

The Accuracy, Efficiency, and Appropriateness of Two Self-Administrative Scales to Screen for Major Depressive Disorder

Running title: Screening Performance of CES-D and K6

Akiyoshi SEKIYA^{1,2}, Naohito TANABE³, Nao SEKI⁴, Noboru FUKISHIMA²,
Satoshi YAMAZAKI¹, Hiroshi SUZUKI¹

¹Division of Public Health, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; ²Mental Health Center, City of Niigata, Niigata Japan; ³Division of Health Promotion, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; and ⁴School of Health Sciences, Faculty of Medicine, Niigata University, Niigata, Japan.

Correspondence: Naohito Tanabe, MD, PhD

Division of Health Promotion, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo Ward, Niigata City, 951-8510, Japan

E-mail: tanabe@med.niigata-u.ac.jp

Phone: +81-25-227-2129, Fax: +81-25-227-0765

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Abstract

Identifying patients with major depressive disorder (MDD) in communities and providing appropriate treatment are important means to prevent suicide. The aim of this study was to find a highly capable scale to identify MDD patients and to clarify the appropriateness of administering screening for MDD after informed consent is given. A mental health questionnaire survey was conducted in Niigata City and was answered by 1,001 persons. After being informed that the survey was to screen for MDD, 153 persons accepted (screening survey).

Two self-administrative scales were administered: the Center for Epidemiologic Studies Depression Scale (CES-D) and the K6 scale. The Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID) was also applied, and seven individuals were judged as positive for MDD. Receiver Operating Characteristic (ROC) curves for MDD, indicated that CES-D (0.932) had a wider area under the curve than K6(0.874). The optimum screening criterion of CES-D was “ ≥ 14 points” based on the Youden index and the ROC curve. By using this criterion, the sensitivity for MDD was 1.00, and its positive predictive value was greater than K6 under any conditions examined. According to the mental health questionnaire survey, the

prevalence of depressive symptoms in 848 non-participants of the screening survey was clearly lower than in the 146 SCID-negative participants for MDD. In conclusion, CES-D is a capable scale to identify patients with MDD. The administration of CES-D to participants of a screening survey can be a practical way to effectively and efficiently find patients with MDD within a community.

Key words: Major depressive disorder, Mass screening, Psychiatric Status Rating Scales, Diagnostic and Statistical Manual of Mental Disorders, ROC Curve

Abbreviations: MDD, Major Depressive Disorder; CES-D, Center for Epidemiologic Studies Depression Scale; DSM-IV, The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders by the American Psychiatric Association; SCID, The Structured Clinical Interview for DSM-IV Axis-I Disorders; ROC, Receiver Operating Characteristic Curve; WHO, The World Health Organization; SDS, Zung Self-Rating Depression Scale; AUC, Area Under Curve; PPV, Positive Predictive Value; NPV, Negative Predictive Value; NNT, Number Needed to Test

Introduction

In Japan, suicide is the fifth leading cause of death and more than 30,000 individuals commit suicide every year; therefore, prevention of suicide is a priority public health issue in Japan.¹⁾ Major depressive disorder (MDD) is an important, treatable, risk factor for suicide,²⁾ and screening for MDD has contributed to a reduction of the suicide rate in schools³⁻⁶⁾ and small cities in Japan.⁷⁻⁹⁾ Identifying patients with MDD in communities and providing appropriate treatment have been recognized as means to prevent suicide. However, the currently available screening processes are limited with respect to efficiency and cost-effectiveness,¹⁰⁾ therefore, it is essential to develop accurate and efficient methods to screen communities and identify MDD patients.

As the language and behavior of patients are the main source of information for the diagnosis of mental diseases, a psychiatric interview is the most appropriate method to judge depression; structured interviews such as the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID)¹¹⁾ are widely used in the clinical setting. However, structured interviews require a trained professional and take 45 to 60 minutes per person; therefore, they cannot be applied to large groups. Hence, many scales have

been developed to screen for psychiatric disorders.

