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REGULAR ARTICLE

Live two-way video versus face-to-face treatment for depression, anxiety, and obsessive-compulsive disorder: A 24-week randomized controlled trial

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Aim: Live two-way video, easily accessible from home *via* smartphones and other devices, is becoming a new way of providing psychiatric treatment. However, lack of evidence for real-world clinical setting effectiveness hampers its approval by medical insurance in some countries. Here, we conducted the first large-scale pragmatic, randomized controlled trial to determine the effectiveness of long-term treatment for multiple psychiatric disorders *via* two-way video using smartphones and other devices, which are currently the primary means of telecommunication.

Methods: This randomized controlled trial compared two-way video *versus* face-to-face treatment for depressive disorder, anxiety disorder, and obsessive-compulsive disorder in the subacute/maintenance phase during a 24-week period. Adult patients with the above-mentioned disorders were allocated to either a two-way video group (≥50% video sessions) or a face-to-face group (100% in-person sessions) and received standard treatment covered by public medical insurance. The primary outcome was the 36-Item Short-Form Health Survey Mental Component Summary (SF-36 MCS) score. Secondary outcomes included all-cause discontinuation, working alliance, adverse events, and the severity rating scales for each disorder.

Results: A total of 199 patients participated in this study. After 24 weeks of treatment, two-way video treatment was found to be noninferior to face-to-face treatment regarding SF-36 MCS score (48.50 vs 46.68, respectively; $p < 0.001$). There were no significant differences between the groups regarding most secondary end points, including all-cause discontinuation, treatment efficacy, and satisfaction.

Conclusion: Two-way video treatment using smartphones and other devices, was noninferior to face-to-face treatment in real-world clinical settings. Modern telemedicine, easily accessible from home, can be used as a form of health care.

Keywords: *anxiety disorder, depression, long-term treatment, obsessive-compulsive disorder, two-way video.*

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Since psychiatric outpatient care primarily involves face-to-face conversations, physician-to-patient telemedicine *via* live two-way video is easily applicable in this field and has long been used.[1] Moreover, this expanded into worldwide use with the coronavirus disease 2019 (COVID-19) pandemic. According to a survey conducted by the World Health Organization, 70% of the 130 countries surveyed had telemedicine in place to continue providing psychiatric and mental health services during the pandemic.[2] This increase in use may partially be due to advances in information and communication technology that have led many people to own smartphones and other devices. As a result, two-way video has become a familiar means of telecommunication that can be easily and conveniently performed using these devices. Another main reason is the deregulation that took place in many countries around the world during the pandemic period.[3,4]

Even before the pandemic, many studies have compared the effectiveness of two-way video and face-to-face treatment and reported that two-way video treatment can provide comparable or better treatment efficacy, patient satisfaction, and medication adherence.[5–8] We recently conducted a meta-analysis including 32 randomized controlled trials (RCTs) and found that, in general, two-way video has comparable treatment effects compared with face-to-face treatment.[9] However, most existing studies focused only on a single disorder, such as depression or posttraumatic stress disorder, and only three RCTs looked at multiple conditions simultaneously.[10–12] Furthermore, these RCTs were conducted under special conditions, such as with a dedicated line set up between clinics and patients visiting one clinic to be seen by a psychiatrist who was physically present at another clinic.[10–12] More importantly, many of these trials did not necessarily examine long-term treatment effects. The majority of psychiatric treatment is subacute or maintenance treatment, and the possibility that long-term treatment *via* two-way video may be less effective or that the physician-patient relationship may differ from face-to-face treatment should be considered. These validations are especially important now that smartphones and tablets with smaller screens are being used by patients treated at home rather than in a dedicated room with a large screen and a dedicated line for two-way video calls.

Although Japan is a developed country with a robust health care infrastructure, the use of two-way video is not widespread because of regulations as well as other factors such as restrictions on prescribing drugs used in psychiatry and reimbursement prices being lower than those for face-to-face treatment.[3,13] Behind this strict regulation of telemedicine was the concern that it would accelerate inappropriate prescribing of benzodiazepine and Z-drugs,[14] which have become a problem in Japanese psychiatric care,[15] and the lack of evidence in Japan.[13,16] Furthermore, although Japan has several unique circumstances, such as universal health insurance, relatively low treatment costs, and a busy medical workforce,[17–19] there is still no evidence regarding the effectiveness, safety, and patient satisfaction of two-way video compared with face-to-face treatment.

Therefore, the current study was designed to validate telemedicine in the new era of easy access to medical care from home, mainly through smartphone usage. To the best of our knowledge, this was the largest pragmatic trial that has followed the course of treatment for 6 months or longer, targeting multiple psychiatric disorders. In particular, this was the first trial of its kind to compare two-way video using smartphones and other devices with face-to-face treatment.

