Supplementary File 2.

Translation of the information for participants and informed consent form.

Supplement to:

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The effect of Intensive Care Unit-specific Virtual Reality (ICU-VR) to improve psychological well-being in ICU survivors: study protocol for a multicentre, randomised controlled trial - the HORIZON-IC study

Participants information for participation in medical scientific research

The effect of Intensive Care-specific Virtual Reality (ICU-VR) on psychological complaints after Intensive Care treatment.

Introduction

Dear Sir / Madam,

Using this letter, we would like to inquire whether you would be interested to participate in medical research. Participation is on voluntary basis. You are receiving this letter because you have been treated in the intensive care unit for more than three days and were mechanically ventilated.
In this letter, we will inform you about the nature of the study, what participation means, and what the benefits and disadvantages are of participation. Would you like to carefully read the entire letter prior to deciding whether you want to participate? If you are willing to participate, you can fill in and sign the form that you can find in Appendix B. You are given 1 to 4 days to consider your participation; we will ask you to make a decision about participation no later than seven days after your discharge from the intensive care unit.

Ask your questions

You can make your decision using the information you will find in this information letter. In addition, we recommend you to:
- Ask questions to the investigator who has provided you with this information.
- Talk about participation in this study with your partner, family or friends.
- Ask questions to the independent expert, [redacted] (Appendix A)
- Read the information provided on www.rijksoverheid.nl/mensenonderzoek.

1. General information

This study was initiated by the Franciscus Gasthuis & Vlietland and Erasmus MC. We will refer to the Franciscus Gasthuis & Vlietland and the Erasmus MC as the 'sponsor'. Investigators, which can be personified by doctors, nurses and student investigators, conduct the study in several hospitals. Hospitals participating in this study include the Erasmus MC, Franciscus Gasthuis & Vlietland, Ikazia hospital, and Maasstad hospital in Rotterdam, the IJsselland hospital in Capelle aan den IJssel, the Van Weel-Bethesda Hospital in Dirksland, the Groene Hart Hospital in Gouda, the Haaglanden Medical Centre in The Hague and the Albert Schweitzer hospital in Dordrecht.
A total of 300 participants are needed for this study. The United Medical Ethics Committee (MEC-U) in Nieuwegein, a medical ethical review committee, has approved this study.

2. What is the aim of the study?

In this study, we investigate whether an Intensive Care-specific Virtual Reality intervention, ICU-VR, can effectively reduce psychological impairments in patients who have been treated in an intensive care unit. Additionally, we study whether ICU-VR improves quality of life.

For this we compare three groups of patients;
1) patients not receiving ICU-VR,
2) patients receiving ICU-VR three times in the first two weeks after ICU discharge and
3) patients who receive ICU-VR during an ICU follow-up visit three months after discharge from the intensive care unit.

ICU-VR is an information film about the intensive care unit that can be watched using virtual reality. This film is implemented in the SyncVR Relax & Distract application. This application is approved for use in patients to help reduce stress and anxiety. Virtual reality, or VR, means virtual reality or apparent reality. The ICU-VR film lasts approximately 12 minutes. During the ICU-VR film, you will be virtually brought back to the intensive care unit and you will receive explanation about various aspects of the intensive care unit environment and treatment. During this explanation, you will be virtually laid down in an intensive care bed. You can always interrupt the ICU-VR film. In the latter case, you may decide to continue watching ICU-VR later on, or to not continue watching ICU-VR.

3. What is the background of the study?

In the Netherlands, approximately 90,000 adult patients are annually treated in an intensive care unit due to a critical illness. The chances of surviving life-threatening conditions such as cardiac arrest, trauma or sepsis have greatly improved over the past twenty years. In recent years, it has become increasingly apparent that surviving an acute and life-threatening critical illness can have long-term consequences on quality of life.