To screen a large group for MDD, a free or low price scale with high accuracy and efficiency is necessary. The Center for Epidemiologic Studies Depression Scale (CES-D) was developed for the epidemiological study of MDD in the USA and is free from copyright,¹²⁾ and therefore has been widely used throughout the world. Although copyright exists for the Japanese version, of which the validity was confirmed,¹³⁾ it can be used at a relatively low cost. The K6 scale^{14,15)} is a simplified screening scale for common mental health disorders developed by the World Health Organization (WHO), and the validated Japanese version is free from copyright.¹⁶⁾ Some governmental organizations such as WHO¹⁷⁾ and the US government¹⁸⁾ have used this scale to screen for mental health disorders. The Japanese version of K6 by Furukawa et al.¹⁶⁾ has been adopted for the Comprehensive Survey of Living Conditions of the People on Health and Welfare from 2007. Therefore, K6 is commonly used to monitor the mental health status of communities. However, few reports have directly compared the screening performances of these scales,²⁾ and it has not been fully considered which can be more effectively administered to screen for MDD. Therefore, we applied a screening survey for MDD in Niigata City, Japan,

with the aim of clarifying which scale can accurately and efficiently screen for MDD.

Because it is practically difficult to screen an entire community for MDD, including those who have no mental disorder, we also investigated the appropriateness of administering the screening survey only to individuals who wished to participate once they understood the motive of the survey.

Methods

Niigata City is the capital of Niigata prefecture in Japan and has a population of 814,000 according to the 2005 national census. We selected four of eight wards in the city as model areas and screened these areas for MDD (screening survey) using the opportunity of a mass screen for gastric cancer (gastric-cancer survey). We used this opportunity because of the following reasons: 1) the gastric cancer survey has a 40-year history and is an accepted major health-related event; 2) it would be easier to obtain cooperation for the MDD screening survey because participants would already be interested in their general health condition; and 3) we could recruit participants to the MDD screening survey and conduct another questionnaire survey concerning mental health status while the subjects

were waiting for their gastric examination. In the four selected wards, 7,509 out of 241,000 residents aged 40 years or over were examined from April to November, and 1,108 in July 2008.

We asked those attendees in July to complete a simple questionnaire concerning their perceived mental health status and 1,001 participated; they were the subjects of the questionnaire survey. At the same time, we provided information concerning the importance of preserving mental health and requested their participation in the screening survey; 153 attendees accepted and they were the subjects of the screening survey. These surveys were conducted by the Mental Health Center, City of Niigata.

For the present analyses, all data were anonymized by the first author (A.S.) of this paper. Other researchers of Niigata University handled these anonymous data given to the University from the mayor of Niigata City based on a research entrustment. We obtained written informed consent from all participants for the handling methods of these data and the publication of research results. We conducted this study in accordance with the 2007 version of Japan's Ethical Guidelines for Epidemiologic Research.

Questionnaire survey related to mental health

We surveyed the presence or absence of perceived mental disorder and symptoms suggestive of depression by a self-administered questionnaire. For the perceived mental disorder, we received a “Yes” or “No” answer to the question “Do you feel stress, distress, or anxiety at present?” For depressive symptoms, we listed nine major symptoms of MDD (Table 1) which are described in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders by the American Psychiatric Association (DSM-IV), and asked participants to tick those symptoms that they recognized in the past month. Based on these ticked items, we tentatively estimated the frequency of possible MDD in the participants by applying the judging methods of DSM-IV.