As mentioned earlier, telemedicine is not fully covered by insurance in Japan. To promote better policy-making, it is important to conduct pragmatic trials tailored to each country's health care system. This trial also plays a role in establishing evidence for telemedicine in Japan, including areas other than psychiatry.

Methods

Study Design

Details regarding the study methods and protocols have been previously published.[20] This was a multisite, prospective RCT. Patients were assigned in a 1:1 ratio to either a two-way video group (at least 50% of treatment sessions to be conducted by two-way video, with at least one face-to-face session within 6 months) or the face-to-face group (all treatments sessions to be face-to-face). Patients in the two-way video group interacted with their psychiatrists from a private location, such as their home or office, using a smartphone, tablet, or personal computer. Both groups received standard treatment covered by public medical insurance for 24 weeks. The intervals between treatments were determined at the discretion of the psychiatrist in charge.

Participants

Participants were recruited at 19 medical institutions providing psychiatric services in 11 prefectures in Japan between April 2021 and February 2022.

Patients were included based on the following inclusion criteria: (1) met DSM-5[21] criteria for depressive disorders, anxiety disorders, or obsessive-compulsive disorder (OCD) and related disorders and were outpatients at a participating medical institution; (2) were 18 years or older at the time of obtaining consent; (3) needed continuous treatment for the next 6 months or more (at the discretion of the attending physician); (4) had a smart phone or personal computer as well as access to video-calling over the internet (even if available only with family support); (5) their psychiatric condition was stable enough for them to undergo two-way video treatment, based on the clinical judgment of the attending physician; (6) their psychiatric condition was stable enough for them to have sufficient capacity to provide consent, based on the clinical judgment of the attending physician; and (7) provided written consent to participate in the study. For patients who were minors (younger than 20 years), written consent had to be obtained from the patient and his/her guardian.

The exclusion criteria were as follows: (1) likelihood of requiring unscheduled or urgent treatment at a hospital in addition to regular treatment because of emergent suicidal ideation, anxiety, or agitation; and (2) patients who would have had difficulty in managing an emergency visit by themselves if their psychiatric condition deteriorated (e.g. the hospital was far away).

Randomization

Participating patients were randomly assigned in a 1:1 ratio to either the two-way video group or the face-to-face group for treatment during the study period. To avoid interinstitutional differences and biases

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among the groups regarding types of disorders, randomization was performed by a blinded, independent third party using a modified minimization method and biased-coin assignment[22] balanced for age group (≥60 years or <60 years), sex (male or female), target disorder, and participating institution. Additionally, the allocation results were not disclosed to the central evaluator to minimize bias.

Assessment Schedule

After randomization, participants completed the following assessments through self-rating scales and interviews as baseline assessments and again at weeks 12 and 24.

Primary Outcome

The primary outcome was the 36-Item Short-Form Health Survey Mental Component Summary (SF-36 MCS) score at week 24. The SF-36, a scientifically validated and reliable instrument for assessing health-related quality of life, consists of a self-administered questionnaire[23] to which patients in this study responded through a dedicated application. The SF-36 MCS focuses on mental items and was used because the present study targets multiple psychiatric disorders.

Secondary Outcomes

The following secondary outcomes were assessed: (1) SF-36 Physical Component Summary (PCS) scores; (2) all-cause discontinuation (in the two-way video group, if the patient discontinued two-way video and switched to face-to-face treatment only, the patient was considered to have dropped out of the two-way video group; (3) Working Alliance Inventory (WAI) score (assessed at weeks 12 and 24) as a measure of treatment alliance[24]; (4) Client Satisfaction Questionnaire (CSQ) score (assessed at weeks 12 and 24) for assessing satisfaction[25]; (5) adverse events; (6) cost and time (assessed using a self-administered questionnaire on costs and time associated with medical treatments); (7) EuroQol 5 Dimension (EQ-5D) score (assessed at baseline and at weeks 12 and 24) as another measure of health-related quality of life[26]; (8) degree of anxiety regarding coronavirus disease 2019 (COVID-19); (9) comments about two-way video; (10) for the depressive disorder group, the Hamilton Depression Rating Scale (HAMD) score[27]; (11) for the anxiety disorder group, the Hamilton Anxiety Rating Scale (HAMA) score[28]; and (12) for the OCD and related disorders group, the Yale-Brown Obsessive Compulsive Scale (YBOCS) score.[29]

Sample Size

The sample size was calculated based on previous psychiatric intervention studies (including those involving psychotherapy and electroconvulsive therapy interventions), in which the evaluation period was 6 months.[30–35]

In previous studies, the mean SF-36 MCS scores ranged from 30 to 50 (SD, 9–14). In the present study, assuming that an SF-36 MCS score of 45 in both the two-way video and face-to-face groups at 6 months (no difference between the two groups), with an SD of 12 and a noninferiority margin of five, the required number of patients in each group would be 92 under the conditions of 80% power and a one-sided significance level of 2.5%.

