1 November 2023 （Ver.1）

Description and consent document for 'Examining the effectiveness and cost-effectiveness of internet-delivered psychotherapy for irritable bowel syndrome: a randomised controlled study

1 About the study

Irritable Bowel Syndrome (IBS) is a condition characterized by symptoms such as constipation, diarrhea, and abdominal pain. In our previous research, we reported that psychotherapy is effective for some individuals who continue to experience symptoms despite pharmacological treatment. In individuals with IBS, there may be anxiety related to abdominal symptoms, and they may engage in behaviors such as avoiding triggers (e.g., certain foods or taking express trains), which can paradoxically worsen symptoms and decrease overall quality of life. Psychotherapy aims to improve thought patterns and behaviors that worsen symptoms and quality of life related to abdominal symptoms.

However, psychotherapy for IBS is not covered by insurance in Japan. Additionally, there is a shortage of facilities and therapists, and the associated costs can be high, making it challenging for individuals with IBS to access psychotherapy. Therefore, we have turned our attention to e-learning-based psychotherapy using the internet. Utilizing the internet allows individuals to receive treatment regardless of their location, and using video materials (videos) enables individuals to progress through treatment at their own pace.

While the effectiveness of such psychotherapy has been reported overseas, it remains unclear in Japan. Therefore, in this study, we aim to provide two types of psychotherapy in e-learning format, evaluating their effectiveness and economic impact. The goal is to make appropriate treatments more easily accessible.

Approval for conducting this research was obtained from the Nagoya City University School of Medicine Research Ethics Committee (located in Mizuho-ku, Nagoya, Mizuho-cho, Kawasumi 1). The committee, consisting of experts and non-experts in medical, dental, pharmaceutical, and other healthcare or research fields, conducted a thorough ethical and scientific review. The research institution's head granted permission for the study to be conducted only after approval was received from the committee. Additionally, the committee will continue to review the study to ensure it is conducted properly. We also obtained approval for the conduct of the research at the institutions where our co-researchers are affiliated, namely Kyoto University, the National Center of Neurology and Psychiatry, Kyorin University, and Tokyo University of Science, in a single, collective approval process.

For further details regarding the regulations associated with this committee, please refer to the following website:

Nagoya City University Hospital Clinical Research and Development Support Center Website "To Patients" http://ncu-cr.jp/patient

2 The names of the principal investigator and collaborators at this study:

The names of the principal investigator and collaborators at this research facility are as follows:

Center for Psycho-oncology and Palliative Care, Core Laboratory, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

Shino Kikuchi
Center for Psycho-oncology and Palliative Care, Core Laboratory, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

Tatsuo Akechi
Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University, Graduate School of Medical Sciences, Nagoya, Japan.

Takeshi Kamiya
Department of Medical Innovation, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

Eiji Kubota
Department of Gastroenterology and Metabolism, Nagoya city University Graduate School of Medicine, Nagoya, Japan.

The study is a collaborative research by several research organisations, and therefore the following research organisations are participating:

Kyoto University: Toshiaki Furukawa
*National Center of Neurology and Psychi*atry: Masaru Horikoshi
Kyorin University: Yuki Oe
Tokyo University of Science: Takashi Sozu

3 Research Purpose and Significance

The aim of this study is to investigate the effectiveness of psychotherapy for irritable bowel syndrome (IBS) through e-learning and examine the associated economic implications of this treatment.

4 The reason for your selection as a participant in this study

In this study, to ensure the safe and appropriate participation in the program, we will conduct interviews and surveys by a gastroenterologist before the program begins. We will confirm whether participants meet the following conditions.

Those who meet all of the following criteria are eligible to participate in this study:

1. Individuals aged 18 or older at the time of registration.
2. Individuals diagnosed with irritable bowel syndrome (IBS) at a medical institution before registration and treated with medication for three months or more before registration.

3. Individuals with moderate or more severe IBS symptoms at the time of registration.
4. Individuals who meet the diagnostic criteria for irritable bowel syndrome**.
5. Individuals who have access to the internet, can participate in online meetings, and preferably have a quiet and private environment.
6. Individuals who can read and write in Japanese and communicate effectively.
7. Individuals who understand the purpose and content of the study and can consent to participate voluntarily.

*The severity and **diagnostic criteria will be assessed by a gastroenterologist (principal investigator) during the explanation at the secretariat.

