ORIGINAL INVESTIGATION

Survival Rate and Causes of Mortality in the Elderly with Depression: A 15-Year Prospective Study of a Japanese Community Sample, the Matsunoyama-Niigata Suicide Prevention Project

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Objective: To compare long-term survival rates and causes of death in community-dwelling elderly with and without depression using the International Research Diagnostic Criteria administered by a psychiatrist.

Method: From 1985 to 2000, we prospectively examined Japanese persons ($N = 920$) aged 65 years or older. Cases with depression ($n = 158$) and a control sample without depression ($N = 762$) were evaluated. The main outcome variables were survival rates and causes of mortality.

Results: By 2000, 61% of the subjects with depression had died. By contrast, 48% had died in the control group at the completion of the 15-year follow-up. Using age-adjusted Kaplan-Meier survival analysis, we found a hazard ratio (HR) of 1.49 (95% confidence interval [CI] 1.16–1.89) for mortality in the depressed group compared with controls ($p = .0009$). Importantly, in female subjects with depression, the HR was 1.55 (95% CI 1.16–2.07; $p = .002$). In males with depression, by contrast, the HR (1.34) was not significant (95% CI 0.84–2.13; $p = .19$). Significantly more subjects died of cerebrovascular disorders, malignant tumors, respiratory disorders, or suicide after the onset of depression compared with controls ($p < .05$).

Conclusions: Depression appears to be associated with a significant increase in the risk of mortality among elderly Japanese subjects, particularly in females. The elderly with a diagnosis of depression may be at an elevated risk of mortality owing to cerebrovascular disorder, malignant tumors, respiratory disorders, or suicide. These prospective data provide a new quantitative insight on gender differences and the long-term public health significance of depression among the community-dwelling elderly.

Key words: depression, mortality, gender-specific survival rate, prospective clinical investigation, cerebrovascular disease, Japanese, elderly

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The lifetime prevalence of major depressive disorder as diagnosed with the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* is 5 to 12% in males and 10 to 25% in females.[1] According to the World Health Organization (WHO), depression is ranked fourth with regard to the influence on overall health, followed by respiratory infectious disease, diarrheal disorder, and perinatal disorder, based on the disability-adjusted life-years.[2] Further, depression is predicted to rank second by 2020. Thus, depression may come to affect one in six to seven individuals in their lifetime and have a prominent influence in both the social and physical dimensions of health.

Several reports in the past have suggested that depression may decrease survival.[3–6] For example,

patients with heart disease,[7–9] cerebrovascular disorder,[10–13] and malignant tumors[14] may have depression, which can influence their survival.[8,15–20] It has also been reported that individuals with depression are likely to develop various physical disorders later (eg, heart disease,[17] cerebrovascular disorder,[18] malignant tumors[19]). Notably, depression may affect causes of death not only directly but also indirectly, through increases in cigarette smoking[20] and alcohol consumption,[21] nonadherence to therapy,[22] or impaired social integration.[23]

Despite the results of singular clinical epidemiologic studies suggesting a link between depression and mortality, the available body of literature does not uniformly support this association. Wulsin and colleagues reviewed 57 reports on survival of depressive patients and found that about half (51%) of the studies reported significantly decreased survival rates in depressed patients, 23% reported the absence of an association, and 26% were inconclusive.[24] Some, but not all, studies suggest that depression may increase the risk of death by cardiovascular disease, particularly in men.[24] Thus, no consistent conclusion concerning the survival rates of depressed patients or the attendant causes of mortality has been clearly established to date.

We noted that the elderly suffer from a high prevalence of depression.[25] This predicament is further accentuated owing to the increasing size of the elderly population globally. In Japan, for example, those aged 65 years or older may account for 26% of the total Japanese population by 2015, becoming the world's most rapidly aging society.[26] Hence, studies in the Japanese elderly population may serve as a model to study the long-term medical outcomes associated with depression.

The aim of the present study was to prospectively investigate, over a course of 15 years, the survival rates and causes of death in community-dwelling elderly Japanese residents who were diagnosed with depression based on established international research diagnostic criteria administered by a qualified psychiatrist.

Methods

Subjects

The subjects were male and female residents aged 65 years and older as of July 1985 in Matsunoyama town, Higashikubiki county, Niigata prefecture (total population in 1985: 4,400; elderly rate: 21%). There were 369 males (65–91 years of age; 73.6 ± 5.9 years) (mean ± SD) and 551 females (65–96 years of age; 74.3 ± 6.7 years), a total of 920 subjects. The survey period was between 1985 and 2000. This survey was performed as the Matsunoyama Suicide Prevention Project,[27] and it is still continuing. Written and informed consent was obtained from all participants.