The all-cause discontinuation rate was expected to be low in this study, because the primary psychiatrist who had been treating a patient until the time of the study would continue to be in charge of the treatment, regardless of whether the patient was in the two-way video or face-to-face group. Assuming an all-cause discontinuation rate of approximately 10%, the total number of required patients was calculated as 200, or 100 in each group.

Data Collection and Management

Data on the SF-36 MCS and SF-36 PCS scores, treatment alliance and satisfaction measures, cost, EQ-5D score, and degree of anxiety about COVID-19 were collected as self-administered patient-reported values. All such electronic patient-reported outcome data were collected through the participants' smartphones using an electronic data capture system. For the HAMD, HAMA, and YBOCS scores, remote centralized ratings were obtained through two-way video. Evaluators were required to have completed a total of at least 30 h of training on these evaluation items.

Statistical Analyses

The full analysis set (FAS), which included all patients who completed at least one SF-36 MCS assessment during the study period and did not present any serious violation of the study protocol or the ethical research guidelines, was used for the analysis of the primary outcome. The per-protocol set (PPS), which is the supplemental analysis population for the primary outcome, was defined as the population excluding patients in serious violation of the study protocol from among the FAS, i.e. (1) violation of selection/exclusion criteria; (2) violation of discontinuation criteria; (3) violations related to therapies for which concomitant use was prohibited; and (4) lack of follow-up data. The primary analysis was performed for FAS and PPS, and secondary efficacy analyses and exploratory analyses were conducted only for FAS. Safety analysis was performed on the safety analysis set, which was defined as the set of patients enrolled in the study and who underwent at least one SF-36 MCS assessment in addition to that at baseline. As appropriate, χ^2 and Fisher exact tests were used for categorical variables, while Wilcoxon rank sum test and *t* test were employed for continuous variables. In the primary analysis, point estimates and their 95% confidence intervals were estimated for each time point using a mixed-effects model for repeated measures. The correlation structure was assumed to be unstructured. Adjustment factors for allocation were adjusted, a restricted maximum likelihood estimator was used as the estimator of each parameter, and the Kenward-Roger method was used to estimate the variance of the parameter estimators and the degrees of freedom.[36] The noninferiority margin was set to −5. The statistical analysis plan was developed by the principal investigator and the biostatistician before the completion of patient recruitment and data fixation. A one-sided *P*-value <0.025 and a two-sided *P*-value <0.05 were considered statistically significant. Statistical analyses were performed with SAS version 9.4 (SAS Institute Inc.).

In addition to the analyses described above, the possibility was considered that there might have been a difference in the efficacy of the treatment in the two-way video group that used as many telemedicine visits as possible versus the group that did not. Therefore, as a *post hoc* analysis, we performed the same analysis for the primary end point in the patients' group that had 100% of their postbaseline visits performed *via* two-way video.

Ethical Considerations

This study was approved by the institutional review board of the National Center of Neurology and Psychiatry and the participating medical facilities. The trial was registered with the Japan Registry of Clinical Trials (jRCT1030210037). Written informed consent was obtained from all participants. The study procedures were conducted according to the Declaration of Helsinki.

Results

A total of 199 patients were assessed for eligibility, provided consent to participate in the study, and were randomized into either the two-way video or face-to-face group. One hundred five patients were allocated to the two-way video group (53 with a depressive disorder, 34 with an anxiety disorder, and 18 with OCD) and 94 patients were allocated to the face-to-face group (45 with a depressive disorder, 32 with an anxiety disorder, and 17 with OCD). Seven patients in the two-way video group discontinued intervention due to the following reasons: withdrawal of consent ($n = 1$), failure to meet the inclusion criteria ($n = 1$), adverse event ($n = 1$), patient request ($n = 1$), time commitment challenges ($n = 1$), and other reasons ($n = 2$). Four patients in the face-to-face group discontinued intervention due to the following reasons: loss to follow-up ($n = 3$) and withdrawal of consent ($n = 1$). The CONSORT (Consolidated Standards of Reporting Trials) diagram for this study is presented in the Fig. 1

Table 1 presents the baseline demographic and clinical characteristics of the participants. No significant differences were noted between the two groups, including in terms of age, sex, disease duration, and total treatment period. In the two-way video group, the average percentage of two-way video use after baseline was 76.95% ± 22.93%. Of these, there were a total of 38 patients who utilized two-way video 100% of the time.

