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## ORIGINAL RESEARCH Assessment of current clinical practices for major depression in Japan using a web-based questionnaire

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Purpose: To investigate the current clinical practice of Japanese physicians in the diagnosis and management of major depression (major depressive disorder [MDD]).

Patients and methods: Japanese physicians specializing in psychiatry or psychosomatic medicine in the medical database of Nihon Ultmarc Inc. (Chuo-Ku, Tokyo, Japan), who had treated  $\geq$ 30 patients with MDD in the past month were invited to complete a web-based questionnaire from January 15 to 29, 2018. The questionnaire was comprised of 28 questions pertaining to the physician's background, the criteria and tools used to diagnose MDD during physician-patient consultation, and actual and preferred duration of physician-patient consultation. Responses were given as single answer numerical values or as multiple-choice answers.

**Results:** From the 518 physicians invited to participate, 340 completed questionnaires were analyzed. Respondents were predominantly male (90%), hospital based (73%), affiliated with the Department of Psychiatry (95%), and members of the Japanese Society of Psychiatry and Neurology (87%). The majority of physicians (84%) agreed that "improvement of cognitive dysfunction caused by major depression is an important factor for patients to return to work" was the most challenging aspect of MDD diagnosis and management. Moreover, 83% of physicians conducted psychological assessments using a cognition evaluation test with most of their patients at the time of MDD diagnosis; the most commonly used tool was the Hasegawa Dementia Scale-Revised. Both hospital-based physicians and general practitioners would prefer to have longer consultations with their patients.

**Conclusion:** Physicians acknowledge the importance of the assessment and management of cognitive dysfunction in patients with MDD. However, most physicians would prefer to have longer consultation times with their patients for the diagnosis of MDD. In the future, it may be useful to introduce digital tools (eg, THINC-it<sup>®</sup>) for the initial screening of cognitive dysfunction.

Keywords: Japan, survey, diagnosis, management, major depression disorder

#### Introduction

Major depression (major depressive disorder [MDD]) is a common, costly, and heterogeneous psychiatric disorder, associated with decreased social functioning and increased mortality.<sup>1-3</sup> The 12-month prevalence of major depressive episodes in Japan is 2.2%, which is lower than high-income countries, including the US (8.3%), France (5.9%), and Germany (3.0%).<sup>1</sup> However, the prevalence of MDD in Japan is suggested to be higher than reported, as MDD is often underdiagnosed and therefore remains either inadequately treated or untreated.<sup>4–6</sup> Lower treatment rates

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of MDD in Japan compared with high-income Western countries may be due, in part, to the stigma associated with mental illness in Japan.<sup>6</sup>

In 2010, MDD was the leading cause of disabilityadjusted-life-years and the second leading cause of years lived with disability.<sup>7</sup> Severe MDD is a major contributor to suicide, which was a leading cause of death and accounted for approximately 788,000 deaths worldwide in 2015.<sup>8</sup> Lack of adherence to antidepressants poses additional challenges. There is a strong association between non-adherence and worsening patient clinical and economic outcomes.9 It has been reported that patients non-adherent to antidepressant medication were more likely to experience suicidal ideation, and were at increased risk of relapse and/or recurrence, emergency department visits, hospitalization rates, and increased severity of depression.<sup>9</sup> Several predictors of non-adherence have been reported including patient concerns about treatment-related side effects, medication dependence, and patients' beliefs, clinical factors (lack of patients education and follow-up), and social factors (isolation, poverty, lack of social support, low income, and educational level).<sup>10-14</sup> In addition to these, Pompili et al have reported younger age (<40 years), comorbidity with substance use and personality disorders, severity of illness, and poor therapeutic alliance between the patient and physician as indicators of non-adherence.<sup>15</sup> Given the high social, clinical, and economic impact of non-adherence among patients who are affected by mood disorders it is imperative to identify key predictors in order to recognize patients at risk for non-adherence.<sup>15</sup>

MDD is diagnosed by the appearance of mood disturbances; however, a multitude of symptoms are often present, and there is accumulating evidence that symptomatic treatment for mood disturbances may be insufficient for the treatment of MDD.<sup>16–19</sup> Cognitive dysfunction has been associated with psychosocial dysfunction and work impairment, including decreased work productivity and/or increased absenteeism.<sup>16,20–23</sup> Evidence suggests that management of cognitive function may improve patient outcomes in MDD.<sup>16</sup>