Study Procedures and Data Collection

The following tests were performed annually in July as a geriatric depression screening test: Zung's Self-Rating Depression Scale (SDS)[28] in 1985 and a modified SDS, the Niigata University Self Rating Depression Scale (NSDS),[29,30] after 1986. NSDS was established and validated by slight modification of the SDS: 5 items were added (25 items in total) to the questions of SDS, and the maximum score was set at 100, to facilitate the interpretation of rating scores.[29,30] The questions were structured to be as comprehensible as possible for the Japanese elderly to answer the contents of the questions appropriately. NSDS is commonly used to screen for depression in Japanese patients.[29,30] When the SDS score rate was 60% or higher or the NSDS score was 60 points or higher, the subject was interviewed by a psychiatrist to establish the diagnosis. These threshold values are recommended for screening of subjects for further clinical interview by a psychiatrist.[29] Subjects whose scores did not meet the criterion above (ie, 60% score rate) were also interviewed if they expressed suicidal intent to a physician (internist) of a regional medical institution or a public health nurse or had experienced the death of their spouse, discharge from a medical institution, or a suicide incident in their neighborhood immediately prior to their annual study visit.

As part of the diagnostic procedure, whether the depression met the diagnostic criteria of major or minor depressive disorder was evaluated using the Research Diagnostic Criteria.[31] The subjects diagnosed with major and minor depressive disorders were collectively designated as the depressive group, and the other subjects were designated as the nondepressive group. When a subject in the nondepressive group was later diagnosed with major or minor depressive disorder on diagnostic interview, the subject was transferred to the depressive group in that year. That is, if subjects were not depressed at study entry, they were in the nondepressed group unless they later developed depression. For all subjects diagnosed with depression, pharmacologic treatments were immediately initiated at a medical office or a psychiatric hospital with a hospitalization facility.

Assessment of the Survival Rate

The behavioral rating scores for depression, the presence or absence of depression in subjects interviewed for diagnosis, and the study outcomes, such as

death and moving to another geographic area, were investigated for individual subjects on an annual basis. When survival could not be confirmed, the study outcomes were ascertained by the Basic Resident Register. When the registration was not kept, permission to read the death certificate kept at medical offices in the town was obtained. The subjects who were hospitalized or admitted to a facility at the time of distribution of the questionnaire were regarded as having moved out. Among the subjects who moved out, subjects who reparticipated in the survey later were handled as survivors, whereas those who did not reparticipate remained in the 'moved out' category.

In the nondepressive group, the ratio of survivors was calculated by dividing the annual number of surviving subjects by the total number of surviving and deceased subjects in the fiscal year (July to June). In the depressive group, the number of surviving subjects was divided by the total number of surviving and deceased subjects in each follow-up year, designating the year of discovery of depression as the '0' year of follow-up.

The survival rates were also calculated separately in males and females in both depressive and nondepressive groups. The ratio of subjects younger than 69 years of age was particularly higher in the nondepressive group than in the depressive group, whereas the mean age was higher in the depressive group (Table 1). To eliminate the effect of different age distribution in the nondepressed group, representative samples were drawn from each age group of the nondepressive group using random numbers. The ratio of the subjects 85 years or older was higher in the depressive group; thus, samples of this age group were drawn from the depressive group by the same procedure using random numbers. As a result, 153 and 382 ($n = 535$) subjects in total were respectively drawn from the depressive and nondepressive groups; these two age-adjusted groups showed no significant difference in age distribution ($p > .05$). For example, in females, the mean age in the first year was 76.9 ± 6.1 (SD) and 77.0 ± 6.4 years in the depressive and nondepressive groups, respectively ($p > .05$). This age-adjusted sample of subjects was then used in the Kaplan-Meier survival analysis, including the attendant gender-stratified analysis.

Assessment of Cause of Death

The causes of death were ascertained from the Resident Population Dynamics Questionnaire or death certificates and classified as heart disease, malignant tumor, cerebrovascular disorder, respiratory disorder, suicide, and others using the WHO *International Classification of Diseases*.[32] The mortality rates from each cause in the age-adjusted depressive and nondepressive groups and relative risk (RR) of death of the depressive group compared with the nondepressive group for all subjects, males and females, were calculated.

