

## Research

# Happy Science Prayers Reduce Interpersonal Difficulties among University Graduates with Depression: A Double-Blind Randomized Controlled Trial

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## Abstract

### Background and Objectives

Recent decades have witnessed a tremendous increase in scientific interest regarding the relationship between religion and health. Especially, researches on intercessory prayer is ongoing but, to date, the findings have been equivocal. This study aimed to evaluate the efficacy on depressive symptoms by the intercessory prayer of Happy Science, which is one of the largest Japanese religious institutions, in a double-blind randomized controlled trial.

### Methods

The trial participants (n=177) were treated with the intercessory prayer twice a day (in the morning and in the evening) for one month; the morning and evening prayer are “Byoki-HeiyuKigan” (spiritually healing prayer) and “Akurei-GekitaiKigan” (exorcism prayer), respectively, while the control patients (n=187) received usual care including medication. Mental status was assessed at three time-points before, after, and three months following the intervention using the Center for Epidemiologic Studies Depression scale. In an analysis comparing the intervention and control conditions, we adjusted for important cofounders such as diagnosis, illness duration, medication, religious background, smoking, drinking, body mass index, marital status, and education.

### Results

The treatment group, particularly those who were university graduates, showed a significant reduction in interpersonal difficulties both at post-intervention and at the 3-month follow-up.

### Conclusions

These prayers might ameliorate interpersonal difficulties in depressive symptoms.

**Keywords:** Distant intercessory prayer; El Cantare; Happy Science; Religion and health; Master Ryuho Okawa

## Introduction

Historically, there has been a strong connection between religion

and medicine (Koenig 2012) [1]. In the West, the church built the first public hospitals (as early as the fourth century), and religious orders trained and registered doctors, right up until the time of the Reformation. Beginning in the 17<sup>th</sup> century and the Enlightenment, however, a nearly total separation developed between religion and medicine, as evidenced by the widespread cultural turn to science and technology for explanations of disease and healing. Around this time, there was a major focus on the physical management of disease, which left spiritual or psychological approaches to be considered as, at best, alternative or complementary forms of medicine. Nonetheless, more recently, perception of this separation has undergone a “swing of the pendulum” of sorts. Outside of the medical profession, the healing benefits of prayer are, in many countries, widely held and frequently reported in the mainstream media. Likewise, in some parts of the world, such as the United States, “prayer” has increasingly become the subject of scientific investigation [2]. In recent years, a number of prayer typologies, briefly summarized in a previous paper of ours [3], have been proposed within the field of healthcare, which has provided further confirmation of the recognition, even within the medical field, of the potential efficacy of prayer in alleviating ill health.

### Studies of Intercessory Prayer

Paloma and Gallup, after observing American prayer practices [4], described the following four-part typology of prayer:

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1. Conversational prayer: speaking to God as you would to a friend;
2. Ritual recitation: reciting ritualized prayers, from both written texts and from memory;
3. Meditation: nonverbal communication with God; and
4. Prayer of petition: requesting of God something for oneself or for others.

In the present study, I focus on the last type, the prayer of petition, otherwise known as an intercessory prayer or prayer for others. Prayers for others can be offered either with or without knowledge of the person to whom they are directed, and can be conducted with the person present (such as by making physical contact with the person), or at a distance, with the prayee located elsewhere. Three sequential Cochrane Collaboration literature reviews have been conducted on research of the use of intercessory prayer to alleviate illness. These reviews were published in 2000, 2004, and 2009 [5,6,7] and all acknowledged that intercessory prayer is one of the oldest and most common intervention types used by many faiths to alleviate illness. In the review by Roberts et al. (2010) [7], the authors searched ten databases and analyzed ten trials with a randomized sample totaling 7,646 people. The authors determined that the findings were equivocal: although some of the results from individual studies suggested positive effect, the majority did not. Overall, the evidence did not appear to support a recommendation either in favor of or against the use of intercessory prayer.

Likewise, the reporting of data on clinical outcomes was heterogeneous and equivocal, suggesting that what the studies assumed to be the object of intercessory prayer varied significantly and was open to different interpretations. One of the problems here is that few of the studies used scientific methodologies such as standardized published scales, which leaves the reliability and validity of the outcomes unknown [2]. Another problem identified by the Cochrane authors is the evident heterogeneity of prayee illness types treated [7].