In recent years, guidelines have been generated and revised to standardize diagnostic tools for the diagnosis of psychiatric disorders.<sup>20,24–27</sup> Efforts have been made to determine clinical practices in the diagnosis of cognitive function in patients with MDD. For example, a web-based questionnaire targeting psychiatrists in the USA, France, Germany, Spain, Australia, and Hong Kong examined how

physicians assessed cognitive function among their patients with MDD;<sup>20</sup> however, cognitive evaluation was difficult to determine because of reliance on patient history rather than cognitive evaluation tools.<sup>20</sup> In Japan, there are a number of evaluation tools that can be used to measure MDD as well as cognitive function, including the Hamilton Depression Rating Scale (HAM-D), Montgomery-Åsberg Depression Rating Scale (MADRS), and Digit Symbol Substitution Test (DSST). The Perceived Deficits Questionnaire-Depression (PDQ-D) test is also available, however the Japanese version had not been validated at the time of the current survey.<sup>28</sup> We therefore designed a web-based questionnaire to investigate current clinical practice in the diagnosis and management of MDD. Our questionnaire included sections that focused on the challenges of accurate diagnosis and disease management of MDD; evaluation tools used for psychological and cognitive assessments; active assessments of physiological and psychological parameters of patients; and the duration of initial and follow-up consultations.

## Materials and methods Study design

This was a population-based, prospective, observational study conducted from January 15 to 29, 2018. Physicians in Japan were asked to complete a web-based questionnaire, which consisted of five sections and a total of 28 questions. There were two to seven questions per section pertaining to: 1) physician background (including the type of facility they practiced in, physicians age, expertise, and departmental affiliation); 2) criteria used to assess and diagnose MDD during patient consultation; 3) evaluation tools used to assess patients and their frequency of use; and 4) whether physicians were aware of cognitive dysfunction as a symptom of MDD and whether physicians actively diagnosed and managed such symptoms. Responses were given as single answer numerical values or as multiple-choice answers.

The questionnaire was delivered to physicians using a Social information service (Social Survey Research Information Co. Ltd., Tokyo, Japan) via Japan's medical professional website m3.com (<u>https://www.m3.com/</u>). Participants could save partially completed questionnaires for completion by January 29, 2018. The minimum number of responses by January 29, 2018 was set as 300.

Sample questionnaires are included in the supplementary materials (Tables S1 and S2).

## Study population

Hospital physicians and general practitioners who were registered on m3.com (<u>https://www.m3.com/</u>) were invited to participate in the survey. Physicians were screened via the Marc Inc. database in Japan and invited to participate if they were registered as specializing in psychiatry (code O01) or psychosomatic medicine (code A82) in the medical database of Nihon Ultmarc Inc. (Chuo-Ku, Tokyo, Japan), and had treated a minimum of 30 patients with MDD in the past month. There were no age restrictions.

Respondents consented to personal information protection guidelines, which stated that any information disclosed could not be used to identify individuals. All responses were anonymized. Physicians were not required to enter their name or other personal details. Due to multiple-choice or numerical response options, personal information of patients could not be disclosed. Due to the absence of direct patient involvement and clinical data ethics, approval was not required.

## Objectives

The primary objective was to examine the clinical practice of physicians in relation to the diagnosis and management of MDD in Japan. It can be hypothesized that 1) issues surrounding the clinical practice of MDD may differ depending upon the physicians' facilities, age, expertise, and participation in academic societies, 2) the diagnostic approach for MDD may not be standardized, 3) the use of the assessment batteries for MDD may be limited, 4) there may only be a small number of physicians who refer to the Japanese Society of Mood Disorders treatment guidelines,<sup>24</sup> and 5) clinical practices that consider cognitive impairment in MDD may be limited.