Screening survey for MDD

We asked all participants to complete the CES-D¹²⁾ and K6 surveys.^{14,15)} CES-D is a screening scale consisting of 20 questions developed by Radloff in the USA. We used the Japanese version for which the validity was confirmed by Shima et al.¹³⁾ Although the Japanese version of the Zung Self-Rating Depression Scale (SDS) is also available as a validated scale for depressive symptoms, we chose the CES-D due to its lower usage fee (84 Japanese yen,

0.9 US dollars, for CES-D and 147 yen, 1.6 US dollars, for SDS for one test in 2008). K6 consists of six questions with the aim of screening for common mental health disorders such as mood and anxiety disorders, including MDD. We used the Japanese version of K6 by Furukawa et al.¹⁶⁾

Thereafter, we applied SCID to all participants and made judgments about MDD. SCID is a psychiatric interview method based on DSM-IV, and its questioning and judging procedures are structured so that the judgment of multiple surveyors can be standardized.¹¹ Three mental health counselors performed the interviews for the present study. All these surveyors are licensed psychiatric social workers, and work at the Mental Health Center, City of Niigata. They are proficient in the use of SCID in their daily duties. We carefully standardized the survey methods between surveyors before initiating this study.

Statistical analysis

The statistical differences of the numerical data between groups were tested by the Student's t-test and those of categorical data were tested by the chi-square test. Receiver operating characteristic (ROC) curves were drawn for CES-D and K6, using judgments of MDD by SCID as the gold standard,

and the area under the curve (AUC) was calculated to assess the global screening performance of each scale to identify patients with MDD. Three different criteria for positive screening were used to calculate sensitivity and specificity as indices of screening accuracy, and with positive predictive value (PPV), negative predictive value (NPV), and number needed to test (NNT) as indices of screening efficiency. The NNT can be calculated by “ $1/PPV$ ”, indicating the number of SCID tests required to identify one patient with MDD from screening positive subjects. One of the three criteria was the conventional criterion, i.e., “ ≥ 16 points” for CES-D which was the originally proposed criterion and “ ≥ 5 ” for K6 which was the criterion proposed by Furukawa et. al. for the Japanese population.¹⁶⁾ Two other criteria were determined based on the Youden index and the ROC curve graph¹⁹⁾ in order to impartially compare the screening accuracy and efficiency between scales. The Youden index was calculated by “ $sensitivity + specificity - 1$ ”, and the cutoff point was determined to maximize this value. The criterion based on the ROC curve graph was determined using a cutoff point which minimized the distance between the curve and the upper-left corner of the graph (i.e., $sensitivity = 1$ and $specificity = 1$): the distance can be calculated by “ $(1-sensitivity)^2 + (1-specificity)^2$ ”.

All statistical analyses were performed with SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA), and a two-tailed $P < 0.05$ was considered statistically significant.

Results

Men were less likely to participate in the screening survey ($P = 0.008$) (Table 1). In the screening survey, 7 out of 153 participants (4.6%) were judged as positive for MDD by SCID [SCID(+)]. These SCID(+) participants had most depressive symptoms more frequently than those who were negative for MDD [SCID(-)] ($P < 0.05$) in the questionnaire survey. The frequency of perceived mental disorder and most depressive symptoms were lower in the non-participants of the screening survey than in the total and SCID(-) participants. The prevalence of possible MDD (2.0%, $P = 0.014$) in the non-participants was significantly lower even when compared with SCID(-) participants (5.5%).

In the screening survey with conventional criteria, 22 participants (14.4%) were positive for CES-D and 61 (39.9%) were positive for K6 (Table 2). All positive cases for CES-D were also positive for K6. The positive rates were higher for K6 in all sex and age classes except for 45–54-years-old

males. SCID(+) was observed in subjects from 45–74 years of age, and 6 of 7 cases were women.

In ROC analyses, both CES-D (AUC = 0.932, $P < 0.001$) and K6 (AUC = 0.874, $P < 0.001$) showed a high performance in screening for MDD, but the AUC was wider for CES-D (Fig. 1). Using conventional criteria, CES-D overlooked one SCID(+) person (sensitivity = 0.86), but there was no oversight in K6 (sensitivity = 1.00). The specificity for K6 (0.63) was lower than for CES-D (0.89) (Table 3).