More problematically, intercessory prayer literature lacks a theoretical and theological basis [7,8]. To address this, in a previous review, [3] proposed the following set of five theological factors, taken from Happy Science theory, that are said to determine the effectiveness of prayer interventions: (1) strength of faith, (2) a becalmed state of mind, (3) readiness to pursue self-help measures, (4) a wish likely to be approved by guiding spirits, and (5) a positive spiritual environment.

### Happy Science and Prayer

Happy Science, originally established in Japan as *Kofuku-no-Kagaku* (literally, “the Science of Human Happiness”) in 1986, has grown into one of the most influential religious organizations in Japan. It currently includes a global base with members from

over 100 countries across the world, with more than 10,000 local branches, temples, and Shojas all over Japan and the world. The founder and leader is Master Ryuho Okawa, who, as of January 2016, has presented more than 2,400 lectures and published over 2,000 books. His lectures cover a large range of genres and topics including spirituality, health, science, relationships, business, politics, and education [9].

The basic tenets of Happy Science, and the core of its teachings, are known as “The Principles of Happiness,” which consist of the fourfold path of “love,” “wisdom,” “self-reflection,” and “progress” [10]. Based on these principles, [11,12] developed a novel religious/spiritual group psychotherapy and reported its efficacy with various mental disorders in randomized controlled trials. Happy Science believers receive a sutra book, “The Dharma of the Right Mind,” and a set of prayer books upon joining. “The Dharma of the Right Mind” was inspired by Shakyamuni Buddha’s consciousness and therefore has the power to purify minds with the light of Buddha. This prayer has been described as possessing 10,000 times more power than Buddhism’s Lotus or Heart Sutras [9]. Happy Science members’ spiritual life, of which prayer constitutes a core component, revolves around recitation of the sutras and prayers contained in these books.

Happy Science has a unique cosmology. It is believed that the universe has a multi-dimensional structure, within which the material world is three-dimensional, whereas the other world (i.e., the spirit world) refers to the fourth dimension and above. The spirit world of planet Earth continues up to the ninth dimension, which is the highest limit of personified spiritual existences. Happy Science believers believe in the existence of the Supreme Being, known as El Cantare, which is the same entity that many of the major religions (e.g., Christianity and Islam) refer to as God. El Cantare is the leader of 10 ninth-dimension spirits, including Jesus Christ, Confucius, Zeus, and Moses [2]. In the Happy Science cosmology, human souls are repeatedly reincarnated for the purpose of spiritual evolution. The material world is considered the “training ground” for souls, which helps them to evolve and progress through the dimensions. Upon progressing above the seventh, or the world of angels, these souls begin to act as guiding spirits.

When one prays, a response is ostensibly received from the guiding spirits of the particular spiritual group defined by one’s religious affiliation. For example, a Christian prayer would be heard by Christian guiding spirits. Thus, it can be said that spiritual affiliation is one of the conditions for a prayer to be effective. Spiritual affiliation is defined by one’s faith. By the same token, Happy Science is blessed by a large number of guiding spirits who can provide support and guidance to Happy Science believers. However, the question arises as to whether prayers made by nonbelievers would have any effect.

Although doubtlessly some spirits may recognize the prayers made by nonbelievers, it is uncertain whether a response can be expected from them and which type of spirit would be expected to respond.

For the Happy Science faithful, the spirit world is the world of thought, and thought is the form of existence of souls in the spirit world. Since the three-dimensional world is a uniquely material world, our physical existence is not compatible with the form of existence in the spirit world. However, thoughts can be transmitted between these two worlds. Prayer, in essence, can be seen as a form of thought transmission, which is received and responded to by guiding spirits in the spirit world. The Happy Science doctrine distinguishes among the various types of thought and emotion according to their respective frequencies. Joy, gratitude, anger, and hatred, for instance, all have different frequencies. However, although each thought and emotion has a different frequency, repeatedly emitting the same sorts of thoughts and emotions can cause certain tendencies in the soul to arise.