## Statistical analysis

Completed questionnaires were excluded if completed within 2 mins, or if the answers to a select number of questions were identical. Results were presented descriptively as percentages of physicians responding to the options provided for each question. Factors relating to: challenges in the clinical diagnosis and management of MDD; evaluation tools used for the diagnosis of MDD and assessment of cognitive dysfunction; and psychological and physiological parameters assessed for the diagnosis of MDD; and duration of initial and follow-up consultations, were assessed using the chi-squared test by physician facility. Physicians practicing at clinics were defined as general practitioners and those working in other facilities were categorized as hospital physicians. All statistical analyses were performed on Microsoft<sup>®</sup> Excel by Social Survey Research Information Co. Ltd.

## Results

## Physician background and demographics

A total of 518 physicians identified in the m3.com database (https://www.m3.com/) completed questionnaires. Of these, 164 questionnaires were excluded for the following reasons: the physician reported no adverse events (n=13), the clinical department was listed as "other" (n=25), the number of patients seen with MDD were <30 patients (n=119), or the questionnaire was not fully completed (n=7). Of the remaining 354 completed questionnaires, 14 were excluded for the following reasons: the number of patients was >2000 (n=1), the duration of the initial visit was shorter than follow-up (n=2), the questionnaire was completed within 3 mins (n=9), or the answers to questions 12, 14, 15, 16, 27, and 28 were the same (n=2). The remaining 340 completed questionnaires were included in the analysis. Responding physicians were predominantly male (90%), hospital-based (73%), worked in a city or urban area (77%), affiliated with a department or advertised their specialty as psychiatry (95%), or members of the Japanese Society of Psychiatry and Neurology (87%; Table 1). In addition, 47% of respondents were hospital physicians at psychiatric hospitals, 40.3% had treated between 30 and 49 patients in the past month, 36% had 10-19 years of experience in psychiatric treatment, and were predominantly in the 30-39 year-old, and 40-49 year-old age group (both 34%; Table 1). The median and mean time taken to complete the questionnaire was 6 and 32 mins, respectively. The variation was observed because physicians could save and later return to complete the questionnaire.

# Challenges in the clinical diagnosis and management of MDD

Of the 340 physicians, 285 (84%) agreed that "Improvement of cognitive dysfunction caused by major depression is an important factor for patients to return to work" was the most challenging clinical task in the diagnosis and management of MDD. In addition, 59% of physicians agreed that "Clinical manifestations alone are insufficient to understand individual symptoms" (Figure 1). There were no significant differences between hospital physicians and general practitioners

Table	I	Background	and	demographic	characteristics
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	(N=340)
Background	
Sex	
Male	306 (90)
Age in years	
≤29	6 (2)
30–39	65 (19)
40–49	114 (34)
50–59	116 (34)
≥60	39 (11)
Years of experience of psychiatric disorder	
assessment	<b>F</b> (1)
≤3	5 (1)
3–9	43 (13)
10–19	121 (36)
20–29	112 (33)
≥30	59 (17)
Number of patients with MDD treated in the past month	t
30-49	137 (40.3)
50-99	107 (31.5)
100–199	64 (18.8)
200–299	16 (4.7)
≥300	16 (4.7)
Facility	
Туре	
University hospital	40 (12)
Psychiatric hospital	159 (47)
General hospital	48 (14)
Clinic	93 (27)
Number of hospital beds in entire facility	
≤19	93 (27)
20–99	7 (2)
100–199	35 (10)
200–299	70 (21)
300–499	83 (24)
500–799	31 (9)
≥800	21 (6)
Location <sup>a</sup>	
Urban area	262 (77)
Other	78 (23)
Departmental affiliation and society memberships	
Departmental affiliation	
Psychiatric	324 (95)
Psychosomatic	16 (5)

Table I (Continued).

	Physicians, n (%)
	(N=340)
Graduate medical department	
Psychiatry	324 (95)
Psychosomatic	12 (4)
Others	4 (I)
Society membership	
The Japanese Society of Psychiatry and Neurology	297 (87)
Japanese Society of Mood Disorders	50 (15)
The Japanese Society of Clinical Neuropsychopharmacology	29 (9)
The Japanese Society of Neuropsychopharmacology	23 (7)
Japanese Association of Behaviour Therapy	14 (4)
Other	92 (27)
None	29 (9)

**Note:** <sup>a</sup>The definition of "Urban area" was left to the respondent's discretion. **Abbreviation:** MDD, major depressive disorder.

in their responses (Figure S1). For example, 85% of hospital physicians and 81% of general practitioners agreed that the factor most challenging in clinical practice was the treatment of MDD-caused cognitive dysfunction, which is important for patients to return to work (Figure S1).

