Original research

Executive dysfunction and risk of suicide in older adults: a population-based prospective cohort study

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ABSTRACT

Objective It is uncertain what factors increases the risk of suicide in older adults without depression, and it is unknown whether executive dysfunction (ED) is one of those factors. We aimed to examine the effect of ED on the risk of suicide in non-demented older adults without depression.

Methods In an ongoing population-based prospective cohort of Korean older adults, we identified suicide using the National Mortality Database and suicidal ideation or attempt (SIA) based on the Korean version of the Mini International Neuropsychiatric Interview. We defined ED as performing below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of following tests: Frontal Assessment Battery, Trail Making Test A, Digit Span Test or Verbal Fluency Test.

Results The mean age of the 4791 participants at baseline was 69.7 (SD 6.4) years, and 57.1% of them were women (mean follow-up duration=4.9 years). ED at baseline increased the risk of suicide by about seven times (HR 7.20, 95% CI 1.84 to 28.12, p=0.005) but did not change the risk of SIA. However, cognitive impairment without ED did not change the risks of suicide and SIA. In participants with ED, being aged 75 years or above, living alone, and having a low socioeconomic status were associated with the risk of suicide.

Conclusion ED is a strong risk factor of late life suicide independent from depression, particularly in very old adults living in disadvantaged environments.

INTRODUCTION

With advancing age, suicide rate increases[1] and suicide attempts become more lethal.[2] Although depression is a well-established risk factor of suicide in older adults,[3] more than 80% of older adults who died by suicide did not have depressive disorders before they died by suicide.[2] However, it is not yet known what factors other than depression raise the risk of suicide among the elderly.

In older adults with depressive disorders, executive dysfunction (ED) was found to increase the risk of suicidal ideation or attempt (SIA),[4] although it has never been investigated whether ED may increase the risk of suicide per se. In many robust case–control studies, older adults with depressive disorder who had SIA consistently showed more impairments in executive functions such as decision making, problem solving, cognitive inhibition and delayed reward discounting than those who did not have SIA.[5–13] In a prospective cohort study, marked ED predicted suicide attempts and emergency psychiatric admissions within 3 years in older adults with major depressive disorder.[14]

If ED increases the risk of suicide by prohibiting adaptive and flexible coping of the difficult demands of contextual and vulnerable factors, it may also increase the risk of suicide in older adults without depressive disorders, particularly in those under disadvantaged environments. ED is also common in older adults without depressive disorders and increases with advancing age.[15] However, it has never been investigated whether ED may increase the risks of SIA or suicide in older adults without depressive disorders, probably because suicide itself is a rare outcome in community settings.[16]In addition, the effect of ED on suicide may be different from that on SIA because the epidemiological characteristics differ between older adults with SIA and those who died by suicide.[2]

In this nationwide, population-based prospective cohort study, we examined the effects of ED on the risks of suicide and SIA in non-demented older adults without depressive disorders.

METHODS

Study design, setting and participants

We acquired data from the Korean Longitudinal Study on Cognitive Aging and Dementia (KLOSCAD), an ongoing nationwide prospective cohort study.[17] In the KLOSCAD, 6818 community-dwelling Koreans aged 60 years or above were randomly sampled from the residents of 13 districts across South Korea using the national residential roster at the end of 2009. The baseline assessment was conducted from November 2010 to October 2012, and follow-up assessments have been conducted every 2 years (the first follow-up assessment was from November 2012 to October 2014, the second follow-up assessment was from November 2014 to October 2016, and the third follow-up assessment was from November 2016 to October 2018). Since the fourth follow-up assessment is underway (from November 2018 to October 2020), we included the data from the baseline assessment to the third follow-up assessment in the current study. We included 4791 participants

after excluding those who had dementia (n=343), major depressive disorder (n=116), other neurological or major psychiatric disorders (n=101) or a history of SIA (n=78) at the baseline assessment and those who did not respond to all follow-up assessments.

All participants were fully informed about the study protocol and provided written informed consent.