Happy Science further expounds on an important law said to be operating in the spirit world. Known as “the law of same wavelengths attraction,” thoughts can only be successfully communicated to the spirit world when they “match” the frequency of a given spirit. The spirit world is thought of as a huge conglomerate of realms divided according to wavelengths of collective thoughts. This distinction is held to occur in both vertical and horizontal manners. Vertically, spirits are divided into dimensions in accordance with their spiritual development, whereas horizontally, they are divided into homogeneous communities defined by belief, taste, personality, and so on [13]. In principle, spirits who belong to different dimensions cannot communicate with one another because their frequencies are not compatible. However, the thoughts of a living person in the material world transition to other dimensions, and the frequency of these thoughts determines which dimension or realm they transition to.

As further defined in Happy Science doctrine, frequencies vary from the realm of Hell to the ninth dimension. Therefore, if one has a “hellish” thought, that thought is instantaneously communicated to spirits in the Hell dimension, while a “heavenly” thought is communicated to those in the heavenly dimensions. In this way, people who maintain a hellish tendency in their thoughts are thus destined for Hell, which Happy Science holds is located in a corner of the fourth dimension and is made up of a collection of realms of different negative-frequency spirits. A negative thought is communicated to spirits in the realm corresponding to its wavelength. When one’s soul is attuned to a frequency of Hell, it can result in the phenomenon known as possession. In Happy Science, possession is considered to be the root of problems such as physical and mental illness and misfortune [14,15]. Along this same line, because prayers—which are a form of thought transmission—are

responded to by guiding spirits who belong to a higher dimension, they must have a frequency compatible with those of the guiding spirits. It therefore follows that the quality of a thought is considered one of the requisites for prayer to be effective. In general, negative thoughts and wishes such as curses and egotistic desires are said to be rejected by guiding spirits, whereas positive prayers such as expression of altruistic desires are likely to be responded to by higher-dimension spirits [16].

### The Present Trial

As discussed above, the major factors making prayer efficacious in treating illness may be (1) strong faith, (2) a positive state of mind, (3) a commitment to self-help, (4) a wish that is worthy of approval by guiding spirits, and (5) a positive spiritual environment. One must also consider the heterogeneity of trial procedures and prayee illness types treated. The present trial addressed these major factors directly. Specifically, those who carried out the distant intercessory prayers (DIPs) were Happy Science devotees—believers who had stronger faith and who wanted to improve themselves through daily practice of the Fourfold Path of Love, Wisdom, Self-reflection, and Progress to a greater degree than did student members [9]. Furthermore, the DIPs were conducted in front of an El Cantare statue, which is regarded as a sort of spiritual portal connecting with El Cantare’s consciousness [17,3]. By praying in front of the El Cantare statue, one can have direct connection with El Cantare, and therefore with the higher dimensions. It is believed spiritual light is constantly flowing out of the El Cantare statue and gradually filling the surrounding environment with heavenly vibrations. Taken together, the present trial can be said to convincingly address the five theological factors (i.e., strong faith, a positive state of mind, a commitment to self-help, a wish that is worthy of approval by guiding spirits, and a positive spiritual environment) comprising effective prayer.

In this study, 450 Japanese outpatients were enrolled in order to investigate the effect of Happy Science DIPs (specifically, the “Prayer for Recovery from Illness” and “Prayer for Exorcising Evil Spirits”) on depressive symptoms. The protective role of religious involvement in against the incidence and persistence of depressive symptoms or disorders has been relatively known well [18,19,20]. In this DIP trial, a double-blind design was utilized, and all of the enrolled patients suffered from only major depression. As a result, I was able to control for the heterogeneity of trial procedures and prayee illness type. More significantly, employing the double-blinded design means that none of the enrolled patient-prayees (i.e., the individuals who were the object of prayer) knew whether they were being prayed for or not. Additionally, prayees were not in any way apprised of the major factors that comprise prayer efficacy. In taking these actions, I expected the DIP trial results to identify the statistically positive effects of prayer on depressive symptoms.

The effectiveness of the DIPs was evaluated not only at post-intervention but also at a 3-month follow-up. I also investigated the relationships of descriptive and demographic characteristics with responses to DIP.