Table 1 Description of the Subjects Prior to Age Adjustment for Kaplan-Meier Survival Analysis

	Depressive Group	*Nondepressive Group*
Number of subjects	158	762
Major depression	111	NA
Minor depression	47	NA
Male:female	40:118	329:433
(% composition)	25:75	43:57
Age distribution (%)		
65–69 yr	11	34
70–74 yr	22	26
75–79 yr	33	21
80–84 yr	20	12
85 yr or older	14	7
Outcomes (fiscal year 2000)*		
Number of subjects		
Survival	7	230
Death	96	365
Suicide	8	7
Moving out	55	167

NA = not applicable.
*Refers to the full sample ($N = 920$) prior to age adjustment for the Kaplan-Meier survival analysis.

Statistical Analysis

The significance of differences in the survival rate between patients with depression ($n = 153$) and the control group without depression ($n = 382$) was evaluated by the Kaplan-Meier survival analysis, including the attendant gender-stratified survival analysis. *SPSS* (version 11.0J, SPSS Inc., Tokyo) was used for all statistical analyses.

Results

The subject characteristics are shown in Table 1. There were 158 depressed patients (17.2%) for all 15 years (see Table 1). The mean age at onset for depression was 77.4 ± 6.3 (SD) years. Fifty-five (34.8%) and 167 (21.9%) subjects moved out of the region in the depressed and control groups, respectively. Matsunoyama is geographically located in rural Japan. For the elderly residents, it is not uncommon to relocate to a larger metropolitan district (eg, Niigata) for familial reasons (eg, for close proximity with younger family members). The duration of follow-up was 5.8 ± 4.6 years (mean ± SD; range 1–15 years) in the group with depression and 8.5 ± 5.1 years (range 1–15 years) in the control group. In the entire study

sample ($N = 920$), by 2000, 96 and 365 subjects were ascertained to have died, whereas 8 and 7 subjects had committed suicide in the depressed and control groups, respectively (see Table 1). As a caveat, it is noteworthy that patients who committed suicide in the nondepressed (control) group might have had depression between the annual study assessments.

Survival Rates in the Depressive and Nondepressive Groups

From 1985 to 2000, there were 153 depressed and 382 nondepressed controls ($n = 535$). From this age-adjusted sample, by 2000, the number of surviving subjects in depressed and nondepressed groups was 7 and 86, respectively. Kaplan-Meier survival analysis (males and females combined) found a hazard ratio of 1.49 (95% confidence interval [CI] 1.16–1.89) for mortality in the age-adjusted depressed group compared with controls without depression ($p = .0009$).

Importantly, in female subjects with depression, the hazard ratio for mortality was 1.55 (95% CI 1.16–2.07; $p = .002$) (Figure 1B). In males with depression, by contrast, the hazard ratio for mortality (1.34) was not significant (95% CI 0.84–2.13; $p = .19$) (Figure 1A).

Hazard ratios for mortality in depressed subjects aged 65 to 74 and > 74 years were 1.84 (95% CI 1.08–3.12, $p = .02$) and 1.54 (95% CI 1.16–2.04; $p = .0013$), respectively (Figure 2).

Causes of Death

Table 2 shows the mortality rates from each cause of death in the depressive and nondepressive groups and RR of the depressive group. Using the age-adjusted sample of depressed and control subjects without depression, we found a significant difference in mortality rates, particularly from cerebrovascular disorders, as well as from malignant tumors, respiratory disorders, and suicide in the depressive group ($p < .05$).

Discussion

There have been limited long-term observational studies of major depression and mortality in community-dwelling elderly.[33–39] Previous studies in the field tended to have relatively shorter survey periods (eg, as short as 6 months) and a smaller number of study subjects, included an ethnically heterogeneous group of patients, lacked a control group in some reports, and focused solely on inpatients, or the diagnosis of depression was made based on a questionnaire instead of a clinical interview by a psychiatrist.[24] In the present investigation, we prospectively followed all elderly residents aged 65 years or older in Matsunoyama town, Higashikubiki county, Niigata prefecture for 15 years, identified a sample of individuals who presented with depression (at least once during the 15-year observation period) among these subjects, and investigated the age-adjusted survival rate and causes of death in the elderly with depression. Three principal observations were made in our study.