Assessments

Geriatric psychiatrists performed a face-to-face standardised diagnostic interview and physical and neurological examinations to all participants using the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-K) Assessment Packet Clinical Assessment Battery[18] and the Mini International Neuropsychiatric Interview (MINI-K).[19 20]

Neuropsychological researchers or trained research nurses administered a comprehensive neuropsychological battery that included the Korean version of the CERAD Neuropsychological Assessment Battery (CERAD-K-N),[18 21] Digit Span Test Forward and Backward (DST-F and DST-B)[22] and Frontal Assessment Battery (FAB).[23] The CERAD-K-N consists of nine subtests: Mini Mental Status Examination, Trail Making Test A (TMT-A), Verbal Fluency Test (VFT), 15-item Boston Naming Test (BNT-15), Word List Memory Test (WLMT), Word List Recall Test (WLRT), Word List Recognition Test (WLRcT), Constructional Praxis Test (CPT) and Constructional Recall Test (CRT).

Trained research nurses administered the Medical Outcome Study Social Support Survey (MOS-SSS) to evaluate the level of social support,[24 25] the Cumulative Illness Rating Scale (CIRS) to evaluate the burden of comorbidities,[26] and the Geriatric Depression Scale (GDS) to evaluate the level of depressive symptoms.[27] Additionally, they calculated the metabolic equivalent task (MET) to evaluate participants' exercise level.[28]

Researchers also administered comprehensive laboratory tests including complete blood cell counts, chemistry panels, serologic test for screening syphilis, serum levels of folate and vitamin B_{12}, thyroid function test and apolipoprotein E genotyping.

Diagnosis and ascertainment of SIA and suicide

A panel of geriatric psychiatrists confirmed the diagnosis of dementia and major psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria.[29] We defined cognitive impairment as performing below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in one or more tests among FAB, TMT-A, DST-F, DST-B, VFT, WLMT, WLRT, WLRcT, CRT, CPT or BNT-15, and ED as performing below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in one or more tests among FAB, TMT-A, DST-F, DST-B or VFT. We defined poor social support as having an MOS-SSS score of below the 25th percentile among the participants,[24 25] a high burden of comorbidities as having a CIRS of 5 points or higher[26] and a low socioeconomic status (SES) as being covered by the National Medicaid Programme. We categorised exercise into three levels using MET: below 600 min/week as low, 600–3000 min/week as moderate and 3000 min/week or over as high.[28]

We ascertained death by suicide using the National Mortality Database (NMD). All deaths in Korea, which have to be reported to the local governments, are registered into the NMD, which is operated by the Statistics Korea. The NMD has the date and the cause of all deaths in Korea confirmed by a physician. We gathered death data for the follow-up period of 7 years based on the longest observation period from the baseline assessment to the third follow-up assessment. We ascertained the presence of SIA using the single question from the MINI-K, 'Did you repeatedly think about death or have any thoughts of killing yourself, or have any intent or plan to kill yourself? Did you attempt suicide?'[19 20] We categorised suicide-related outcomes into four levels: (1) participants who did not report SIA at all follow-up assessments while they were alive during the follow-up period (non-suicidal control), (2) participants who did not respond to one or more follow-up assessments but were alive during the follow-up period and did not report SIA at the follow-up assessment to which they responded (uncertain SIA; USIA), (3) participants who reported SIA at one or more follow-up assessments but did not die by suicide or were alive during the follow-up period (confirmed SIA; CSIA) and (4) participants who passed away due to suicide.

Statistical analysis

We compared the categorical variables using Pearson's chi-square tests and continuous variables using Student's t-tests between groups. We analysed the effects of baseline cognitive impairments on the risk of incident suicide-related outcomes using Cox proportional hazard analyses adjusted for age, sex, education level, SES, cohabitant, social support, alcohol drinking, exercise, comorbidities and GDS score. Additionally, we analysed the association between the number of neuropsychological tests with poor performances and the risk of suicide-related outcomes, and also analysed the association between each neuropsychological test for ED and that risk using Cox proportional hazard analyses. We performed Kaplan-Meier analysis and log-rank tests to estimate the cumulative suicide-free survivals by the presence of cognitive impairments. To analyse the factors associated with the risk of suicide within the participants with ED, we performed multivariate Cox proportional hazard analyses.

All statistical analyses were performed using IBM SPSS Statistics, V.19.0 (IBM).