#### Assessments for the diagnosis of MDD

The majority of physicians (n=281; 83%; Figure 2A) stated that they conducted psychological tests using an assessment tool with all or most of their patients at the time of mood disorder diagnosis. More than 50% of physicians were aware of, and performed, the Hasegawa Dementia Scale-Revised (HDS-R), Mini-Mental State Examination (MMSE), Zung Self-Rating Depression Scale (SDS), and HAM-D at time of mood disorder diagnosis (Figure 2B); whereas, overall, the Young Mania Rating Scale (YMRS), MADRS, Quick Inventory of Depressive Symptomatology-Japan (QIDS-J), and DSST were used by less than approximately 20% of physicians (Figure 2B). Hospital physicians were significantly more likely to use evaluation tools than general practitioners (Pvalue of <0.001 to 0.029; Figure 2C). A small but significantly higher proportion of hospital physicians used the MADRS (21%) compared with general practitioners (10%; P=0.015; Figure 2C); whereas neither group often or regularly used the DSST (hospital physician: 5%; general practitioners: 2%; Figure 2C).

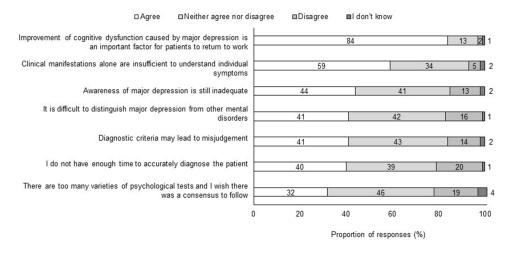
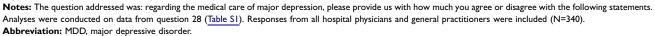


Figure I Challenges in the clinical diagnosis and management of MDD.



At diagnosis, the top three most assessed psychological and physiological parameters by physicians were: the patient's history of mental illness (91%), sleep patterns (91%), and background (89%; development, academic, and employment history, and marital status) (Figure 3A). Hospital physicians conducted significantly more physiological tests than general practitioners (all P<0.001) (Figure 3B). Types of physiological tests conducted included, basic physiological tests (eg, height, weight, vital signs), blood and urine tests, other physiological tests (scans, eg, electrocardiogram, electroencephalogram), and imaging (computed tomography, magnetic resonance imaging, and/or single photo emission computed tomography). There were no significant differences between hospital physicians and general practitioners with regard to the psychological tests that they performed during the initial diagnostic assessment by physician facility (Figure 3B).

## Consultation duration for initial and follow-up visits

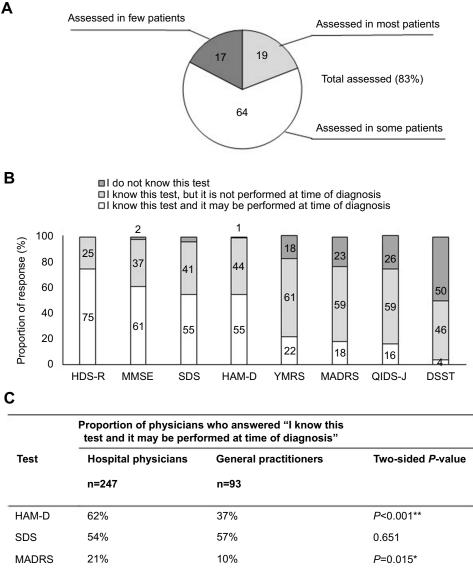
The mean most common duration of the initial consultation visit was approximately 30 mins, although physicians would ideally spend 45 mins or longer on the initial consultation (Figure 4A). Furthermore, 40% of physicians agreed that the duration of the initial visit was insufficient to make an accurate diagnosis. There was no significant difference between hospital physicians and general practitioners in the actual duration of the initial consultation (*P*=0.462; Figure 4B); however, further analysis demonstrated that hospital physicians' preferences regarding the ideal duration of the consultation were significantly different compared with that of general practitioners (*P*=0.008). The ideal duration of consultation preferred by 39% of hospital practitioners was >1 hr compared with 22% of general practitioners (*P*=0.003), and 41% of general practitioners preferring approximately 30 mins compared with 25% of hospital physicians (*P*=0.003).