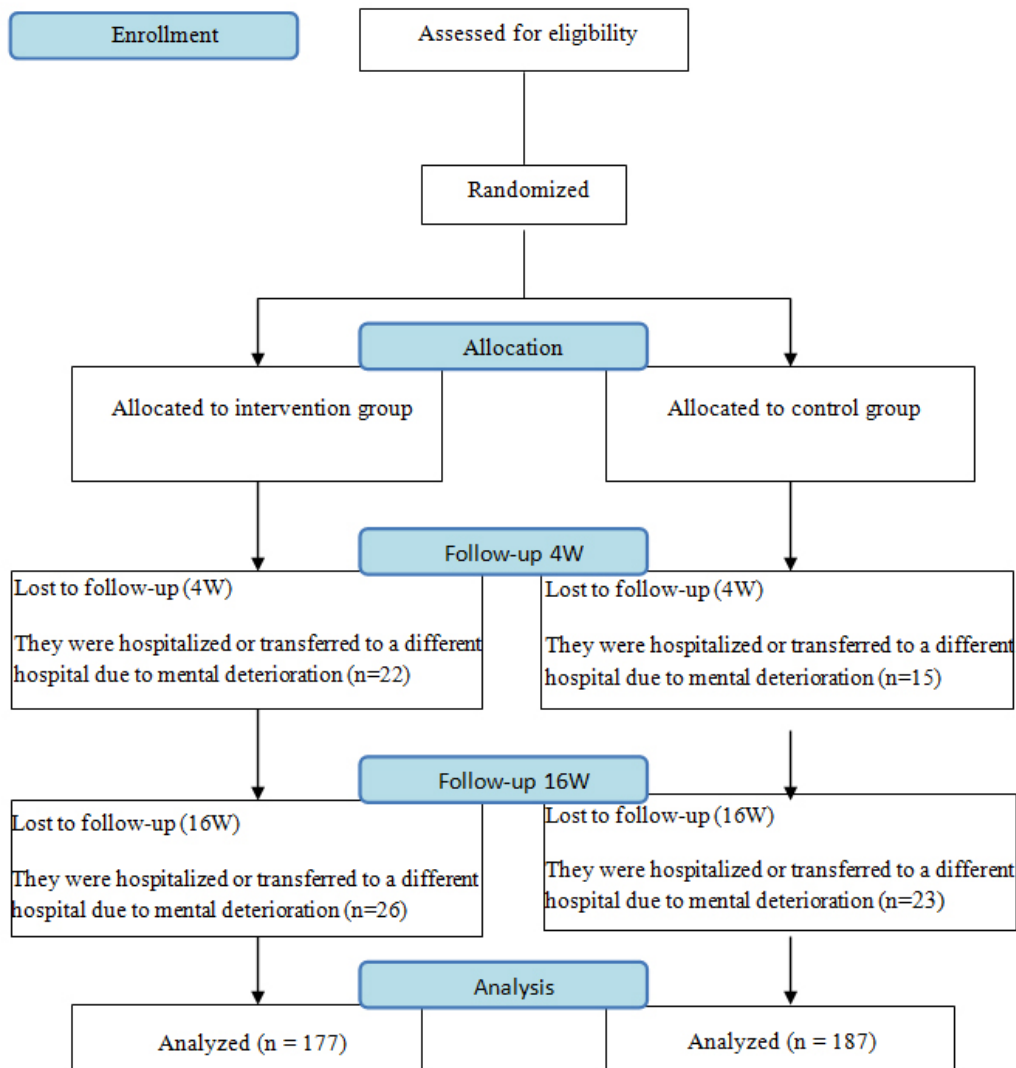
## Materials and Methods

### Design and Study Participants

The CONSORT (Consolidated Standards of Reporting Trials) 2010 statement [21], was followed to conduct this double-blind randomized controlled trial. The study used a two-group (intervention vs. control) double-blind randomized trial design with three assessment times (pre-intervention, post-intervention, and 3 months after intervention), and was conducted at the [Happy Smile Clinic] in Kawasaki City, Kanagawa, Japan, between May and November 2014.