For the criteria based on the Youden index and the ROC curve graph, ≥ 14 points in every method of CES-D, and ≥ 6 points and ≥ 7 points in each method of K6 were determined as the optimal positive criteria. When these criteria were used, CES-D did not overlook the SCID(+) individual. Although the NNT (4.1) for CES-D (≥ 14 points) was slightly increased from the NNT with the conventional criterion (3.7), this value was lower than for K6 at every criterion. The PPVs were higher and the NPVs were equal to or higher for CES-D than for K6 in any setting studied, indicating the higher screening efficiency of CES-D than K6.

Discussion

As a result of the screening survey administered to 153 participants aged ≥ 40 years, CES-D (≥ 14 points) could identify MDD cases more efficiently than K6 without missing cases. Thus CES-D is a more capable tool than K6 to screen for MDD.

Kawakami et al also directly compared the screening performance of CES-D and K6 for identifying mood disorders (MDD and dysthymic disorder).²⁾ Their study population consisted of outpatients with mood disorders and volunteers with no psychiatric disorders. Despite the differences in study design, they also determined that the accuracy and efficiency of CES-D were better than for K6.

Differences in the target disorders between the two scales could partly explain the superiority of CES-D in screening for MDD. CES-D is a specialized scale to identify subjects with depressive symptoms, whereas K6 is designed to identify both mood and anxiety disorders. Therefore, many patients with mental disorders other than MDD can be determined as K6 positives. To prevent suicides, identifying patients with MDD could be a key tool because MDD is a treatable risk factor for suicide.²⁻⁸⁾ When screening large groups for MDD, selecting an accurate and efficient scale to eliminate wasted effort and budgets is a substantive problem. Therefore, CES-D would

be a better tool than K6 for community-based suicide prevention measures.

However, the conventional criterion, CES-D ≥ 16 points, overlooked one of seven MDD patients, with a sensitivity of 0.86. In the validation study for the Japanese version by Shima et al., a similar sensitivity (0.88) was reported, indicating that the conventional criterion can overlook some patients with MDD. In this study, the optimum criterion of CES-D was determined as ≥ 14 points, with a sensitivity of 1.00. Although indices for screening efficiency were slightly reduced, they were better than those for K6 in any settings. Therefore, it would be reasonable to lower the positive criterion of CES-D to ≥ 14 if we account for the increased use of K6 in Japan. However, future studies with larger sample sizes are necessary to determine the most appropriate criterion of CES-D for the screening of MDD in communities.

The larger effort required from respondents could be problematic for the use of CES-D; CES-D consists of 20 questions whereas K6 has 6, and CES-D contains some reverse-scored questions. Some of our participants declared that CES-D was hard to answer, as was also reported by Kawakami et al.²⁾ However, this should not be a big problem for CES-D given the accuracy and efficiency of this test. The usage fee of CES-D could be another

problem for its use in Japan; the fee is 84 yen (0.9 US dollars) for one individual test (in 2008). However, this cost could be acceptable because human and financial resources could be saved for further examinations due to the high screening efficiency of CES-D compared to K6.

In this study, we recommended that 1,001 candidates should participate in the screening survey, however, only 153 people accepted. Therefore, we cannot deny that there will be non-ascertained patients with MDD in the non-participants. However, the frequency of perceived mental disorder, and the prevalence of possible MDD were significantly lower in the non-participants even when these were compared with the SCID(-) participants. Consequently, the probability of including MDD patients in the non-participants would be very low. It is possible that some candidates did not judge themselves as MDD, and did not feel the necessity to participate. Furthermore, it would be ethically difficult to force people to receive screening when they do not want it. The low participation rate in this study was possibly due to the inclusion of SCID testing in the screening survey, the rate is expected to increase if only CES-D is used. Thus, administering CES-D testing to subjects who wish it would be a practical and efficient way to conduct a screening survey for MDD.