RESULTS

Among 4791 participants (mean age, 69.7±6.4 years; women, 57.1%), 143 (3.0%) had incident CSIA and 15 (0.3%) died due to suicide. The incidence rates of SIA and suicide were 606.0 and 63.6 per 100 000 persons per year, respectively. Their mean duration of follow-up was 4.9±1.5 years. While the current study was being conducted, the annual suicide rate of Koreans aged 60 years or above had steadily reduced from 70.9 per 100 000 persons in 2010 to 43.6 per 100 000 persons in 2018.[30]

As summarised in table 1, participants with cognitive impairment were more depressive, older and more likely to be men, and they exercised less than those with normal cognition. Among the 2136 participants with cognitive impairments at baseline, 73 (3.4%) reported CSIA and 12 (0.6%) died due to suicide during the follow-up period. Participants with cognitive impairments showed slightly higher rates of CSIA and USIA than those with normal cognition (3.4% vs 2.6%, p=0.058 for CSIA; 36.8% vs 34.1%, p=0.021 for USIA). Although suicide was far less common than SIA in both participants with cognitive impairments and those without cognitive impairments, those with cognitive impairments showed a substantially higher rate of suicide than did those with normal cognition (0.6% vs 0.1%, p=0.004). In the Cox proportional hazard models, baseline cognitive impairment was found to increase future risk of suicide by about five times, but not the risk of CSIA, during the 7-year follow-up period (table 2). Cognitive impairments in multiple neuropsychological tests increased risk of suicide 5.4-fold higher

Table 1 Baseline characteristics of the participants

	Normal cognition[a]	Cognitive impairment			Statistics		
	(n=2655)	All[b] (n=2136)	With ED[c] (n=1185)	Without ED[d] (n=951)	P value*	P value†	Post hoc†
Age, years, mean (SD)	68.6 (5.9)	71.0 (6.6)	71.4 (6.6)	70.6 (6.5)	<0.001	<0.001	c>d > a
Men, n (%)	1192 (44.9)	864 (40.4)	453 (38.2)	411 (43.2)	0.002	0.001	c<a, d
Suicide-related outcomes					<0.001	0.001	
USIA, n (%)	906 (34.1)	787 (36.8)	447 (37.7)	340 (35.8)			c>a
CSIA, n (%)	70 (2.6)	73 (3.4)	34 (2.9)	39 (4.1)			d>a
Suicide, n (%)	3 (0.1)	12 (0.6)	9 (0.8)	3 (0.3)			c>a
GDS score, mean (SD)	8.6 (5.8)	10.1 (6.3)	10.5 (6.4)	9.6 (6.1)	<0.001	<0.001	c>d > a
Low education, n (%)‡	1075 (40.5)	1130 (52.9)	658 (55.5)	472 (49.6)	<0.001	<0.001	c>d > a
Low SES, n (%)§	72 (2.7)	120 (5.6)	76 (6.4)	44 (4.6)	<0.001	<0.001	c, d>a
Living alone, n (%)	324 (12.2)	342 (16.0)	198 (16.7)	144 (15.1)	<0.001	<0.001	c, d>a
Poor social support, n (%)¶	522 (20.1)	498 (24.2)	296 (26.0)	202 (21.9)	0.001	<0.001	c>a, d
Current drinking, n (%)**	377 (14.3)	247 (11.7)	132 (11.3)	115 (12.2)	0.007	0.022	c<a
Low exercise, n (%)††	1125 (42.9)	1122 (53.1)	647 (55.2)	475 (50.5)	<0.001	<0.001	c>d > a
High comorbidities, n (%)‡‡	1065 (40.7)	976 (46.2)	552 (47.1)	424 (45.1)	<0.001	<0.001	c, d>a