However, those who meet any of the following criteria are not eligible to participate in this study:

1. Individuals who have received psychotherapy for irritable bowel syndrome, including current treatment, in the past two years or plan to undergo such treatment in the future.
2. Individuals participating in or planning to participate in another clinical trial for IBS at the time of registration or during the participation period.
3. Individuals currently undergoing treatment for a mental illness in psychiatry or psychosomatic medicine, and their attending physician has deemed participation in this study inappropriate.
4. Pregnant individuals.
5. Individuals with conditions other than irritable bowel syndrome where abdominal symptoms occur, currently undergoing treatment or strongly suspecting the presence of the disease. ***
6. Other individuals deemed unsuitable for this study by the principal investigator or research collaborators.

***A gastroenterologist may conduct an interview and may recommend consultation if another disease is suspected.

5 Methods and Duration of the Study

《**Study Duration**》

Registration Period: Approval Date to June 30, 2025

Overall Research Period: Approval Date to March 31, 2027

Your Participation Period: Registration Date to approximately 1 year after the completion of the evaluation in the 52nd week.

《**Anticipated Number of Study Participants**》

132 individuals (the number may vary due to progression).

《**Specific Research Procedures, Content, Observation Period, and Presence of Placebo**》

The research procedures and content are as follows:

① Participants will be randomly assigned to one of two programs. Following the instructions of the assigned program, participants will engage in the program for 10 weeks. This involves videos (approximately 5-15 minutes), mini-tests, and online consultations with the therapist, estimating a time commitment of 30 minutes to 1 hour per week.

② In addition to ①, tasks (homework) will be presented in each session. These tasks should be completed within the time frame you find suitable. It is acceptable to complete them daily or even just once.

③ Participants will also respond to surveys at predetermined intervals. The content of the surveys may vary slightly over time but will generally take 10-15 minutes each.

④ The observation period extends beyond the 10-week program. Approximately 1 year after initial consent, 6 surveys will be conducted, and evaluations will be performed.

⑤ There is no placebo (dummy medication or sham treatment). Participants, upon completion of the research participation period (after 1 year), have the option to view videos and materials from another program.

《Data to be Collected as Study Data》

Irritable bowel syndrome cannot be diagnosed through blood tests or imaging examinations. Therefore, surveys will be used to assess the quality of life, severity, and psychological state. These surveys, referred to as evaluation forms, will be conducted a total of 6 times during participation. Additionally, information will be collected about your educational and professional background to understand how irritable bowel syndrome affects your life, work, and studies. This background information survey, conducted once before assignment, is referred to as the baseline survey. Furthermore, some parts of the treatment may be recorded for therapist evaluation purposes.

《Survey Items, Implementation Frequency, and Timing of Evaluation Forms》

The evaluation forms will be administered a total of six times: before initiation (Week 0), after 4 weeks of initiation, 9 weeks, 13 weeks (1 month after treatment completion), 26 weeks (6 months), and 52 weeks (1 year). The content varies depending on the evaluation period, as outlined below.

Time (week)	0	4	9	13	26	52
Background	×					
Primary outcomes	×	×	×	×	×	×
Secondary outcomes						
Economic evaluation	×	×	×	×	×	×
Psychological evaluation	×	×	×	×	×	×
Stool properties	×	×	×	×	×	×
Expectation	×					
Satisfaction/improvement				×		×
Adverse Events	←	—	—	—	—	→

《Treatment and Examinations During the Participation Period》

For tests, treatments, rehabilitation, etc., related to diseases other than irritable bowel syndrome (IBS), please continue as usual. However, during the participation in this study (approximately 1 year), there are two requests.

Firstly, try not to change the medication for irritable bowel syndrome that you were taking before participating in the study unless instructed otherwise by your primary physician. If your primary physician deems it necessary, please follow their instructions.

Secondly, during the participation period, try to avoid undergoing any other psychological therapy as much as possible. Not only limited to psychological therapy for irritable bowel syndrome, if the content of psychological therapy is similar, there may be issues with the timing and accuracy of the study, leading to discontinuation of participation. Therefore, if you need to undergo psychological therapy during the participation period, please inform the study office so that we can review the content. Please note that there is no need to inform us when seeking psychological therapy after the study concludes.

Furthermore, there are no specific restrictions on daily activities such as diet and exercise.