For this study, we selected 1,108 attendants during one month of a gastric-cancer survey, in model areas, as the target population, and identified 7 patients with MDD. If we extrapolate this discovery rate, we could expect to find approximately 100 patients with MDD if the target population was extended to all attendees of the gastric-cancer survey in Niigata City over a year (17,000 attendees/year). Meanwhile, approximately 200 people commit suicide every year in Niigata City. As socially inactive residents would not attend a voluntary event such as mass health screening, extending the benefits of the screening survey for such high risk MDD subjects²⁰⁻²⁴⁾ would be problematic. We observed that the number of consultations related to mental health disorders within the health-care sections of the municipality increased in the model areas following the screening survey.²⁵⁾ We also observed a similar increase in consultations in areas in which we conducted a different version of the screening survey in the previous year.²⁶⁾ As we provided information concerning the importance of preserving mental health to all attendants of the gastric-cancer survey, some attendants might have noticed signs of mental health disorders in their family members or acquaintances, and might have recommended that they consult with public health services. We will examine such indirect effects in

the future.

In summary, for the purpose of identifying MDD, CES-D is a more capable scale than K6 due to its increased accuracy and efficiency. In order to reduce the non-ascertainment of patients with MDD, the use of a more adequate criterion with a lower cutoff value than the conventional criterion (≥ 16 points) should be considered; we propose " ≥ 14 points" as the optimal criterion based on the data generated in this study. Administering CES-D testing to those who wish it after the proposal could be a practical way to efficiently identify patients with MDD.

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Figure legends

Figure 1 Screening performances of CES-D and K6 for identifying major depressive disorder evaluated by receiver operating characteristic curve analyses

CES-D, the Center for Epidemiologic Studies Depression Scale

The gold standard was major depressive disorder as determined by the Structured Clinical Interview for DSM-IV Axis-I Disorders.

Table 1. Characteristics of the study subjects and results of the mental health questionnaire survey by participation status in the screening survey for major depressive disorder and the results of SCID testing

	Participants in the screening survey				Non-participants		
	Total (n = 153)	SCID(+) (n = 7)	SCID(-) (n = 146)	<i>P</i>	(n = 848)	<i>P</i> vs. Total participants SCID (-)	
Age, years	63.7 ± 10.3	62.6 ± 8.6	63.7 ± 10.4	0.369	65.0 ± 10.1	0.161	0.191
Sex, number (%) of men	40 (26.1)	1 (14.3)	39 (26.7)	0.562	344 (40.6)	0.008	0.013
Perceived mental disorder†	94 (61.4)	6 (85.7)	88 (60.3)	0.402	319 (37.6)	<0.001	<0.001
Depressive symptoms during the last month							
Any	115 (75.2)	7 (100.0)	108 (74.0)	0.438	393 (46.3)	<0.001	<0.001
(1) depressed mood	26 (17.0)	5 (71.4)	21 (14.4)	<0.001	53 (6.3)	<0.001	<0.001
(2) reduction of interest or pleasure	18 (11.8)	3 (42.9)	15 (10.3)	0.014	48 (5.7)	0.007	0.041
(3) gain or loss of weight	21 (13.7)	2 (28.6)	19 (13.0)	0.278	79 (9.3)	0.112	0.728
(4) increased or decreased sleep	48 (31.4)	4 (57.1)	44 (30.1)	0.213	107 (12.6)	<0.001	<0.001
(5) increased or decreased levels of psychomotor activity	43 (28.1)	5 (71.4)	38 (26.0)	0.027	111 (13.1)	<0.001	<0.001
(6) fatigue	66 (43.1)	7 (100.0)	59 (40.4)	0.019	197 (23.2)	<0.001	<0.001
(7) feelings of guilt or worthlessness	16 (10.5)	3 (42.9)	13 (8.9)	<0.001	24 (2.8)	<0.001	<0.001
(8) diminished ability to concentrate	52 (34.0)	5 (71.4)	47 (32.2)	0.082	120 (14.2)	<0.001	<0.001
(9) recurring thoughts of death or suicide	4 (2.6)	2 (28.6)	2 (1.4)	<0.001	7 (0.8)	0.052	0.523
Possible major depressive disorder judged by the questionnaire survey‡	14 (9.2)	6 (85.7)	8 (5.5)	<0.001	17 (2.0)	<0.001	0.014