The mean most common consultation duration at follow-up was 5 mins; however, similar to the results for initial visits (Figure 4), physicians would ideally have longer consultation durations than currently available at followup (10 mins; Figure 5).

#### Discussion

Cognitive dysfunction affects patients at varying degrees during phases of MDD.<sup>29</sup> Improvements in cognitive dysfunction are essential to improve patient outcomes, and therefore advances in assessing cognitive dysfunction are imperative. Such developments are not only important in Japan but also on a global scale given that depressive disorders are ranked as the single largest contributor to non-fatal decline in health worldwide (7.5% of all years lived with disability).<sup>8</sup> Our findings highlight important challenges to the diagnosis and management of MDD in Japan, which can be targeted to improve future clinical practice.

Overall, our study revealed that the majority of physicians valued the importance and challenges of diagnosis



Test	Hospital physicians	General practitioners	Two-sided <i>P</i> -value	
	n=247	n=93		
HAM-D	62%	37%	<i>P</i> <0.001**	
SDS	54%	57%	0.651	
MADRS	21%	10%	<i>P</i> =0.015*	
QIDS-J	18%	9%	<i>P</i> =0.029*	
YMRS	26%	10%	<i>P</i> <0.001**	
DSST	5%	2%	0.263	
HDS-R	75%	74%	0.833	
MMSE	66%	48%	<i>P</i> =0.002**	

Figure 2 Psychological assessments employed for the diagnosis of MDD.

Notes: (A) Proportion of physicians who employ psychological assessments. The question addressed was: in how many patients do you confirm and/or perform the following tests when you are diagnosing mood disorders? Analyses were conducted on data from question 14 (Table S1), and responses from all hospital physicians and general practitioners were included (N=340). (B) Psychological tests used to diagnose patients (all physicians). The question addressed was: are you aware of the following psychological tests? Do you perform these tests in clinical practice, when diagnosing a mood disorder? Analyses were conducted on data from question 15 (Table SI) and responses from all hospital physicians and general practitioners were included (N=340). (C) Psychological tests employed by physician facility. Analyses were conducted on data from question 15 (Table S1). Two-sided P-value was calculated using hypothesis testing for the difference in the population proportions (\*P<0.05; \*\*P<0.01).

Abbreviations: DSST, Digit Symbol Substitution Test; HAM-D, Hamilton Depression Rating Scale; HDS-R, Hasegawa Dementia Scale-Revised; MADRS, Montgomery-Åsberg Depression Rating Scale; MMSE, Mini-Mental State Examination; QIDS-J, Quick Inventory of Depressive Symptomatology-Japan; SDS, Zung Self-Rating Depression Scale; YMRS, Young Mania Rating Scale; MDD, major depressive disorder.

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A		В			
Assessed in most patients	ed in some patients Assessed in few patients		Proportion of physicians who answered "Assessed in most patients"		
History of mental illness	91 6 2	Psychological and physiological parameters	Hospital physicians	General practitioners	Two-sided <i>P</i> -value
Sleep patterns	91 6 2		n=247	n=93	
Patient background (development, academic, and employment history, and marital status)	89 8 3	Basic physiological assessments (height, weight, and vital signs)	51%	27%	<i>P</i> <0.001**
History of physical illness	84 14 2	Neurological assessments <sup>a</sup>	24%	15%	0.066
Family history of mental illness	83 14 3	History of mental illness	91%	92%	0.685
State prior to disease onset	81 17 2	History of physical illness	85%	81%	0.379
		Family history of mental illness	84%	80%	0.358
Stress evaluation Personality traits and habits before disease onset	78 18 5   68 27 5	Patient background (development, academic, and employment history, and marital status)	90%	86%	0.314
Blood and/or urine analysis	44 46 10	Personality traits and habits before disease onset	69%	65%	0.406
Basic physiological assessments (height, weight, and vital signs)	44 44 12	State prior to disease onset	81%	81%	0.946
Neurological assessments <sup>a</sup>	22 58 21	Stress evaluation	77%	78%	0.818
Psychological tests	19 64 17	Sleep patterns	91%	90%	0.733
rsychological tests	19 64 17	Blood and/or urine analysis	55%	16%	P<0.001**
Other physiological tests (ECG and EEG) Imaging (CT, MRI, and/or SPECT)	17 57 26 16 60 23	Other physiological tests (ECG and EEG)	22%	4%	<i>P</i> <0.001**
	0 20 40 60 80 100	Imaging (CT, MRI, and/or SPECT)	21%	5%	<i>P</i> <0.001**
	Proportion of responses (%)	Psychological tests	18%	23%	0.319