6 Expected Benefits and Anticipated Burdens or Risks of Your Participation in This Study

《Benefits》

Participants are expected to gain knowledge and learn various methods for dealing with symptoms and stress related to irritable bowel syndrome through this study. It is anticipated that their understanding of the disease will deepen. However, the specific benefits derived from this program are not currently clear. It should be noted that this program is not available to individuals other than research participants.

《Disadvantages (Burden or Risks) 》

Participation in this program may lead to increased burdens such as time and communication expenses. While the likelihood of experiencing health-related issues during the program is minimal, in the unlikely event of such occurrences, participants are encouraged to promptly consult the designated contact point and, if necessary, be referred to a specialist.

Any medical costs or compensation will not be provided for any health problems that may arise as a result of participating in this study.

7 Freedom to Withdraw Consent

Participation in this study is voluntary and based on your free will. Even after giving consent for this study, you have the right to withdraw your participation at any time. If you wish to withdraw your consent, please contact the study office and sign the consent withdrawal document. Additionally, if you fail to submit the background information and evaluation questionnaire within two weeks after providing consent, it will be considered a voluntary withdrawal of consent, and any collected information up to that point will be deleted. Furthermore, if you do not wish to permit the use of information collected after withdrawing consent, your data will be erased. However, please note that in certain circumstances, such as post-data analysis, it may not be possible to remove your data based on

the progress of the research. In the event that we lose contact without receiving an expression of intent to withdraw consent, we will assume your continued permission for the use of information.

8 If you do not consent to participate in this study or choose to withdraw your participation midway, you will not experience any disadvantages in future treatments or otherwise.

9 Disclosure of Study Information

An overview and status of this study will be registered and made publicly available on the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CT), a clinical trial registration system of the University Hospital Medical Information Network Research Center.

URL: http://www.umin.ac.jp/ctr/index-j.htm

Results obtained from this study are planned to be published through academic journals or conferences in the future. However, rest assured that information identifying individuals, such as names and addresses of participants, will not be included or disclosed.

10 Access to Research Proposal and Methodology Documents

Within the limits that do not compromise the protection of personal information of other participants or the originality of the study, you may access documents related to the research plan (research implementation plan). If you wish to view these documents, please contact the "15. Contact Information." Additionally, after the conclusion of this study and the compilation of its results, if you express interest, we can inform you of the outcomes.

11 Handling of Personal Information

Your information will have personally identifiable details such as your name removed, and instead, it will be assigned a number (Research ID) with unidentifiable pseudonymization. The correspondence table linking you to this number will be securely stored at the research institution where we received your information, ensuring that personal information is carefully managed to prevent any leaks.

12 Storage and Disposal Methods for Samples and Information

Information obtained from this research will be stored in a pseudonymized state on a secure server throughout the research period. The management team will regularly backup the data to confirm its protection. If your information needs to be shared with collaborating research institutions for analysis, it will be encrypted in a pseudonymized state and exchanged using a password-protected cloud. Recordings and videos will not be stored on the server but will be promptly downloaded to media after the session ends, password-protected, and managed securely.

This information will be stored for a period of five years from the date of reporting the end of this research or the latest date of reporting the final publication of the research results, whichever is later. After the storage period expires post-research completion, the information will be discarded. In such cases, electronically stored data that is irrevocable will either be physically destroyed to make data reading impossible, or overwritten multiple times with dummy data before being disposed of, ensuring the original data is irretrievable.

13 Potential Use in Future Research or Provision to Other Research Institutions

The stored information may be provided or shared with third parties in the future for the advancement of medical and scientific knowledge or for the maintenance and improvement of people's health. In such instances, a research proposal for that study will be submitted to and approved by the Medical Research Ethics Committee. Additionally, measures will be taken to protect personal information, and your consent will be obtained again. Unauthorized use of your information will not occur.

14 Future disease information from the study

The results obtained from this study are based on surveys and do not lead to the discovery of specific diseases. Therefore, there is no specific information to convey.

15 Contact for Inquiries about the Study or Health Concerns

Contact Information for Inquiries about the Study and Medical Institution in Case of Health Issues. If you have any questions or concerns about this research, please feel free to consult us.

【Contact Information at Our Facility】

Research Institution: Nagoya City University Graduate School of Medicine

Contact: Email - suciri117@gmail.com (Available Hours): Weekdays 9:00-18:00

While emails are accepted 24 hours, responses will be provided during the specified hours.