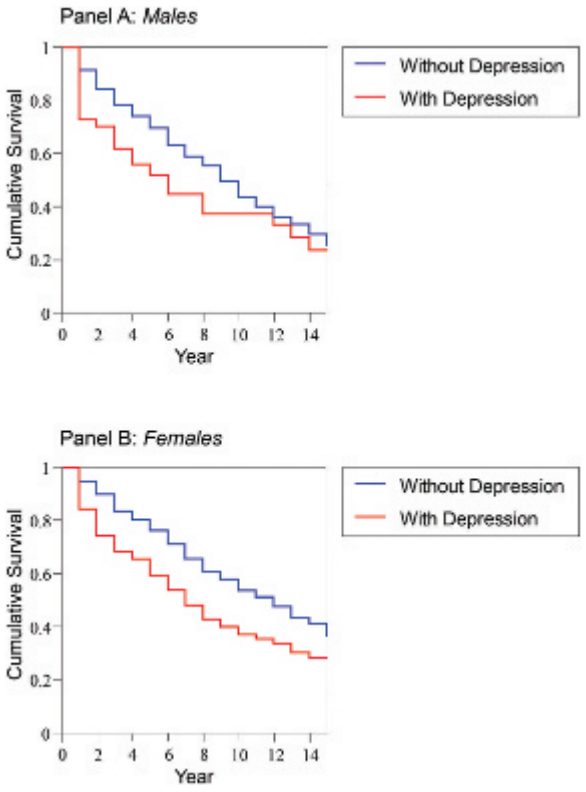

Figure 1 Kaplan-Meier survival curves from 1985 (year 0) to 2000 (year 15) in an age-adjusted and gender-stratified study sample aged 65 years and older (*A*, males; *B*, females). $A = 40$ depressed and 100 nondepressed male subjects; $B = 113$ depressed and 282 nondepressed female subjects (total $n = 535$).

First, the survival rate was significantly lower in the depressive group than in the nondepressive group throughout the 15-year prospective long-term follow-up. Second, and importantly, the survival rate was significantly lower in elderly females with depression compared with female controls without depression. By contrast, males with depression did not exhibit a significantly increased hazard ratio for mortality. Third, regarding the cause of death, the mortality rates from cerebrovascular disorders, malignant tumors, respiratory disorders, and suicide were significantly higher in the depressive group than in the nondepressive group. Collectively, these prospective long-term observations

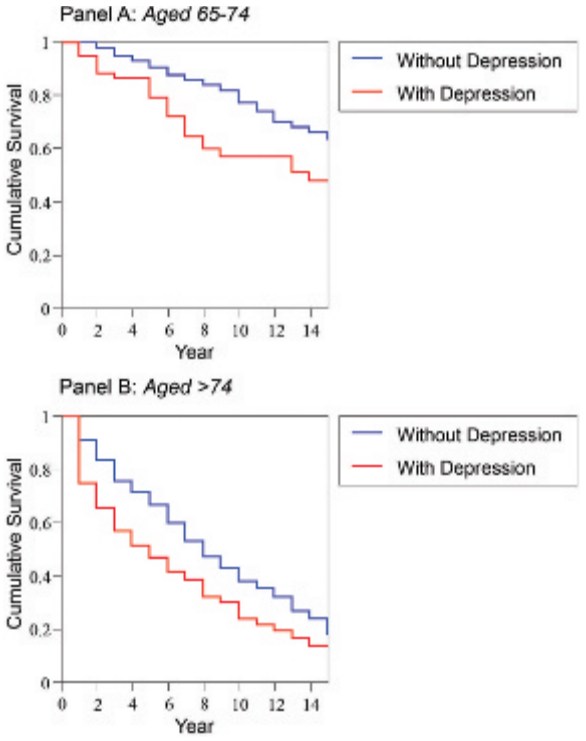

Figure 2 Kaplan-Meier survival curves from 1985 (year 0) to 2000 (year 15). All depressed subjects and the control group without depression were adjusted for age distribution prior to survival analysis (total $n = 535$). Subjects aged 65 to 74 and > 74 years are shown in *A* and *B*, respectively. *A* = 51 depressed and 129 nondepressed subjects; *B* = 102 depressed and 253 nondepressed subjects.

provide a new quantitative perspective on gender differences and the public health significance of depression in the community-dwelling elderly.