Primary Outcome

The SF-36 MCS scores at week 24 in the two-way video and face-to-face groups were 48.50 ± 9.57 and 46.68 ± 10.58, respectively. The criteria for noninferiority, for which the margin was set as −5.0, were met (mean between-treatment group difference, 1.82; 95% confidence interval, −1.12 to 4.77; $P < 0.0001$) (Table 2). With regard to sensitivity analysis based on the PPS, the criteria for noninferiority were also met, with a mean between-treatment group difference of 1.90 points (48.50 ± 9.57 vs 46.60 ± 10.62 in the two-way video and face-to-face groups, respectively [95% confidence interval, −1.06 to 4.86]; $P < 0.0001$). As a *post hoc* analysis, only the patients who utilized two-way video 100% of the time were extracted. The SF-36 MCS scores at week 24 for that group were 47.58 ± 9.16, and the criteria for noninferiority in the face-to-face group were also met (Supplementary Table S1).

Secondary Outcomes

There was no significant difference between the two-way video and face-to-face groups with regard to the SF-36 MCS score at week 12 ($P = 0.38$) or the SF-36 PCS scores at weeks 12 and 24 (Table 3).

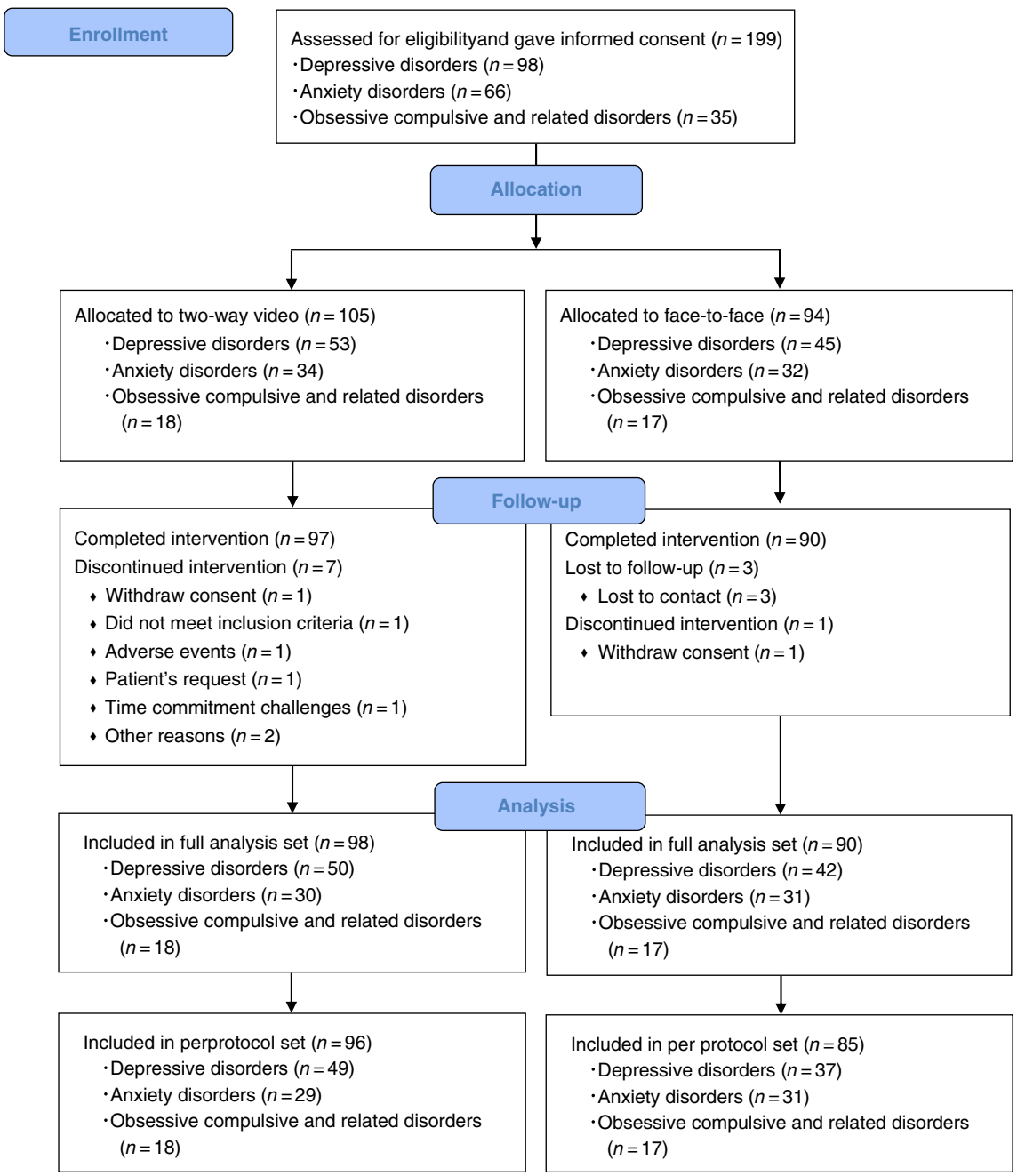

Fig. 1 CONSORT (Consolidated Standards of Reporting Trials) diagram of participant flow through the study.

Table 1. Baseline demographic and clinical characteristics

	Two-way video ($n = 98$)	Face-to-face ($n = 90$)	*P*-value
Age (years)	39.7 ± 11.9	40.7 ± 11.9	0.55
Sex (female), *n* (%)	48 (49.0)	46 (51.1)	0.88
Psychiatric history			
Duration since the first episode (months)	105.1 ± 90.3	105.7 ± 99.5	0.97
Duration since current episode (months)	82.7 ± 78.5	72.2 ± 83.2	0.38
Duration of total treatment (months)	78.5 ± 73.6	79.9 ± 78.9	0.90
Duration of treatment by a current physician	38.0 ± 45.5	35.4 ± 37.5	0.66