[b]Performed below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of following neuropsychological tests; Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward, Verbal Fluency Test, Word List Memory Test, Word List Recall Test, Word List Recognition Test, Constructional Praxis Test, Constructional Recall Test or 15-item Boston Naming Test
[c]Performed below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of following neuropsychological tests; Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward or Verbal Fluency Test
[d]Performed below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of Word List Memory Test, Word List Recall Test, Word List Recognition Test, Constructional Praxis Test, Constructional Recall Test or 15-item Boston Naming Test but performed −1.5 SD or above of age-adjusted, gender-adjusted and education-adjusted norms in all of Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward and Verbal Fluency Test
*Comparisons between normal cognition group and cognitive impairment group using χ^2 test for categorical variables and Student's t-test for continuous variables
†Comparisons between normal cognition group, cognitive impairment with ED group and cognitive impairment without ED group using χ^2 test for categorical variables and analysis of variance for continuous variables with Bonferroni post hoc comparisons
‡Formally educated 6 years or less
§Covered by the National Medicaid Programme
¶Medical Outcomes Study Social Support Survey scores under 25 percentiles
**Drinking above 7 standard units per week within the past 1 year
††Under 600 metabolic equivalent task minutes per week
‡‡The Cumulative Illness Rating Scale total scores of 5 points or higher
CSIA, confirmed suicidal ideation or attempt but did not die in suicide; ED, executive dysfunction; GDS, Geriatric Depression Scale; SES, socioeconomic status; USIA, uncertain suicidal ideation or attempt.

than normal cognition, whereas the impairment in only one test did not increase that risk significantly (online supplemental table 1).

Among the 2136 participants with cognitive impairments at baseline, 1185 (55.5%) had ED. Compared with participants with normal cognition, those with ED showed higher rates of suicide (0.8% vs 0.1%, p=0.001) but comparable rates of CSIA (2.9% vs 2.6%, p=0.459). In contrast, participants with cognitive impairment but no ED showed higher rates of CSIA (4.1% vs 2.6%, p=0.015) but comparable rates of suicide to those with normal cognition (0.3% vs 0.1%, p=0.166). In the Cox proportional hazard models, baseline cognitive impairment with ED was found to increase the risk of suicide by about seven times during the 7-year follow-up period. However, baseline cognitive impairment without ED did not significantly increase the risk of suicide. Baseline cognitive impairment did not increase the risk of CSIA regardless of the presence of ED (table 2). Compared with the normal cognition, cognitive impairments with ED in multiple neuropsychological tests and only one test demonstrated 7.8-fold and 4.3-fold higher risk of suicide, respectively (online supplemental table 1). In particular, poor performances in TMT-A, DST-F, and VFT increased the risk of suicide which implies that impairments in attention, working memory, and psychomotor speed were significantly associated with suicide risk (online supplemental table 2).

As shown in figure 1, participants with ED showed lower rates of suicide-free survival than did those with normal cognition (log-rank test=11.49, p=0.001) while participants with cognitive impairment but no ED showed comparable survival rates to those with normal cognition (log-rank test=1.86, p=0.172). In participants with ED, nine died by suicide within 3.5±2.1 years from the baseline assessment and 2 of them died by suicide within 2 years before the first follow-up assessment. Among the seven participants who died by suicide but survived 2 years or longer from the baseline assessment, two responded to one or more follow-up assessments and showed ED in their final follow-up assessments. Among the participants with cognitive impairment but no ED, three died by suicide within 4.8±0.4 years from the baseline assessment. Two of them responded to one or more follow-up assessments and showed ED in their

Table 2 Effects of cognitive impairment on the risks of incident suicidal ideation or attempt and suicide*

	USIA		CSIA		Suicide	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Normal cognition	1 (reference)		1 (reference)		1 (reference)	
Cognitive impairment†	1.08 (0.98 to 1.20)	0.115	1.00 (0.70 to 1.41)	0.978	4.89 (1.31 to 18.32)	0.018
Cognitive impairment without ED‡	1.06 (0.93 to 1.20)	0.419	1.32 (0.88 to 1.98)	0.180	2.10 (0.34 to 12.90)	0.423
Cognitive impairment with ED§	1.11 (0.98 to 1.25)	0.089	0.76 (0.49 to 1.17)	0.216	7.20 (1.84 to 28.12)	0.005

*Cox hazard regression analyses adjusted for age, sex, education level, socioeconomic status, cohabitant, social support, alcohol drinking, exercise, comorbidities and Geriatric Depression Scale score
†Performed below −1·5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of neuropsychological tests as follows; Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward, Verbal Fluency Test, Word List Memory Test, Word List Recall Test, Word List Recognition Test, Constructional Praxis Test, Constructional Recall Test and 15-item Boston Naming Test
‡Performed below −1.5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of Word List Memory Test, Word List Recall Test, Word List Recognition Test, Constructional Praxis Test, Constructional Recall Test or 15-item Boston Naming Test but performed −1·5 SD or above of age-adjusted, gender-adjusted and education-adjusted norms in all of Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward and Verbal Fluency Test
§Performed below −1·5 SD of age-adjusted, gender-adjusted and education-adjusted norms in any of following neuropsychological tests; Frontal Assessment Battery, Trail Making Test-A, Digit Span Test-Forward, Digit Span Test-Backward or Verbal Fluency Test
CSIA, confirmed suicidal ideation or attempt but did not die in suicide; ED, executive dysfunction; USIA, uncertain suicidal ideation or attempt.

