated with cognitive function (34–37), which are important for higher-level functional capacity in older people. We add to the literature that the association between childhood SES and high-level functional limitations in older people may be explained by ACEs, because we observed that the point estimate of PR of childhood economic hardship for high-level functional limitation was attenuated after adjusting for ACEs (from 1.23 to 1.16). These results were consistent with a previous study showing that the impact of low childhood SES on mental disorders can be explained by ACEs (38). Moreover, to our knowledge, this is the first study to investigate the association between ACEs and higher-level functional capacity in older people.

The present study has several limitations. First, the retrospective assessment of ACEs may induce recall bias, which can be expected to occur within an older age cohort. However, the prevalence of psychological neglect, for example, was similar across each age cohort, and the

Table 2. Prevalence Ratio (95% Confidential Interval) of ACE for Higher-Level Functional Limitation

Number of ACE	Reversed TIMG-IC (mean ± *SD*)	Crude		Model 1 (adjusted age, sex)		Model 2 (model 1 + childhood disadvantage)		Model 3 (Model 2 + adult sociodemographics)		Model 4 (Model 3 + adult health behavior and health status)	
		PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
0	(1.25 ± 1.70)	Ref.		Ref.		Ref.		Ref.		Ref.	
1	(2.50 ± 1.92)	1.21	1.16–1.26	1.17	1.12–1.22	1.13	1.09–1.18	1.09	1.05–1.14	1.06	1.02–1.10
2+	(2.00 ± 2.22)	1.61	1.51–1.71	1.55	1.46–1.65	1.46	1.37–1.55	1.34	1.26–1.43	1.19	1.12–1.27

Note: ACE = adverse childhood experience; BMI = body mass index; CI = confidence interval; GDS = Geriatric Depression Scale; PR = prevalence ratio; Ref = reference; *SD* = standard deviation; TIMG-IC = Tokyo Metropolitan Institute of Gerontology Index of Competence.

prevalence of parental death was higher among the older age cohort. This is reasonable to expect, as parents of the people in this cohort were more likely to have participated in World War II, suggesting that recall bias may have no significant fault. In addition, there is evidence that severe abuse is often remembered well and that false-positive reports are probably rare, whereas less severe adversities are more likely to be under reported (39). Thus, the association may be underestimated, but is less likely to be overestimated. Second, we assessed seven categories of ACE, each via a single item. Thus, other ACEs, such as sexual abuse and parental substance abuse, were not included, because of the feasibility according to the municipalities. However, childhood sexual abuse and parental substance abuse are rare in Japan (40). Third, there is a common method bias because all measures were assessed by a single self-reported questionnaire. Reuben et al. reported that as compared to prospective ACE studies, retrospective ACE studies showed stronger associations with subjectively assessed outcomes, that is, our results might have overestimated the association (41). Fourth, poor childhood health may also affect a variety of health outcomes, but these were not assessed, and we were unable to examine any effects on functional limitations. Fifth, because we used data from the JAGES study, in which the participants were healthy enough to participate in the survey, surviving bias could result in an underestimation of the association between ACEs and higher-level functional limitations among older people. Finally, our analytical sample excluded people who have a disability, so the generalizability of the findings may not be extended to those with disabilities.

In conclusion, our findings provide evidence for an independent effect of ACEs on higher-level functional limitations among older people in Japan. In addition to interventions aimed at improving health behaviors in adulthood, policies aimed at reducing ACEs may help decrease demand for medical and social care services associated with functional limitations in old age.

Supplementary Material

Supplementary data is available at *Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This study used data from the Japan Gerontological Evaluation Study (JAGES), which was supported by Japan Society for the Promotion of Science (JSPS) KAKENHI grant numbers (JP15H01972, JP20319338, JP22390400, JP23243070, JP23590786, JP23790710, JP24140701, JP24390469, JP24530698, JP24653150, JP24683018, JP25253052, JP25870573, JP25870881, JP26882010), Health Labour Sciences Research Grants (H28-Choju-Ippan-002, H26-Choju-Ippan-006, H 25-Choju-Ippan-003, H25-Kenki-Wakate-015, H25-Irryo-Shitei-003[Fukkou], H24-Junkanki[Seishu]-Ippan-007), the Research and Development Grants for Longevity Science from Japan Agency for Medical Research and development (AMED), the Research Funding for Longevity Sciences from National Center for Geriatrics and Gerontology (24-17, 24-23) , and Japan Foundation for Aging And Health (J09KF00804).