Notably, only six previous reports have investigated gender differences in survival among patients with depression. Among these, two reports were consistent with our study,[40,41] suggesting a greater reduction in survival rate among female patients with depression than males. Conversely, the other four studies reported a significant decrease in the survival rate, particularly among the male depressive patients.[35,39,42,43] However, depression diagnosis in these studies tended to be established by a questionnaire rather than a psychiatrist using research diagnostic criteria.

If our results are representative of the population as a whole, a question remains: Why was the death rate higher in female depressive patients than in male depressive patients? Murphy and colleagues suggested that physical comorbidity might have been more advanced in females even though the degree of depression was similar following diagnosis using a questionnaire.[44] The latter assumption, however, is not supported by the longer average life expectancy in females than in males. Thus, the answer to the above question is not clear at present, but the mortality rate from cerebrovascular disorders was higher in females than in males in our study, suggesting that depression in elderly females may tend to be cerebrovascular; fatal cerebrovascular disorders may occur in the course of depression, or depression may induce cerebrovascular disorder in ways that are not fully elucidated at present.

Few previous long-term studies investigated the age group of 75 years or older. In a sample of 500 elderly community residents aged 85 years or older in England, Vinkers and colleagues found that depression was associated with a decrease in the survival rate even in very elderly subjects (mean follow-up duration 3.2 years).[45] On the other hand, Vinkers and colleagues employed a questionnaire for the diagnosis of depression. In a self-rating questionnaire, subjects may mistake, for instance, malaise associated with physical disorders and physical complaints for symptoms of depression. Thus, the depressive group in their study might have included subjects with physical disorders, or it might have been related to the difference in the average life expectancy between Japan and England.

We found that the mortality rates from cerebrovascular disorders, malignant tumors, respiratory disorders, and suicide were significantly higher in the group with depression compared with controls. These observations require further validation in future prospective studies. Association with mortality from cerebrovascular disorders was apparent in the depressed group as early as within the first 5 years. Major depression can precipitate certain risk factors associated with cerebral infarction, including hypertension, hyperlipidemia, diabetes, and smoking. Cerebral infarction resulting from increased platelet activity owing to an overactive adrenocortical system has also been reported.[46] Cerebral lesions were localized in the deep white matter in elderly depressed patients compared with nondepressed control patients.[47] Thus, a depressive state and cerebrovascular disorders are presumably closely related, and their coexistence is thus likely to increase the risk of mortality.

Association of the depressive group with suicide was significant and consistent with other reports in the elderly persons in the community.[42] Depression is a direct cause of suicide, and attention should be paid to depression cases in this regard as well. In the present prospective study, of the eight subjects who committed suicide after the onset of depression, four (50%)

Table 2 Relative Death Risk (Relative Risk and 95% Confidence Interval) of the Depression Group Compared with the Nondepression Group after Stratification of the Study Sample Based on the Cause of Death