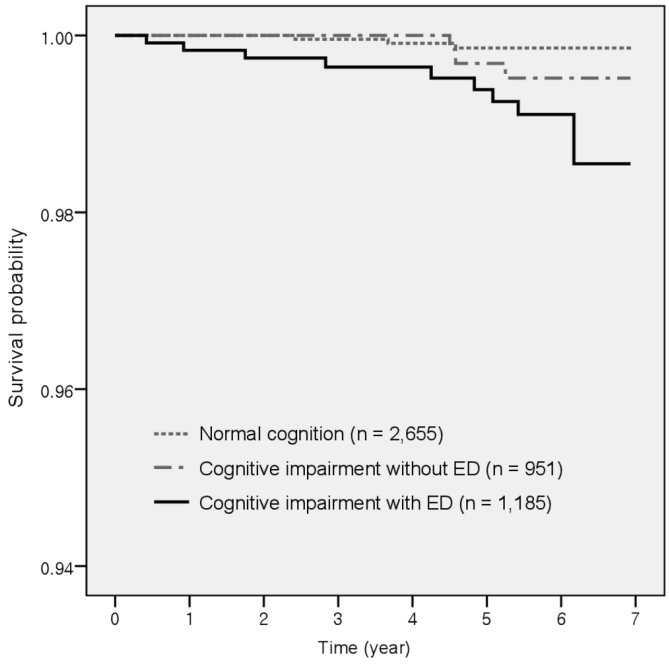

Figure 1 Suicide-free survival according to the cognitive status estimated by Kaplan-Meier survival analysis. ED, executive dysfunction.

final follow-up assessments. Among the participants with normal cognition, three died by suicide within 3.6±1.1 years from the baseline assessment. Two of them responded to one or more follow-up assessments but did not show ED in their final follow-up

In the participants with ED, being aged 75 years or above, low SES, and living alone increased the risk of suicide (table 3). ED was more prevalent in older adults aged 75 years or older than in those aged less than 75 years (33.2% vs 22.2%, p<0.001). Although we could not perform the same analyses in the participants with normal cognition or with cognitive impairment but no ED as we performed in the participants with ED, all participants with normal cognition or with cognitive impairment but no ED who died by suicide did not live alone and their SES was not low.

Table 3 Factors associated with risk of suicide in the older adults with executive dysfunction

	HR (95% CI)*	P value
GDS score	0.98 (0.87 to 1.10)	0.748
Old-old†	10.80 (1.94 to 60.01)	0.007
Men	7.08 (0.78 to 64.45)	0.083
Low education‡	0.79 (0.17 to 3.72)	0.765
Low socioeconomic status§	9.19 (1.76 to 48.05)	0.009
Living alone	11.08 (1.38 to 89.05)	0.024
Poor social support¶	0.15 (0.02 to 1.47)	0.103
Current drinking**	0.94 (0.14 to 6.15)	0.947
Low exercise††	0.50 (0.10 to 2.51)	0.402
High comorbidities‡‡	0.40 (0.09 to 1.80)	0.231

*Multivariate Cox proportional hazard model
†Age of 75 years or above
‡Formally educated 6 years or less
§Covered by the National Medicaid Programme
¶Medical Outcomes Study Social Support Survey scores under 25 percentiles
**Drinking above 7 standard units per week within the past 1 year
††Under 600 metabolic equivalent task minutes per week
‡‡The Cumulative Illness Rating Scale total scores of 5 points or higher assessments.
GDS, Geriatric Depression Scale.