Conflict of Interest

The authors have no conflict of interest directly relevant to the content of this article.

References

1. Weinstein MR. The concept of the disability process. *Psychosomatics*. 1978;19:94–97. doi:10.1016/S0033-3182(78)71019-4

2. Bowen ME. Childhood socioeconomic status and racial differences in disability: evidence from the Health and Retirement Study (1998–2006). *Soc Sci Med*. 2009;69:433–441. doi:10.1016/j.socscimed.2009.06.006
3. Fujiwara T, Kondo K, Shirai K, Suzuki K, Kawachi I. Associations of childhood socioeconomic status and adulthood height with functional limitations among Japanese older people: results from the JAGES 2010 Project. *J Gerontol A Biol Sci Med Sci*. 2014;69:852–859. doi:10.1093/gerona/glt189
4. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med*. 1998;14:245–258.
5. Dong M, Giles WH, Felitti VJ, et al. Insights into causal pathways for ischemic heart disease: adverse childhood experiences study. *Circulation*. 2004;110:1761–1766. doi:10.1161/01.CIR.0000143074.54995.7F
6. Brown DW, Anda RF, Felitti VJ, et al. Adverse childhood experiences are associated with the risk of lung cancer: a prospective cohort study. *BMC Public Health*. 2010;10:20. doi:10.1186/1471-2458-10-20
7. Anda RF, Brown DW, Dube SR, Bremner JD, Felitti VJ, Giles WH. Adverse childhood experiences and chronic obstructive pulmonary disease in adults. *Am J Prev Med*. 2008;34:396–403. doi:10.1016/j.amepre.2008.02.002
8. Anda RF, Whitfield CL, Felitti VJ, et al. Adverse childhood experiences, alcoholic parents, and later risk of alcoholism and depression. *Psychiatr Serv*. 2002;53:1001–1009. doi:10.1176/appi.ps.53.8.1001
9. Gustafson TB, Sarwer DB. Childhood sexual abuse and obesity. *Obes Rev*. 2004;5:129–135. doi:10.1111/j.1467-789X.2004.00145.x
10. Danese A, Moffitt TE, Harrington H, et al. Adverse childhood experiences and adult risk factors for age-related disease: depression, inflammation, and clustering of metabolic risk markers. *Arch Pediatr Adolesc Med*. 2009;163:1135–1143. doi:10.1001/archpediatrics.2009.214
11. Ritchie K, Jaussent I, Stewart R, et al. Adverse childhood environment and late-life cognitive functioning. *Int J Geriatr Psychiatry*. 2011;26:503–510. doi:10.1002/gps.2553
12. Schüssler-Fiorenza Rose SM, Xie D, Stineman M. Adverse childhood experiences and disability in U.S. adults. *PMR*. 2014;6:670–680. doi:10.1016/j.pmrj.2014.01.013
13. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;31:285–293.
14. Moffitt TE, Belsky DW, Danese A, Poulton R, Caspi A. The longitudinal study of aging in human young adults: knowledge gaps and research agenda. *J Gerontol A Biol Sci Med Sci*. 2017;72:210–215. doi:10.1093/gerona/glw191
15. Cornia GA, Danziger S. *Child Poverty and Deprivation in the Industrialized Countries, l945-1995*. New York: Oxford University Press; 1997.
16. Tsurumi K. *Social Change and the Individual: Japan Before and After Defeat in World War II*. Princeton, NJ: Princeton University Press; 2015.
17. Koyano W, Shibata H, Nakazato K, Haga H, Suyama Y. Measurement of competence: reliability and validity of the TMIG Index of Competence. *Arch Gerontol Geriatr*. 1991;13:103–116.
18. Lawton M, Brody E. Instrumental Activities of Daily Living (IADL) Scale. Original observer-rated version. “Does do” form--for women only. *Psychopharmacol Bull*. 1988;24:785–787.
19. Moriya S, Tei K, Miura H, Inoue N, Yokoyama T. Associations between higher-level competence and general intelligence in community-dwelling older adults. *Aging Ment Health*. 2013;17:242–249. doi:10.1080/13607863.2012.717256
20. Matsuyama Y, Fujiwara T, Aida J, et al. Experience of childhood abuse and later number of remaining teeth in older Japanese: a life-course study from Japan Gerontological Evaluation Study project. *Community Dent Oral Epidemiol*. 2016;44:531–539. doi:10.1111/cdoe.12246