Contact Person: Center for Psycho-oncology and Palliative Care, Core Laboratory, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

Assistant Professor - Shino Kikuchi

16 Cost Burden and Compensation for You

There is no need to incur additional treatment expenses to participate in this study. However, participants are responsible for communication costs related to online interviews and e-learning sites. As compensation for the effort and time spent answering evaluation questionnaires, payments of 1000 yen each will be made at 4 weeks, 9 weeks, 13 weeks, and 26 weeks from the start, and 2000 yen at 52 weeks (totaling a maximum of 6000 yen) in the form of Amazon gift cards, etc. No compensation is provided at the baseline (0 weeks).

17 Other Treatment Options

This research is conducted in addition to regular insurance treatments, and participants can receive normal treatment even without participating in this study.

18 Provision of Medical Care Following Research Implementation

There are no restrictions on the treatment or care provided after participating in this study.

19 Compensation for Health Damages Resulting from the Research and its Details

While this study is conducted with great care, in the event of any health damage occurring during participation, you will receive appropriate treatment similar to standard medical care. However, you will be responsible for covering the medical expenses incurred in this case, including the deductible amount from your health insurance.

This research involves psychotherapy, and as the likelihood of health damage is considered very low, we do not enroll in clinical research insurance. We will only provide medical care for health damages resulting from the study implementation. No compensation will be provided through insurance in the event of health damage.

20 Monitoring

Monitoring refers to investigations conducted by third parties to ensure that the research is conducted properly and that the reliability of the research results is confirmed. In this study, a monitoring officer designated by the principal investigator may review your registration information, survey results, and other data to examine whether the research is being conducted correctly while safeguarding your human rights.

21 Source of Funding and Conflict of Interest (COI) in this Study

"Conflict of Interest (COI)" refers to the possibility of research results becoming biased when researchers or companies have financial interests such as money or stocks. Therefore, it is necessary to disclose the sources of research funding and the researchers' conflicts of interest. In this study, these aspects are appropriately addressed. The research is conducted with the support of the Japan Society for the Promotion of Science and the KDDI Foundation, with no funding provided by pharmaceutical manufacturers. The procedures of the Conflict of Interest Committee at Nagoya City University Graduate School of Medicine have been completed, and appropriate measures have been taken in collaboration with other research institutions.

22 Attribution of Research Results

The data or discoveries obtained in this study will be owned by the researcher or the research institution to which the researcher belongs. While analysis results based on the data obtained in this study may lead to the creation of patents, it will never be conducted based on results derived from the data of specific individuals. Therefore, under any circumstances, you will not gain economic benefits, and all rights will remain with the researcher or the research institution to which the researcher belongs.

Informed Consent Form

To: President of Nagoya City University, a Public University Corporation

I have received sufficient explanation and understanding of the research titled " Description and consent document for 'Examining the effectiveness and cost-effectiveness of internet-delivered psychotherapy for irritable bowel syndrome: a randomised controlled study " Based on my own free will, I hereby consent to participate in this study.

《Items for Understanding》 Please check the □ boxes.

☐ 1 About the study
☐ 2 The names of the principal investigator and collaborators at this study
☐ 3 Research Purpose and Significance
☐ 4 The reason for your selection as a participant in this study
☐ 5 Methods and Duration of the Study
☐ 6 Expected Benefits and Anticipated Burdens or Risks of Your Participation in This Study
☐ 7 Freedom to Withdraw Consent
☐ 8 If you do not consent to participate in this study or choose to withdraw your participation midway, you will not experience any disadvantages in future treatments or otherwise.
☐ 9 Disclosure of Study Information
☐ 10 Access to Research Proposal and Methodology Documents
☐ 11 Handling of Personal Information
☐ 12 Storage and Disposal Methods for Samples and Information
☐ 13 Potential Use in Future Research or Provision to Other Research Institutions
☐ 14 Future disease information from the study
☐ 15 Contact for Inquiries about the Study or Health Concerns
☐ 16 Cost Burden and Compensation for You
☐ 17 Other Treatment Options
☐ 18 Provision of Medical Care Following Research Implementation
☐ 19 Compensation for Health Damages Resulting from the Research and its Details
☐ 20 Monitoring
☐ 21 Source of Funding and Conflict of Interest (COI) in this Study
☐ 22 Attribution of Research Results

☐ I agree. ☐I do not agree.

Date of Consent: Year ____ Month ____ Day ____

Consenter（Yourself） Name _____ (Signature) _____