DISCUSSION

This study demonstrated that ED increased the risk of suicide but not the risk of SIA in older adults without dementia or major psychiatric disorders including depressive disorder. To the best of our knowledge, this is the first study on the differential effect of ED on suicide and SIA in older adults without depressive disorders.

In the current study, ED increased the risk of suicide considerably, by about sevenfold, in older adults without dementia or depressive disorder even after adjusting for subthreshold depressive symptoms using GDS scores, indicating that ED may be an independent risk factor of suicide in older adults. Although depression is a well-known risk factor of suicide, only 16.9% of older adults who died by suicide were found to have depressive disorders before they died by suicide.[2] Furthermore, suicide is far more prevalent in older adults compared with younger adults while depressive disorders are less prevalent in older adults compared with younger adults.[31] Therefore, suicide in older adults is likely due to powerful risk factors other than depression. ED is very common in older adults without dementia, regardless of the presence of depressive disorders. ED was found in one thirds of older adults without depressive disorders.[32] Although depressive disorders do not increase with advancing age, ED increases with advancing age.[15] In this study, ED was more prevalent in the very old adults aged 75 years or older compared with the young old adults aged under 75 years, and being very old was associated with the risk of suicide in the older adults with ED. Given that living alone and/or having lower SES were associated with the risk of suicide in older adults with ED, ED may increase the risk of suicide by prohibiting adaptive and flexible coping to these difficult contextual demands.

In Korea, the proportion of adults aged 65 years or older and those aged 75 years or older among the total population are 14.4% and 6.3%, respectively.[30] Among the Korean population aged 65 years or older, 22.5% live alone[33] and 45.7% live in poverty.[34] Globally, among older adults, 11.4%–33.2% live alone and 12.5% live in relative poverty.[33 34] Although ED may be attributable to changes in the frontal-striatal circuit such as frontal white matter lesions and frontal and striatal volume losses,[15 35] it is modifiable through non-pharmacological approaches such as problem-solving therapy and cognitive remediation in older adults without dementia.[36 37] Therefore, ED can be a promising target for the development of prevention strategies against suicide in late life, in particular for older adults living in disadvantaged environments such as living alone or in poverty. Whether an intervention on ED with or without environmental modifications, such as developing social engagements with family members or providing public financial aids, can reduce suicide rates in late life warrants further attention. If these interventions are found to be beneficial for preventing suicide in late life, they should not be delayed, because the mean survival time of older adults with ED was short (3.5 years).

In this study, ED was not associated with the risk of SIA in older adults without depressive disorders. Our observation is in line with those from a few previous studies. In an epidemiologic survey on 1712 randomly sampled, community-dwelling older adults in Israel, passive suicidal ideation was not associated with ED.[38] In a cross-sectional functional neuroimaging study, better-planned suicide attempts were associated with deactivation of the lateral prefrontal cortex in response to value difference favouring the immediate option, indicating that impaired decision processes may be involved in both impulsive and premeditated suicidal behaviours.[39] Although SIA has been reported to be

associated with ED in many previous studies on older adults with depressive disorders,[5–14] whether the effect of ED on the risk of SIA is differentiated by the presence of depressive disorders warrants further research because these previous studies were subject to certain limitations. First, none of the existing research investigated suicide simultaneously with SIA. Their participants with SIA included both older adults with SIA who would die by suicide and those who would not. Therefore, the association of ED with SIA in these studies might have been confounded by results from older adults with SIA who would die by suicide. Second, all but one of these studies were cross-sectional. The only prospective study was conducted on inpatients from psychiatric wards.[14] Therefore, the observations from the extant literature do not infer a causal relationship between ED and SIA, even in older adults with depressive disorders.

This study also has several limitations to be noted. First, details of suicidal behaviours, such as suicidal ideation, low-lethality suicide attempt and high-lethality suicide attempt, were not evaluated. Second, approximately 40% of the participants did not respond to one or more follow-up assessments and, thus, their SIA remained uncertain. Finally, despite the large sample size and the high suicide rate in our sample, the number of suicides was still small.

In conclusion, this is the first prospective study to demonstrate that ED is a strong risk factor of suicide in older adults without depressive disorder. ED is worth being included in the assessment of suicide risk in older adults. This may be especially true when they are very old and/or living in disadvantaged living environments such as poverty and solitude.

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Data availability statement Data are available on reasonable request.

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