Criteria for enrollment were (1) 18 years or older; (2) literate in Japanese; (3) diagnosed with a mood disorder (according to the International Statistical Classification of Diseases and Related Health Problems [ICD-10], codes F32 and F33); (4) no psychotic symptoms; and (5) no other medical condition that precluded completion of the self-report questionnaire without assistance. Participants gave their full informed consent to participate in the study and ethical approval was obtained from the Ethics Committee of the Department of Medical Science, Happy Smile Clinic. A total of 450 eligible patients were enrolled and randomly assigned to the intervention (n=225) or delayed-treatment control condition (n=225; see Figure 1 for details of patient recruitment). Eighty-six patients (48 in the treatment group, and 38 in the control group) dropped out of the study because they were hospitalized or transferred to a different hospital due to mental deterioration.

Figure 1: CONSORT 2010 flow chart illustrating the recruitment of patients for the present randomized controlled trial.



Thus, the dropout rate for the current trial was 19.1%. There were no significant differences in demographic characteristics between patients who dropped out and those who remained in the trial.

### Procedure and Happy Science Intercessory Prayer

Before the intervention, participants completed a set of questionnaires and a written consent form at the clinic. The questionnaires included questions on years of education, marital status, smoking history, alcohol consumption, religious belief, and illness duration. Their body height and weight were measured by the nurses at the clinic. Their mental status was assessed at pre-intervention, post-intervention, and the 3-month follow-up using the Japanese version of the Center for Epidemiologic Studies Depression Scale (CES-D), which has been validated previously [22]. The CES-D comprises 20 items, and assesses overall depression symptoms (according to total CES-D score, normal levels of depression are 0-15; mild are 16-21; moderate are 22-25; and severe are 26-60) as well as four dimensions of depression: depressed affect, lack of positive effect, somatic complaints, and interpersonal difficulties [23].

Patients were randomly assigned to DIP or non-DIP using a random table. Neither the enrolled patients nor those who conducted prayer were informed of the group allocation (double-blind). Additionally, any doctors and nurses involved in patients' treatment were not informed of the treatment assignment. A single researcher carried out this randomization scheme and wrote down a list of the patients in the intervention group, which was then put in a masking envelope. The envelope was then treated with DIP twice a day (in the morning and in the evening) for 4 weeks (6 days/week); the prayers in the morning and evening were the Prayer for Recovery from Illness ("Byoki-HeiyuKigan" in Japanese) and Prayer for Exorcising Evil Spirits ("Akurei-GekitaiKigan" in Japanese), respectively. These prayer booklets are available from Happy Science branches located around the world [9]. Both the trial and control patients received usual care including medication. The DIPs were conducted by 3-6 Happy Science believers (i.e., Happy Science devotee members) in front of the El Cantare statue.

### Statistical Analysis

Descriptive statistics were run on all variables to examine frequency distributions and to identify missing data and outliers. Group comparisons of descriptive data were carried out using *t*-tests for continuous variables (age, education years, body mass index, mood status, and illness duration) and chi-square tests for categorical variables (current smoking and alcohol intake [yes or no for both]; marital status [single, married, or divorced]; religious belief [Buddhism, Shintoism, Christianity, Atheism or Materialism, or impossible to answer]; diagnosis [depression according to the ICD-10, codes F32 and F33]; and medication [antidepressant,

minor tranquilizer, or sleep inducer]). Group comparisons of pre-intervention, post-intervention, and 3-month follow-up mean change scores (CES-D score at each time point - CES-D score at pre-intervention) were carried out using repeated-measures analysis of covariance (ANCOVA), controlling for the descriptive characteristic shown in Table 1.

Table 1. Participant characteristics

	Control group (n=187)	Trial group (n=177)
Age, yrs.	38.6 ± 11.0	39.1 ± 11.0
Men, %	50.3	30.9**
Education, yrs.	13.8 ± 2.4	13.8 ± 2.3
Single/divorced, %	60.9	63.0
Religion		
Buddhism	20.0	21.3
Shintoism	5.1	3.4
Christianity	2.9	4.5
Atheism or Materialism	30.8	32.6
Impossible to answer	25.7	23.0
Current smokers, %	32.6	31.8
Current drinkers, %	53.5	67.4*
Body mass index, kg/m <sup>2</sup>	23.4 ± 4.9	23.4 ± 5.3
Illness duration, yrs.	5.0 ± 5.7	5.6 ± 5.9
Medication, %		
Antidepressant	78.1	80.9
Minor tranquilizer	58.8	60.7
Sleep inducer	59.9	62.9
CES-D total score	24.0 ± 12.0	23.1 ± 12.0
Depressive affect	7.5 ± 5.0	7.0 ± 5.1
Positive affect	5.0 ± 2.8	5.0 ± 3.1
Somatic complaints	9.1 ± 5.3	8.5 ± 5.3
Interpersonal difficulties	1.4 ± 1.7	1.5 ± 1.8