21. Silventoinen K. Determinants of variation in adult body height. *J Biosoc Sci*. 2003;35:263–285.
22. Ministry of Health Labor and Welfare. *National Health and Nutrition Survey in Japan*. Tokyo, Japan: Ministry of Health, Labor and Welfare; 2015.
23. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1982;17:37–49.
24. Capistrant BD, Moon JR, Berkman LF, Glymour MM. Current and long-term spousal caregiving and onset of cardiovascular disease. *J Epidemiol Community Health*. 2012;66:951–956. doi:10.1136/jech-2011-200040
25. Kenny DA. *Mediation with dichotomous outcomes*. 2013. davidakenny.net/doc/dichmed.pdf. Accessed March 16, 2017.
26. Wada T, Ishine M, Sakagami T, et al. Depression, activities of daily living, and quality of life of community-dwelling elderly in three Asian countries: Indonesia, Vietnam, and Japan. *Arch Gerontol Geriatr*. 2005;41:271–280. doi:10.1016/j.archger.2005.03.003
27. Kondo N, Minai J, Imai H, Yamagata Z. Engagement in a cohesive group and higher-level functional capacity in older adults in Japan: a case of the Mujin. *Soc Sci Med*. 2007;64:2311–2323. doi:10.1016/j.socscimed.2007.02.009
28. Fukukawa Y, Nakashima C, Tsuboi S, et al. The impact of health problems on depression and activities in middle-aged and older adults: age and social interactions as moderators. *J Gerontol B Psychol Sci Soc Sci*. 2004;59:P19–P26.
29. Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiol Behav*. 2012;106:29–39. doi:10.1016/j.physbeh.2011.08.019
30. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. *J Epidemiol Community Health*. 2003;57:778–783.
31. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R. Choosing area based socioeconomic measures to monitor social inequalities in low birth weight and childhood lead poisoning: the Public Health Disparities Geocoding Project (US). *J Epidemiol Community Health*. 2003;57:186–199.
32. Black RE, Victora CG, Walker SP, et al.; Maternal and Child Nutrition Study Group. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet*. 2013;382:427–451. doi:10.1016/S0140-6736(13)60937-X
33. Evans GW. The environment of childhood poverty. *Am Psychol*. 2004;59:77–92. doi:10.1037/0003-066X.59.2.77
34. Ment LR, Vohr B, Allan W, et al. Change in cognitive function over time in very low-birth-weight infants. *JAMA*. 2003;289:705–711.
35. Abbott RD, White LR, Ross GW, et al. Height as a marker of childhood development and late-life cognitive function: the Honolulu-Asia Aging Study. *Pediatrics*. 1998;102:602–609.
36. Power MC, Weisskopf MG, Alexeeff SE, Coull BA, Spiro A 3rd, Schwartz J. Traffic-related air pollution and cognitive function in a cohort of older men. *Environ Health Perspect*. 2011;119:682–687. doi:10.1289/ehp.1002767
37. Llewellyn DJ, Lang IA, Langa KM, Naughton F, Matthews FE. Exposure to secondhand smoke and cognitive impairment in non-smokers: national cross sectional study with cotinine measurement. *BMJ*. 2009;338:b462. doi:10.1136/bmj.b462
38. McLaughlin KA, Breslau J, Green JG, et al. Childhood socio-economic status and the onset, persistence, and severity of DSM-IV mental disorders in a US national sample. *Soc Sci Med*. 2011;73:1088–1096. doi:10.1016/j.socscimed.2011.06.011
39. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry*. 2004;45:260–273.
40. Fujiwara T, Kawakami N. Association of childhood adversities with the first onset of mental disorders in Japan: results from the World Mental Health Japan, 2002–2004. *J Psychiatr Res*. 2011;45:481–487. doi:10.1016/j.jpsychires.2010.08.002
41. Reuben A, Moffitt TE, Caspi A, et al. Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *J Child Psychol Psychiatry*. 2016;57:1103–1112. doi:10.1111/jcpp.12621