Diagnosis, *n* (%)			
Depressive disorder	50 (51.0)	42 (46.7)	
Anxiety disorder	30 (30.6)	31 (34.4)	
OCD and related disorders	18 (18.4)	17 (18.9)	
Measures			
HAMD-17 (depressive disorders only)	8.3 ± 1.5	6.1 ± 1.5	0.08
HAMA (anxiety disorders only)	10.2 ± 1.9	11.5 ± 2.1	0.42
YBOCS (OCD and related disorders only)	14.1 ± 1.8	15.6 ± 2.1	0.51

Data are mean ± SD unless otherwise indicated.
EQ-5D, EuroQol 5 Dimension; HAMA, Hamilton Anxiety Rating Scale; HAMD, Hamilton Depression Rating Scale; OCD, obsessive-compulsive disorder; SF-36 MCS, 36-Item Short-Form Health Survey Mental Component Summary; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Table 2. SF-36 MCS

	Weeks	Two-way video	Face-to-face	Difference in mean (95% CI)	*P*-value
Noninferiority tests (margin: −5)					
SF-36 MCS (FAS)	24	48.50 ± 0.57 ($n = 96$)	46.68 ± 10.58 ($n = 86$)	1.82 (−1.12 to 4.77)	<0.0001
MMRM					
SF-36 MCS (FAS)	0 (baseline)	47.96 ± 1.88 ($n = 98$)	45.44 ± 1.92 ($n = 90$)	2.52 (−0.13 to 5.17)	0.06
	12	47.55 ± 1.88 ($n = 98$)	46.36 ± 1.92 ($n = 89$)	1.19 (−1.47 to 3.84)	0.38
	24	48.97 ± 1.90 ($n = 96$)	47.50 ± 1.95 ($n = 86$)	1.48 (−1.33 to 4.29)	0.30
Noninferiority tests (margin: −5)					
SF-36 MCS (PPS)	24	48.50 ± 9.57 ($n = 96$)	46.60 ± 10.62 ($n = 85$)	1.90 (−1.06 to 4.86)	<0.0001
MMRM					
SF-36 MCS (PPS)	0 (baseline)	48.26 ± 1.88 ($n = 96$)	46.13 ± 1.92 ($n = 85$)	2.13 (−0.05 to 4.83)	0.12
	12	47.89 ± 1.88 ($n = 96$)	46.71 ± 1.92 ($n = 85$)	1.18 (−1.50 to 3.86)	0.39
	24	49.30 ± 1.91 ($n = 96$)	47.75 ± 1.95 ($n = 85$)	1.55 (−1.27 to 4.37)	0.28

Data are mean ± SD.
CI, confidence interval; FAS, full analysis set; MMRM, mixed-effect model for repeated measure; PPS, per protocol set; SF-36 MCS, 36-Item Short-Form Health Survey Mental Component Summary.