Values are mean ± SD unless indicated otherwise; CES-D, Center for Epidemiologic Studies Depression Scale; \**p*<0.05 compared with the corresponding value in the control group; \*\**p*<0.001 compared with the corresponding value in the control group.

The main analysis used total CES-D mean change scores as the outcome, while additional analyses were carried out with mean change scores on the separate CES-D subscales as outcome variables. In each repeated-measures ANCOVA, only the descriptive characteristics that were significantly different between the control and treatment groups were controlled for. Sample size calculation was based on the absolute change in depressive symptoms as measured by the CES-D questionnaire from the pre-intervention assessment to the post-intervention and 3-month

follow-up assessments. Specifically, this trial is powered to detect an effect size of 2.5 or larger on the CES-D with a one-sided test ( $\alpha = 0.05$ ) at a power of 80% ( $1-\beta$ ), and assuming a common standard deviation of CES-D scores of 8.4, a total of 354 participants ( $n = 177$  in each group) were needed for the study. All analyses were performed using SPSS version 21.0 and all tests of statistical significance were based on two-sided probability.

## Results

As shown in Table 1, the average age of the depression participants was about 39 years old, and there were significantly larger numbers of men in the control group than in the treatment group ( $p < 0.001$ ). There were also more current drinkers in the treatment group than in the control group ( $p = 0.04$ ); otherwise, there were no other differences in demographic or diagnostic factors. The baseline CES-D scores had an average of over 23 in both groups, indicating moderate levels of depressive symptoms.

A repeated-measures ANCOVA on CES-D total change score and the four CES-D subscales change scores (depressive affect, positive affect, somatic complaints, and interpersonal difficulties) showed that interpersonal difficulties scores were marginally lower in the treatment group than in the control group both at post-intervention (4W) and at the 3-month follow-up (16W) ( $p = 0.11$ ; Table 2).

**Table 2.** Comparison of pre-intervention (0W), post-intervention (4W), and 3-month follow-up (16W) mean CES-D change scores by group

	4W	16W	p
<b>CES-D total score</b>			
<b>Control group (n =187)</b>	-0.25 ± 0.69	-0.68 ± 0.76	0.82
<b>Treatment group (n =177)</b>	-0.91 ± 0.71	-0.44 ± 0.78	
<b>CES-D depressive affect</b>			
<b>Control group (n =187)</b>	-0.34 ± 0.30	-0.50 ± 0.33	0.88
<b>Treatment group (n =177)</b>	-0.43 ± 0.31	-0.30 ± 0.34	
<b>CES-D positive affect</b>			
<b>Control group (n =187)</b>	0.07 ± 0.20	0.29 ± 0.22	0.85
<b>Treatment group (n =177)</b>	0.31 ± 0.20	0.15 ± 0.23	
<b>CES-D somatic complaints</b>			
<b>Control group (n =187)</b>	-0.10 ± 0.33	-0.13 ± 0.37	0.86
<b>Treatment group (n =177)</b>	-0.20 ± 0.33	0.13 ± 0.38	
<b>CES-D interpersonal difficulties</b>			
<b>Control group (n =187)</b>	0.14 ± 0.11	0.06 ± 0.12	0.11
<b>Treatment group (n =177)</b>	-0.12 ± 0.12	-0.19 ± 0.13	

Values are mean ± SE; CES-D, Center for Epidemiologic Studies Depression Scale; change scores were computed using the following formula [CES-D total score at each time point – CES-D total score at pre-intervention]; all analyses controlled for sex and current drinkers; p-values were computed using repeated measures ANCOVAs.