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Figure 3 Psychological and physiological parameters assessed at the time of MDD diagnosis.

**Notes:** (**A**) All physicians. The question addressed was: in how many patients do you confirm and/or perform the following tests when you are diagnosing mood disorders? Analyses were conducted on data from question 14 (Table S1) and responses from all hospital physicians and general practitioners were included (N=340). (**B**) By physician facility. Analyses were conducted on data from question 14 (Table S1) (\*\*P<0.01). <sup>a</sup>Neurological assessments included consciousness/mental state, language, cranial nerve examinations, motor, sensory and reflex system tests, coordination movement, meningeal irritation signs, posture, autonomic system assessments.<sup>43</sup> Two-sided *P*-value was calculated using hypothesis testing for the difference in the population proportions.

Abbreviations: CT, computed tomography; ECG, electrocardiogram; EEG, electroencephalogram; MRI, magnetic resonance imaging; SPECT, single photo emission computed tomography; MDD, major depressive disorder.

and management of cognitive dysfunction in patients with MDD, and agreed that clinical manifestations alone were insufficient to understand individual symptoms. Moreover, most physicians performed psychological tests to examine cognitive function in patients, with the HDS-R being the most popular. Notably, there was a discrepancy between most common and ideal consultation duration for MDD diagnosis.

The key symptoms of MDD include physical manifestations (eg, decreased energy and sleep disturbance) and cognitive symptoms (eg, decreased motivation and difficulty with concentration).<sup>30</sup> Clinical and patient perspective studies suggest that cognitive dysfunction is the primary cause of functional impairment.<sup>16,19,28,30,31</sup> In a previous web-based questionnaire by El Hammi et al, 93% of physicians assessed cognition in MDD. In accordance with this, the majority of physicians in the current study (84%) agreed that improvement of cognitive dysfunction caused by MDD was an important factor in assisting patients to return to work and the most challenging clinical task in the diagnosis and management of MDD (Figure 1). However, MDD is a heterogeneous disorder, with multiple psychological tests used for assessing cognitive dysfunction subjectively (eg, MADRS), and objectively (DSST).<sup>29,32</sup> Cognitive tests to assess cognitive dysfunction are not described in available guidelines;<sup>24,25</sup> however, 59% of physicians in our study agreed that clinical manifestations alone were insufficient to understand individual patient's symptoms in MDD. Most Japanese physicians used psychological tests to assess cognitive dysfunction in their patients (Figure 2A). The HDS-R was the most widely known and used test (Figure 2B). One major reason for the popularity of tests such as HDS-R and MMSE may partially be due to a combination of the aging Japanese population, and the need to distinguish dementia and MDD in older patients. Other tests such as the SDS may be used more often than others, as physicians are reimbursed. Of note, the MADRS, QIDS-J, and DSST assessments are among those that can evaluate aspects of cognitive function in MDD; however, they are the least acknowledged and performed (Figure 2B). The DSST is a simple and easy-to-use test for cognition (assessing a combination of processing speed, working memory, attention and executive function) in MDD, as well as brain damage, and dementia.<sup>28,33–35</sup> The low acknowledgment and use of the test may be because it does not screen for disease or provide