The eight SF-36 subscale scores at weeks 12 and 24 also did not differ significantly between the two groups. All-cause discontinuation was found in one case (1%) in the two-way video group and one case (1.1%) in the face-to-face group, with no statistically significant difference ($P = 0.95$). There was no significant difference in the WAI or CSQ scores ($P = 0.25$) between the two groups at weeks 12 and 24. There were four cases of adverse events in the two-way video group and five in the face-to-face group, with no significant difference between the groups with respect to the risk of adverse events ($P = 0.7$). Most of the adverse events consisted of physical illnesses such as cholecystitis, posterior longitudinal ligament ossification, and abdominal pain, which were not related to the intervention.

Regarding the time required for hospital visits, the two-way video group spent less time than the face-to-face group (42.9 ± 40.8 min in the two-way video group and 79.2 ± 61.6 min in the face-to-face group, respectively; $P < 0.001$). Regarding the costs incurred for hospital visits (including communication costs for two-way video), nonparametric tests were used because there was a large variation in costs and high outliers due to the variety of forms of hospital visits and the readiness of the communication environment. As a result, the two-way video group paid less than the face-to-face group (median, 168.9 [interquartile range, 0–793.3] Japanese yen in the two-way video group and 500.0 [interquartile range, 140.0–1266.7] yen for the face-to-face group, respectively, $P = 0.01$) (Table 4). The number of work days missed for treatment sessions averaged 1.5 ± 2.5 in the two-way video group and 2.6 ± 7.1 in the face-to-face group, with no significant difference between the two groups ($P = 0.15$). The EQ-5D scores did not differ significantly between the two groups ($P = 0.97$).

There were no significant differences in disease severity between the two groups at 12 and 24 weeks as assessed based on the HAMD,

Table 3. Secondary outcomes

	Weeks	Two-way video	Face-to-face	Difference in mean (95% CI)	*P*-value
SF-36 PCS	0 (baseline)	48.19 ± 1.72 ($n = 98$)	48.35 ± 1.77 ($n = 90$)	−0.17 (−2.63 to 2.30)	0.90
	12	47.92 ± 1.71 ($n = 98$)	47.06 ± 1.75 ($n = 89$)	0.86 (−1.51 to 3.24)	0.48
	24	49.48 ± 1.75 ($n = 96$)	47.49 ± 1.79 ($n = 86$)	2.00 (−0.60 to 4.60)	0.13
WAI	12	71.7 ± 2.8 ($n = 98$)	68.1 ± 2.9 ($n = 87$)	3.6 (−0.1 to 7.4)	0.06
	24	71.6 ± 2.8 ($n = 96$)	69.5 ± 2.9 ($n = 85$)	2.1 (−1.9 to 6.0)	0.31
CSQ	12	26.9 ± 0.9 ($n = 98$)	26.2 ± 0.9 ($n = 87$)	0.7 (−0.5 to 2.0)	0.24
	24	27.3 ± 0.9 ($n = 96$)	26.5 ± 1.0 ($n = 85$)	0.8 (−0.6 to 2.1)	0.25
EQ-5D	0 (baseline)	0.811 ± 0.029 ($n = 98$)	0.823 ± 0.030 ($n = 89$)	−0.011 (−0.052 to 0.029)	0.58
	12	0.807 ± 0.030 ($n = 98$)	0.822 ± 0.031 ($n = 88$)	−0.014 (−0.062 to 0.033)	0.55
	24	0.828 ± 0.029 ($n = 96$)	0.829 ± 0.030 ($n = 86$)	−0.001 (−0.0045 to 0.043)	0.97
Degree of anxiety about COVID-19 (VAS)	0 (baseline)	46.3 ± 5.3 ($n = 98$)	49.0 ± 5.5 ($n = 89$)	−2.7 (−10.7 to 5.2)	0.50
	12	44.3 ± 5.4 ($n = 98$)	47.0 ± 5.5 ($n = 87$)	−2.8 (−11.0 to 5.4)	0.50
	24	43.2 ± 5.3 ($n = 96$)	44.2 ± 5.4 ($n = 86$)	−0.9 (−8.7 to 6.9)	0.82
HAMD-17 (depressive disorders only)	0 (baseline)	8.3 ± 1.5 ($n = 50$)	6.1 ± 1.5 ($n = 42$)	2.2 (−0.3 to 4.6)	0.09
	12	8.8 ± 1.5 ($n = 50$)	6.0 ± 1.6 ($n = 41$)	2.8 (0.2 to 5.4)	0.03
	24	7.9 ± 1.6 ($n = 48$)	5.9 ± 1.7 ($n = 39$)	2.0 (−1.0 to 5.0)	0.18
HAMA (anxiety disorders only)	0 (baseline)	10.2 ± 1.9 ($n = 30$)	11.5 ± 2.1 ($n = 31$)	−1.3 (−4.7 to 2.0)	0.42
	12	9.7 ± 2.0 ($n = 29$)	12.2 ± 2.1 ($n = 31$)	−2.5 (−6.1 to 1.0)	0.15
	24	8.7 ± 1.8 ($n = 29$)	9.0 ± 1.9 ($n = 30$)	−0.3 (−2.8 to 2.2)	0.81
YBOCS (OCD and related disorders only)	0 (baseline)	14.1 ± 1.8 ($n = 18$)	15.6 ± 2.1 ($n = 17$)	−1.5 (−6.2 to 3.2)	0.52
	12	14.0 ± 1.8 ($n = 18$)	15.0 ± 2.1 ($n = 16$)	−1.0 (−5.8 to 3.8)	0.67
	24	12.9 ± 1.8 ($n = 18$)	14.0 ± 2.1 ($n = 16$)	−1.1 (−5.7 to 3.5)	0.62