As shown in Table 3, further subgroup analyses on the CES-D interpersonal difficulties change scores showed that depression patients with a score of  $\geq 16$  on the CES-D total score ( $p = 0.078$ ) and non-religious patients ( $p = 0.079$ ) tended to show improvements in interpersonal difficulties over the trial. More intriguingly, university graduates ( $\geq 16$  years education) exhibited a significant improvement in interpersonal difficulties ( $p = 0.007$ ) both at post-intervention (4W) and at the 3-month follow-up (16W) (Fig. 2).

**Table 3.** Comparison of pre-intervention (0W), post-intervention (4W), and 3-month follow-up (16W) mean CES-D interpersonal difficulties change scores by subgroup

	4W	16W	p
<b>Depression patients</b>			
<b>Control group (n =138)</b>	0.12 ± 0.16	0.05 ± 0.16	0.078
<b>Treatment group (n =123)</b>	-0.26 ± 0.17	-0.34 ± 0.17	
<b>Non-religious patients</b>			
<b>Control group (n =54)</b>	0.25 ± 0.23	0.12 ± 0.26	0.079
<b>Treatment group (n =58)</b>	-0.24 ± 0.22	-0.53 ± 0.25	
<b>Patients with &lt;16 years of education</b>			
<b>Control group (n =119)</b>	0.02 ± 0.15	-0.30 ± 0.15	0.92
<b>Treatment group (n =119)</b>	-0.01 ± 0.15	-0.04 ± 0.15	
<b>Patients with <math>\geq 16</math> years of education</b>			
<b>Control group (n =68)</b>	0.39 ± 0.20	0.23 ± 0.21	0.007
<b>Treatment group (n =58)</b>	-0.39 ± 0.22*	-0.52 ± 0.23*	

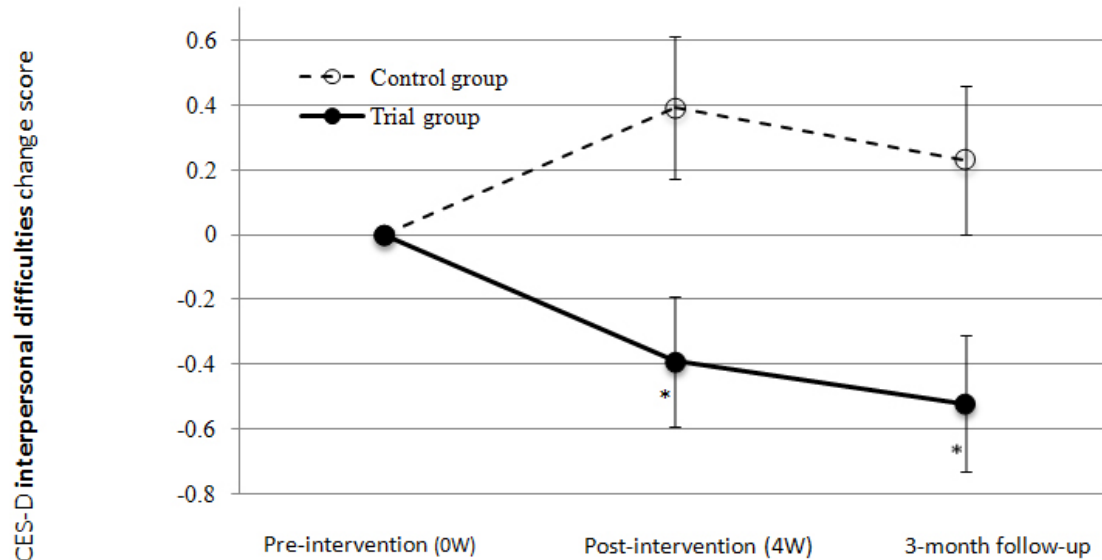
Values are mean ± SE; CES-D, Center for Epidemiologic Studies Depression Scale. "Depression patients" means those with  $\geq 16$  of CES-D total score, while "non-religious patients" means those who are at heist or materialist. Change scores were computed using the following formula [CES-D total score at each time point – CES-D total score at pre-intervention]. All change scores were adjusted for sex in the analysis of depression patients or patients with <16 years of education; for sex, current drinkers, and illness duration in the analysis of non-religious patients; and for sex and current drinkers in the analyses of patients with  $\geq 16$  years of education. The p-values were computed using repeated measures ANCOVAs;

\*  $p < 0.05$  compared with the corresponding value in the control group.