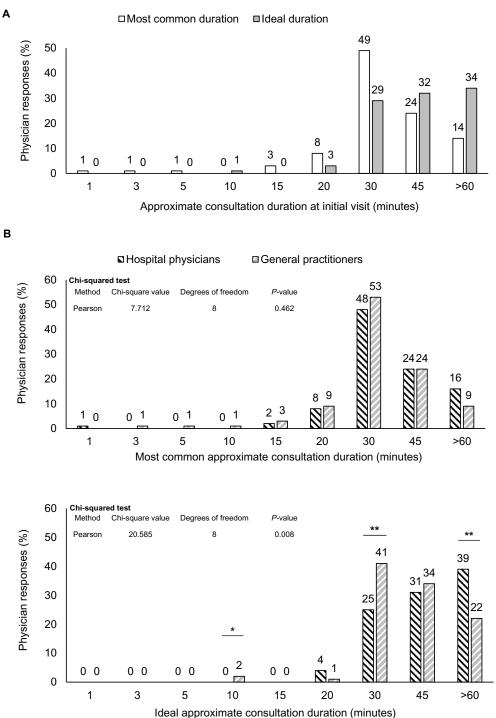
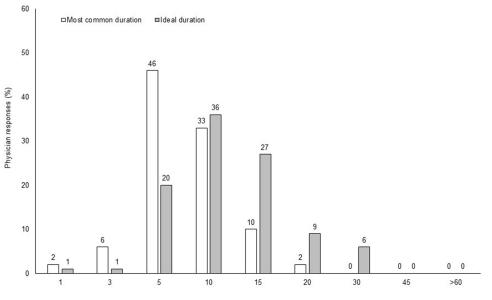


Figure 4 Most common and ideal consultation duration at initial visit.

**Notes:** (**A**) All physicians. The question addressed was: what is the most common consultation duration for your patients with major depression? What is the ideal consultation duration for an accurate diagnosis and evaluation? Analyses were conducted on data from question 19 (Table S1) and responses from all hospital physicians and general practitioners were included (N=340). Consultation durations are approximate lengths. (**B**) By physician facility. Analyses were conducted on data from question 19 (Table S1) (\*P=0.021; \*\*P=0.003). Consultation durations are approximate lengths.

insurance reimbursement in Japan, like other tests such as the SDS.

Hospital physicians were significantly more likely to know and use the psychological tests HAM-D, MADRS, QIDS-J, YMRS, and MMSE during mood disorder diagnosis than general practitioners (*P*-value between <0.001 and 0.029). The differences observed in this study between hospital physicians and general practitioners may be because clinical



Consultation duration at follow-up visit (minutes)

Figure 5 Most common and ideal consultation duration for follow-up visit.

Notes: The question addressed was: what is the most common consultation duration for your patients with major depression? What is the ideal consultation duration for an accurate diagnosis and evaluation. Analyses were conducted on data from question 19 (<u>Table S1</u>) and responses from all hospital physicians and general practitioners were included (N=340). Consultation durations are approximate lengths.

research is often performed in hospitals versus clinics. Additionally, hospital physicians examined physiological parameters significantly more often than general practitioners at the time of diagnosis, with <20% of general practitioners conducting blood and/or urine analysis, neurological assessments, scans, and imaging. This discrepancy may be due to the differences between routine examinations at a hospital versus a clinic and the lack of accessibility of facilities, eg, imaging tools.

Notably, both hospital physicians and general practitioners preferred to have longer initial and follow-up than actual consultation duration. Although the most common consultation length was comparable between hospital physicians and general practitioners, hospital physicians preferred to have significantly longer consultation length at first visit compared with general practitioners (P=0.008). One possible reason for this difference may be because patients with severe MDD are more likely to visit a hospital than a clinic and thus, require more time for a differential diagnosis. In addition, physicians may not be using some tests due to limited duration of consultation with patients. For example, the HAM-D test takes approximately 20-40 mins to complete (Table 2). It may be useful to introduce digital tools for the initial screening of cognitive dysfunction. THINC-it® (http://thinc.progress.im/en/content/thinc-it-tool) is a cognitive functioning screening tool that assesses subjective and

Table 2	Average	times	taken	to	perform	cognitive-behavioral
tests						

Test	Time taken (minutes)
HDS-R <sup>39</sup>	Approximately 10
MMSE <sup>40</sup> *	10–15
SDS*	10–15
HAM-D <sup>41</sup> *	2040
YMRS <sup>42</sup>	15–30
MADRS*	2040
QIDS-J*	10–15
DSST*	2

Note: \*In authors personal experience.