	Heart Diseases					*Cerebrovascular Disorder*					*Malignant Tumor*					*Respiratory Disorder*					*Suicide*				
	Death Rate (%)					*Death Rate (%)*					*Death Rate (%)*					*Death Rate (%)*					*Death Rate (%)*				
Year	*Depressive*	*Non-depressive*	p	*RR*	*95% CI*	*Depressive*	*Non-depressive*	p	*RR*	*95% CI*	*Depressive*	*Non-depressive*	p	*RR*	*95% CI*	*Depressive*	*Depressive*	p	*RR*	*95% CI*	*Depressive*	*Depressive*	p	*RR*	*95% CI*
Male																									
(yr)																									
1	7.9	3.1	.348	2.58	0.54–12.22	2.6	1.0	.482	2.58	0.17–40.19	5.3	1.0	.189	5.16	0.48–55.23	0.0	0.0	—	—	—	5.3	1.0	.189	5.16	0.48–55.23
2	8.1	6.2	.707	1.31	0.35–4.97	2.7	2.1	1.000	1.31	0.12–14.03	5.4	3.1	.616	1.75	0.30–10.04	2.7	1.0	.477	2.62	0.17–40.83	5.4	1.0	.185	5.42	0.49–56.11
3	13.9	7.3	.310	1.93	0.65–5.68	5.6	3.1	.612	1.80	0.31–10.32	5.6	4.1	.662	1.35	0.26–7.04	2.8	3.1	1.000	0.90	0.10–8.36	5.6	1.0	.178	5.39	0.50–57.63
4	18.2	7.4	.080	2.47	0.89–6.82	6.1	3.2	.600	1.91	0.34–10.99	9.1	5.3	.424	1.73	0.44–6.84	3.0	4.2	1.000	0.72	0.08–6.21	6.1	1.1	.163	5.76	0.54–61.44
5	18.8	7.4	.066	2.55	0.92–7.02	9.4	3.2	.170	2.97	0.63–13.98	9.4	5.3	.425	1.78	0.45–7.04	9.4	5.3	.415	1.78	0.45–7.04	6.3	1.1	.156	5.94	0.56–63.31
10	22.6	17.8	.557	1.27	0.58–2.80	12.9	10.0	.738	1.29	0.43–3.90	12.9	5.6	.232	2.32	0.67–8.11	9.7	12.2	1.000	0.79	0.24–2.65	6.5	1.1	.161	5.81	0.55–61.84
15	28.0	18.4	.295	1.52	0.71–3.28	16.0	12.6	.740	1.27	0.44–3.63	20.0	6.9	.066	2.90	0.97–8.72	16.0	18.4	1.000	0.87	0.32–2.37	8.0	1.1	.125	7.00	0.66–73.63
Female																									
1	0.9	0.4	.488	2.52	0.16–39.98	5.5	2.5	.148	2.16	0.74–6.29	3.7	0.4	.024*	10.09	1.14–89.28	1.8	1.1	.625	1.68	0.29–9.93	2.8	0.7	.141	3.78	0.64–22.34
2	3.7	1.5	.176	2.50	0.64–9.80	8.4	4.5	.137	1.87	0.81–4.31	3.7	1.1	.046*	4.16	1.01–17.10	2.8	1.9	.574	1.50	0.36–6.16	4.7	0.7	.022*	6.24	1.23–31.67
3	3.8	2.3	.480	1.67	0.48–5.79	12.5	6.5	.062	1.91	0.96–3.79	3.8	1.9	.128	2.50	0.74–8.46	2.9	2.7	1.000	1.07	0.28–4.06	4.8	1.2	.046*	4.17	1.01–17.12
4	4.0	2.4	.479	1.68	0.48–5.82	13.9	8.3	.111	1.68	0.89–3.17	5.0	2.0	.125	2.52	0.74–8.50	3.0	2.8	1.000	1.08	0.28–4.09	5.0	1.6	.125	3.14	0.86–11.47
5	5.1	2.4	.193	2.13	0.67–6.83	14.3	10.0	.249	1.43	0.78–2.64	5.1	3.2	.209	1.92	0.68–5.39	5.1	3.2	.396	1.60	0.54–4.77	6.1	1.6	.033*	3.84	1.11–13.32
10	10.5	8.4	.562	1.25	0.59–2.66	22.1	17.6	.367	1.25	0.77–2.04	8.1	7.0	.504	1.32	0.59–2.97	11.6	5.7	.074	2.03	0.93–4.46	7.0	2.2	.077	3.17	0.99–10.11
15	16.2	12.9	.391	1.39	0.66–2.94	25.7	22.1	.181	1.16	0.73–1.84	10.8	9.2	.204	1.65	0.76–3.57	14.9	7.8	.038*	2.26	1.03–4.93	8.1	2.8	.034*	3.52	1.11–11.19
Total																									
1	2.7	1.1	.231	2.54	0.64–10.01	4.8	2.1	.108	2.22	0.82–6.01	4.1	0.5	.008**	7.61	1.55–37.29	1.4	0.8	.625	1.69	0.29–10.02	3.4	0.8	.044*	4.23	1.02–17.47
2	4.9	2.7	.233	1.77	0.69–4.56	6.9	3.8	.138	1.81	0.82–3.97	4.2	1.6	.039*	2.95	1.01–8.63	2.8	1.6	.480	1.69	0.48–5.88	4.9	0.8	.007**	5.90	1.55–22.50
3	6.4	3.7	.176	1.76	0.77–4.03	10.7	5.6	.046*	1.91	1.01–3.62	4.3	2.5	.161	1.98	0.75–5.21	2.9	2.8	.977	1.02	0.32–3.19	5.0	1.1	.008**	4.45	1.32–14.97
4	7.5	3.7	.158	1.80	0.79–4.12	11.9	6.9	.040*	1.85	1.02–3.32	6.0	2.9	.107	2.08	0.84–5.17	3.0	3.2	.887	1.19	0.42–3.34	5.2	1.4	.017*	3.65	1.18–11.29
5	8.5	3.8	.074	2.05	0.92–4.55	13.1	8.1	.058	1.71	0.98–2.99	6.2	3.8	.181	1.54	0.82–2.87	5.4	4.0	.329	1.52	0.65–3.54	6.2	1.4	.005**	4.26	1.42–12.78
10	13.7	11.0	.606	1.16	0.66–2.05	19.7	15.5	.212	1.33	0.86–2.06	9.4	6.6	.326	1.42	0.71–2.85	11.1	7.6	.151	1.58	0.85–2.95	6.8	1.9	.010**	3.61	1.28–10.19
15	19.2	14.5	.374	1.26	0.76–2.07	23.2	19.4	.302	1.25	0.82–1.90	13.1	8.6	.257	1.64	0.70–3.86	15.2	10.9	.161	1.49	0.86–2.59	8.1	2.3	.008**	3.51	1.31–9.43