## Discussion

The current trial failed to confirm that the Happy Science DIPs had an ameliorating effect on depressive symptoms in a double-blind randomized controlled trial with Japanese depression outpatients. As described in the Method section, a total of 354 participants ( $n = 177$  in each group) were suggested to be needed in this study, as per the power analysis. However, the actual effect size was around 1.2 on the total CES-D, which suggests that around 2,500 participants ( $n = 1,250$  in each group) would be necessary to confirm the efficacy of DIPs.

**Figure 2:** Average CES-D interpersonal difficulties change scores for patients with  $\geq 16$  years of education at pre-intervention (0W), post-intervention (4W), and 3-month follow-up (16W)



Values are mean  $\pm$  SE; CES-D, Center for Epidemiologic Studies Depression Scale. Change scores were computed using the following formula [CES-D total score at each time point – CES-D total score at pre-intervention]; all analyses controlled for sex and current drinking; \* $p < 0.05$  compared with the corresponding value in the control group.

Despite the small sample size for detecting subtle effects, the CES-D interpersonal difficulties change scores were marginally lower in the treatment group than in the control group both at post-intervention (4W) and at the 3-month follow-up (16W). Furthermore, in the subgroup of university graduates ( $\geq 16$  years education), the Happy Science DIPs appeared to have a significant improvement in interpersonal difficulties both at post-intervention (4W) and at the 3-month follow-up (16W). There were no other differences in demographic factors between university graduates ( $\geq 16$  years education) and non-university graduates ( $< 16$  years education) except for sex (men: 55.0% in university graduates vs. 45.0% in non-university graduates,  $p < 0.001$ ) and number of current smokers (22.9% in university graduates vs. 77.1% in non-university graduates,  $p = 0.01$ ). However, given that the present trial controlled for these two differences of sex and current smokers, I need to further investigate the possible mechanisms underlying the efficacy of Happy Science DIPs in alleviating interpersonal difficulties among university graduates. Especially, since there are evidence showing that sexual dimorphic phenomenon in both the animal models and human beings [24-29], gender differences in the possible mechanisms should be addressed in the future studies focusing more male or female patients. This study indeed found that the score of interpersonal difficulties in female was significantly higher than those in male (male 1.25 vs. female 1.58,  $p < 0.05$ ).

In this study, only 28.6% of participants reported believing in

Buddhism, Shintoism, or Christianity. However, there was no significant difference in religious beliefs between the control and treatment groups. In line with the present data, an Angus Reid survey (2006) [30] indicated that 24% of Japanese respondents considered religion to be very important in their daily lives (Angus Reid 2016), compared to the average of 48% of respondents from the rest of the world. Thus, given that the prayer effect tended to be evident in non-religious patients but not in religious patients, Happy Science DIPs might be more effective in Japanese patients than in patients from other, more religious nations (e.g., 63% of US respondents indicated that religion was very important in their daily lives). However, further research is needed to determine whether there are international differences in the efficacy of Happy Science DIPs. Follow-up trials should include a measure of religiosity in order to investigate why only non-religious patients were responsive to the Happy Science DIPs.

Few previous religious/spiritual interventions have reported any treatment effects on specific CES-D subscales. In this study, the treatment effect appeared to be stronger for interpersonal difficulties than for the other CES-D subscales. If this is a genuine effect, it could be mediated in part by interpersonal behavioral pathways. For example, religiosity/spirituality has been related to increased social support and better human relationships [1]. It would be useful to evaluate whether the Happy Science DIPs could be used to improve individuals' interpersonal relationships.

## Limitations

Since the actual effect size was small (around 1.2) on the total CES-D, future trials should enroll more participants (at least a total of 2,500 participants) in order to confirm the efficacy of Happy Science DIPs. A relatively longer follow up should be taken so that it could supply more informative cues to the readers and clinical treatment. In addition, future studies using the fMRI are needed for clarifying the changes in specific brain regions before and after the treatment by intercessory prayer, and finally the potentially neural circuits mechanism underlying the religious treatment for depression.

## Conclusion

The findings of this trial indicate that Happy Science DIPs may have benefited interpersonal difficulties in a sample of Japanese university graduates with depression.

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