Data are mean ± SD.
CI, confidence interval; CSQ, Client Satisfaction Questionnaire; EQ-5D, EuroQol 5 Dimension; HAMA, Hamilton Anxiety Rating Scale; HAMD, Hamilton Depression Rating Scale; OCD, obsessive-compulsive disorder; SF-36 PCS, 36-Item Short-Form Health Survey Physical Component Summary; VAS, visual analog scale; WAI, Working Alliance Inventory; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Table 4. Hospital visit costs and time

	Two-way video ($n = 98$)	Face-to-face ($n = 90$)	*P*-value
Number of hospital visit during the study period			
Mean ± SD	6.3 ± 2.8	5.7 ± 2.5	0.12
95% CI	5.7–6.8	2.1–6.2	
Time required per hospital visit (minutes)			
Mean ± SD	42.9 ± 40.8	79.2 ± 61.6	<0.0001
95% CI	34.7–51.1	66.3–92.1	
Cost per hospital visit (Japanese yen)			
Median	168.9	500.0	0.0104
IQR	0.0–793.3	140–1266.7	
Number of work days missed for hospital visits			
Mean ± SD	1.5 ± 2.5	2.6 ± 7.1	0.15
95% CI	1.1–2.0	1.2–4.1	

CI, confidence interval; IQR, interquartile range.

HAMA, and YBOCS scores, except that the HAMD score at 12 weeks in the two-way video group was higher than that in the face-to-face group ($P = 0.03$). Data regarding other secondary outcomes, including the changes from the respective baseline values in the two groups, are presented in the Supplementary Tables S2 and S3.

Discussion

Here, we report the results of a large-scale, long-term study comparing two-way video and face-to-face treatment in the real-world clinical setting. The most important feature of this pragmatic trial is that it adapted relatively broad inclusion criteria, namely depressive disorder, anxiety disorders, OCD and related disorders, and examined the effect of long-term treatment over 6 months. The treatment provided was the same as that in general outpatient care with no restrictions on the number of visits or treatment content. In other words, the psychiatrists in the study provided the best insurance-covered treatment they considered appropriate in a two-way video or face-to-face setting. In addition, the study was validated in a modern telemedicine setting, where patients easily accessed and received treatment from a psychiatrist at home or in the office using smartphones, tablets, or personal computers. Most of the telemedicine RCTs to date have been relatively short-term trials for a single disorder, often with some form of specific treatment. To our knowledge, there are very few pragmatic RCTs validating two-way video treatment that incorporate multiple psychiatric disorders.[9] In addition, each trial design has limitations, such as a limited follow-up period of less than 6 months[11] or, in the case of long-term follow-up studies, the number of participants is limited to a few dozen[12] to 140.[10] Through the COVID-19 pandemic, two-way video appointments became established as a common method of psychiatric care delivery. Patients can now easily see their

psychiatrists remotely using their smartphones and other devices from home. The fact that two-way video was determined noninferior to face-to-face treatment in this study is an important finding, given that this type of health care will continue to be used around the world.

Another important aspect of this trial is that it is the first pragmatic two-way video trial in Japan, a country with universal health insurance where people can choose their preferred medical facilities and receive medical care at a relatively low cost. The flip side to low health care prices is the extremely busy treatment environment where health care providers have to see many patients in a short period of time. There was some concern that two-way video treatment would be difficult to implement in such an environment. Since Japan is considered a relatively restrictive country for telemedicine,[3,13] it was important to verify that two-way video treatment is equally effective in light of existing individual and cultural regulatory environments in order to appropriately promote its use.