Data are mean ± standard deviation or number (%)

SCID, The Structured Clinical Interview for DSM-IV Axis-I Disorders; SCID(+) and SCID(-), positive and negative SCID testing for major depressive disorder, respectively

† Positive for perceived stress, distress, or anxiety

‡ Considered positive when any of (1) or (2) plus any three of other symptoms

Table 2. Results of the scales and SCID by sex and age

Age, years	n	Positive at conventional criteria				SCID(+)	
		CES-D(≥ 16)		K6(≥ 5)		n	(%)
		n	(%)	n	(%)	n	(%)
Men and women							
-44	10	0	(0.0)	4	(40.0)	0	(0.0)
45-54	19	5	(26.3)	6	(31.6)	2	(10.5)
55-64	44	9	(20.5)	26	(59.1)	2	(4.5)
65-74	62	5	(8.1)	19	(30.6)	3	(4.8)
75-	18	3	(16.7)	6	(33.3)	0	(0.0)
Total	153	22	(14.4)	61	(39.9)	7	(4.6)
Men							
-44	4	0	(0.0)	2	(50.0)	0	(0.0)
45-54	2	0	(0.0)	0	(0.0)	0	(0.0)
55-64	9	1	(11.1)	5	(55.6)	0	(0.0)
65-74	21	2	(9.5)	4	(19.0)	1	(4.8)
75-	4	0	(0.0)	1	(25.0)	0	(0.0)
Total	40	3	(7.5)	12	(30.0)	1	(2.5)
Women							
-44	6	0	(0.0)	2	(33.3)	0	(0.0)
45-54	17	5	(29.4)	6	(35.3)	2	(11.8)
55-64	35	8	(22.9)	21	(60.0)	2	(5.7)
65-74	41	3	(7.3)	15	(36.6)	2	(4.9)
75-	14	3	(21.4)	5	(35.7)	0	(0.0)
Total	113	19	(16.8)	49	(43.4)	6	(5.3)

CES-D, the Center for Epidemiologic Studies Depression Scale

Table 3. Screening performances of CES-D and K6 for identifying subjects with major depressive disorder using SCID as the gold standard

Criteria	Screening positive		Screening negative		Sensitivity	Specificity	Predictive value		NNT for SCID	
	SCID (+) [†]	SCID (-) [‡]	SCID (+) [§]	SCID (-) [¶]			Positive	Negative		
CES-D										
Conventional	≥16	6	16	1	130	0.86	0.89	0.27	0.99	3.7
Based on both YI ^{††} and ROC curve ^{‡‡}	≥14	7	22	0	124	1.00	0.85	0.24	1.00	4.1
K6										
Conventional	≥5	7	54	0	92	1.00	0.63	0.11	1.00	8.7
Based on YI ^{††}	≥6	7	44	0	102	1.00	0.70	0.14	1.00	7.3
Based on ROC curve ^{‡‡}	≥7	6	29	1	117	0.86	0.80	0.17	0.99	5.8

CES-D, Center for Epidemiologic Studies Depression Scale

NNT, number needed to test = 1/(positive predictive value), indicating the number of SCID tests required to identify one case with depression from screening positive subjects

[†], [‡], [§], [¶]; corresponds to true positives, false positives, false negatives, and true negatives of the screening test, respectively

^{††} The cutoff point was determined to maximize the Youden Index (YI; sensitivity + specificity - 1).

^{‡‡} The cutoff point was determined to minimize the distance between the receiver operating characteristic (ROC) curve and the upper-left corner of the graph (i.e., sensitivity = 1 and specificity = 0).

Fig. 1