CI = confidence interval; RR = relative risk.
*$p < .05$.
**$p < .001$.

committed suicide within 1 year, and seven subjects (87.5%) committed suicide within 2 years. These observations corroborate earlier associations between depression and suicide in older individuals.[48]

As a limitation of our study, we caution the reader from drawing direct causal links between depression and increased risk of mortality because some of the potential confounding factors, such as physical comorbidity and concomitant medications at the time of the survey, smoking habits and alcohol consumption, access to health insurance, or socioeconomic conditions, were not characterized in our study. After detailed review of the medical literature, however, we were struck by the paucity of prospective and long-term outcome studies on major depression (particularly as determined by a psychiatrist using research diagnostic criteria) in relation to mortality and the influence of gender on longitudinal mortality rates in the elderly. Hence, our study was designed to balance these considerations to account for all possible confounders against the feasibility of, and the need for, long-term prospective evaluations of mortality in community-dwelling older persons with depression.

Disease outcome studies often reach different conclusions owing to heterogeneity in age and gender distribution in study samples, discrepancies in establishing the diagnosis for depression by research staff, uneven delivery of health care services, or inadequate access to treatment, particularly in countries where medical insurance is privatized. Interethnic and cross-cultural differences in lifestyle factors or environmental factors may further confound clinical outcome studies in ethnically diverse populations. However, Matsunoyama town is located in a stable socioeconomic setting, and all residents have a Japanese ethnic background and uniform lifestyle preferences (eg, reliance on a traditional Japanese diet enriched with seafood). Importantly, the national social welfare services in Japan ensure that all residents have access to health insurance and medical treatment for physical and psychiatric comorbidity. For example, all patients in the present study had access to antidepressant pharmacotherapy promptly after the diagnosis of depression was established. These considerations and our analysis of the survival data after stratification by gender and accounting for deaths owing to suicide reduce the risk of confounding by patient-to-patient heterogeneity in ethnic background, gender or age distribution, access to health care services, medical insurance, or antidepressant treatment in the study sample.

Monitoring medical conditions comorbid with depression is important to discern the causal link between depression and mortality and for differentiation of 'cause' and 'effect' relationships. For example, cardiovascular disease may first present as new-onset depression in the elderly, that is, cardiovascular disease may cause depression rather than vice versa.[49] However, this is a formidable challenge, especially in long-term prospective studies in which patients tend to agree with a more limited clinical assessment battery in exchange for an increased cooperation for long-term follow-up of their health. The shifting emphasis in health care policies toward establishment of large population biobanks (eg, UK Biobank, the Estonian Genome Project, GenomEUtwin, the CARTAGENE in Quebec) and prospective assembly of patient phenotypic data in these and similar biobanks may allow an integrated study of depression and other risk factors in relation to long-term survival rates in the near future.[50–52]

In summary, these prospective data from the Matsunoyama-Niigata Suicide Prevention Project over a period of 15 years collectively suggest that depression is likely associated with a significant decrease in the survival rates of the Japanese elderly subjects, particularly in females. The survival rate was also lower when the subjects who committed suicide were excluded. In addition, elderly with a diagnosis of depression may be at an elevated risk of cerebrovascular disorder malignant tumors, respiratory disorders, or suicide. Further detailed clinical investigations in other populations are warranted to elucidate the link between depression and mortality.

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Survival Rate and Causes of Mortality in the Elderly with Depression: A 15-Year Prospective Study of a Japanese Community Sample, the Matsunoyama-Niigata Suicide Prevention Project

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