The results of this study are consistent with those of previous meta-analyses that have reported comparable efficacies of two-way video and face-to-face treatment.[9,37,38] In the evaluation of the primary outcome, treatment *via* two-way video was noninferior to face-to-face treatment. Although the difference did not reach significance, numerically, the SF-36 MCS was higher in the two-way video group at 24 weeks. There were no significant differences between the two groups on the gold standard rating scales for each disease. The only exception was that the HAMD score at 12 weeks for patients with depression was significantly higher in the two-way video group than in the face-to-face group. The reason for this is unclear, but both psychiatrists and patients may have been unfamiliar with two-way video and may have had some difficulty with the initial treatment. However, the baseline HAMD score of the face-to-face group was originally higher than that of the two-way video group at the trend level, and the difference may have been significant only incidentally. At the final 24-week time point, the significant difference between the two groups disappeared. This study had a low dropout rate, and there were no differences between the two groups in terms of measures related to treatment alliance, such as the WAI and CSQ scores. Reflecting such patients' positive attitudes toward two-way video, the percentage of two-way video use was relatively high. In this study, the two-way video group was supposed to use two-way video for more than 50% of visits, but the average rate of two-way video use after baseline was approximately 77%. Furthermore, approximately one-third of patients in the two-way video group received only two-way video treatment, demonstrating the noninferiority of two-way video compared with face-to-face treatment in this group as well. At the same time, the reasons for not using two-way video 100% of the time should have been examined in detail. This study did not collect detailed data on the reasons why the two-way video group chose face-to-face care for some visits, and this is an issue for future studies.

As expected, two-way video was also found to reduce the burden of hospital visits for the patients; patients in the two-way video group spent less time in hospital visits and had fewer expenses than patients in the face-to-face group. The value that telemedicine can provide to patients is significant, not to mention the time and cost-savings associated with hospital visits. These include the provision of medical care in medically underserved areas, access to highly specialized psychiatrists, and easier access for patients who may have difficulty seeing a psychiatrist due to symptoms and/or stigma.

The following limitations of this study should be noted. First, we targeted only three disorder groups, namely depressive disorders, anxiety disorders, and OCD and related disorders. Although the three disorder groups considered in this study can be assumed to represent a large number of patients in psychiatric outpatient clinics, they do not cover all psychiatric disorders, such as schizophrenia, bipolar disorder, substance-related disorder, and neurodevelopmental disorder. Thus, a comparison between two-way video and face-to-face treatment for diseases not covered in this study remains a subject for future research. Second, it was not possible to blind psychiatrists or patients in this study comparing two-way video to face-to-face. However, our study implemented a centralized rating, and we were able to implement blinding of the raters who performed the HAMD, HAMA, and YBOCS assessments. This is part of the design advantage of this study over other studies, but, despite this, it cannot be ruled out that the fact that physicians as well as patients knew the assignments may have worked in favor of telemedicine when, for example, expectations for telemedicine were high. Third, although the present study followed patients for a relatively long period (6 months), there is still room for further evaluation of the effects over even longer follow-up periods, as psychiatric disorders often have a long course. While long-term use of two-way video is likely to reduce the financial burden on patients, it may take longer to establish a good rapport or reduce the quality of an established rapport, compared with face-to-face treatment.[39] Future research should examine the usefulness of two-way video for longer periods of time and the desirable methods of operation.

Conclusion

The study showed that two-way video treatment over a 6-month period was no less effective than face-to-face treatment in patients with depressive disorders, anxiety disorders, OCD and related disorders. Many of the patients accessed their psychiatrists from home using smartphones, which is meaningful in that the study demonstrated the effectiveness of a modern form of telemedicine. In addition, this was the first RCT conducted in a real-world clinical setting in Japan, and the results indicate that two-way video is a practical option in Japan and can be used equally with face-to-face treatment. In future studies, longer follow-up and further validation of the usefulness of disease-specific two-way video treatment will be desirable.

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Author contributions

All authors were involved in designing the study. Akitoyo Hishimoto, Takeshi Asami, Akira Suda, Shogyoku Bun, Toshiaki Kikuchi, Akihiro Takamiya, Takashi Nakamae, Yoshinari Abe, Tetsufumi Kanazawa, Yasuo Kawabata, Hiroaki Tomita, Koichi Abe, Seiji Hongo, Hiroshi Kimura, Aiko Sato, Hisashi Kida, Kei Sakuma, Michitaka Funayama, Naoya Sugiyama, Kousuke Hino, Toru Amagai, Maki Takamiya, Hideyuki Kodama, Kenichi Goto, and Shuichiro Fujiwara contributed to the recruiting of patients and collecting the data. Yasunori Sato, Ryo Takemura, and Kengo Nagashima analyzed the data. Taishiro Kishimoto and Shotaro Kinoshita prepared the original draft. All authors contributed to the final draft. All authors have read and approved the final manuscript.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section at the end of this article.