Abbreviations: DSST, Digit Symbol Substitution Test; HAM-D, Hamilton Depression Rating Scale; HDS-R, Hasegawa Dementia Scale-Revised; MADRS, Montgomery–Åsberg Depression Rating Scale; MMSE, Mini-Mental State Examination; QIDS-J, Quick Inventory of Depressive Symptomatology-Japan; SDS, Zung Self-Rating Depression Scale; YMRS, Young Mania Rating Scale.

objective cognitive function, in conjunction with a patientreported questionnaire.<sup>36</sup> THINC-it has been developed to fulfill an unmet need for a reliable, valid, and sensitive assessment tool to evaluate cognitive function impairment in patients with MDD. Using a battery of domain-specific tests, THINC-it comprises four validated objective tests; nback memory task (Symbol Check), digit symbol substitution (CodeBreaker), trail making test – part-B (Trails), and choice reaction time (Spotter). These tasks test working memory, visuospatial coordination, set shifting and

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psychomotor speed. Subjective cognition is evaluated using a five-item Perceived Deficits Questionnaire (PDQ-D5). All of the components can be completed within 20 mins. THINC-it has demonstrated high levels of reliability and stability<sup>37</sup> and validation has shown that subjective and objective cognitive function were impaired in patients with MDD relative to healthy controls.<sup>38</sup>

This study has several limitations. The key limitation of this study was that physicians were surveyed about which evaluation tools they acknowledged and used in general, and did not investigate their use of each evaluation tool for the phase of MDD, or at what stage in consultations, eg, initial or follow-up. Moreover, not all choices of evaluation tools for the assessment of cognitive dysfunction were included in the survey, eg, PDQ-D and the Brief Assessment of Cognition in Schizophrenia. Future studies may be required to determine what evaluation tools are used at different time points. This study was limited to physicians practicing in Japan, and moreover the target population may not be representative of all MDD-treating physicians in Japan because it was a web-based survey of an existing online database. Systematic bias and random variance may have occurred due to the questionnaire design (eg, ambiguous, confusing or biased questions and/or response options) or respondents (eg, misreporting true attitudes). Furthermore, 90% of the respondents were male, which may have created a bias toward the clinical preferences of male practitioners.

## Conclusion

In conclusion, physicians in Japan acknowledge the importance and challenges of the diagnosis and management of cognitive dysfunction in patients with MDD. The majority of physicians reported a preference for a longer duration of physician–patient consultations for the diagnosis of MDD. There was a significant difference between hospital physicians and general practitioners regarding the ideal duration of initial consultation. Currently, it may be a challenge difficult for physicians to immediately implement longer consultations with their patients. Therefore, in the future, it may be useful to ensure collaborative team-based strategies whereby cognitive tests are administered by other practitioners such as a nurse, counselor, or pharmacist, or introduce digital tools such as THINC-it for the initial screening of cognitive dysfunction.<sup>38</sup>

## Ethics approval and informed consent

All participants consented to the personal information protection law and their guidelines. All responses were anonymized and ethics approval was not required.

## **Abbreviations**

DSST, Digit Symbol Substitution Test; ECG, electrocardiogram; EEG, electroencephalogram; HAM-D, Hamilton Depression Rating Scale; HDS-R, Hasegawa Dementia Scale-Revised; MADRS, Montgomery–Åsberg Depression Rating Scale; MDD, major depressive disorder; MMSE, Mini-Mental State Examination; PDQ-D, Perceived Deficits Questionnaire-Depression; QIDS-J, Quick Inventory of Depressive Symptomatology-Japan; SDS, Zung Self-Rating Depression Scale; YMRS, Young Mania Rating Scale.

## Data sharing statement

Takeda makes patient-level, de-identified data sets and associated documents available after applicable marketing approvals and commercial availability have been received, an opportunity for the primary publication of the research has been allowed, and other criteria have been met as set forth in Takeda's Data Sharing Policy (see <u>https://www.takedaclinicaltrials.com</u> for details). To obtain access, researchers must submit a legitimate academic research proposal for adjudication by an independent review panel, who will review the scientific merit of the research and the requestor's qualifications and conflict of interest that can result in potential bias. Once approved, qualified researchers who sign a data sharing agreement are provided access to these data in a secure research environment.

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#### Disclosure

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