Many patients experience an intensive care unit treatment as stressful due to the different experiences and emotions they have during the intensive care unit stay. Think of moments of shortness of breath, having pain, feelings of powerlessness and fear of dying. Former intensive care unit patients therefore have an increased risk of developing psychological impairments, such as post-traumatic stress disorder (PTSD), anxiety, or depression. About 1 out of 5 former intensive care unit patients develop symptoms that are suitable with PTSD in the first year after discharge from the intensive care unit and 1 out of 3 develop symptoms of depression or symptoms that are suitable with an anxiety disorder. Although symptoms of PTSD, anxiety disorders and depression are most common in the first months after discharge, these can also last for years after discharge from the intensive care unit.

Recent studies show that treatment with Virtual Reality (VR) is beneficial for non-ICU patients with various psychological problems such as anxiety, PTSD and depression. We have previously shown that the use of Intensive Care-specific Virtual Reality is safe in intensive care unit patients. Additionally, ICU-VR appears to have a positive effect on the psychological recovery of patients treated for sepsis in the intensive care unit. In this study, we aim to investigate the effect of ICU-VR again in a larger group, to be sure whether ICU-VR can help to reduce psychological impairments and improve quality of life.

4. How is the study progressing?

How long does the study take?

Are you participating in this study? Participation will last until twelve months after your discharge from the intensive care unit.

Step 1: Are you eligible to participate?

We first want to know if you are eligible to participate.

All patients who have been treated in the intensive care unit for at least three days and who have been mechanically ventilated at least 24 hours, are eligible to participate in this study. However, it is important that you are clear in mind and can make a well-considered decision. In addition, you must have enough understanding of the Dutch language to understand ICU-VR and to complete the questionnaires.

Step 2. Informed Consent

Within the first week after you are discharged from the intensive care unit, a doctor, nurse or investigator has given information about the study. You have also received this information letter. We ask you to carefully and thoroughly read this letter, and consider participation.

You will be given one to four days for your consideration. Here after, the doctor, nurse or investigator will visit you again. You will then have the opportunity to ask questions about the study. If you want to participate in the study, you, together with the doctor, investigator or nurse, will sign the consent form on the last page of this letter. By signing the informed consent form, you indicate that you have received sufficient information about the study, that you have had the opportunity to ask questions about the study, and that you want to participate in this study on that basis. After that, a short check-up will be carried out to determine whether you are clear in mind.

Step 3. Questionnaire and randomization

Once you have signed the consent form, you will receive the first questionnaire. First, we want to investigate how your psychological state and quality of life were before you were admitted to hospital. Secondly, we want to investigate your current psychological state and quality of life. It takes approximately 40 minutes to complete this questionnaire.

In addition, participants in this study will be randomly assigned to **three groups.** This randomization, comparable with a lottery, decides to which group you are assigned and will be conducted after having singed the informed consent form. The investigator or doctor **does not have any influence** on the outcome of the randomization. You therefore do not know in advance which group you will end up in, and you are not allowed to indicate a preference for this.

The three groups are as follows:

1) The control group. Participants in this group **will not receive ICU-VR.** You will receive the same care as if you did not participate in this study, but are additionally asked to fill out questionnaires.
2) The **early ICU-VR** group. Participants in this group will receive ICU-VR for **a maximum of three times**, between 8 and 15 days after your discharge from the intensive care unit, if you are still in the hospital ward. When you are discharged from the hospital, you will no longer be offered ICU-VR.

3) The **late ICU-VR** group. Participants in this group will receive **ICU-VR during a visit to our intensive care unit follow-up clinic**, where you will be invited three months after your discharge from the intensive care unit.

Step 4. Intensive Care Unit-specific Virtual Reality

Participants in the early or late ICU-VR group will receive ICU-VR at least once. As previously described, ICU-VR is a 12-minute informational film about the Intensive Care Unit. To view ICU-VR, we use our Virtual Reality glasses. **Image 1** shows what these glasses look like (left), and how the VR glasses are used (right). You will also be explained how to use the VR glasses and how to behave in the virtual environment when you receive ICU-VR.

Image 1. On the left you see the VR glasses that will be used during this study. You put the glasses over your eyes, as shown on the right. The VR glasses use light that is harmless to your eyes. You can keep your glasses on while using the VR glasses.

Step 5: Intensive care unit follow-up clinic

Three months after your discharge from the intensive care unit, we will invite you to visit our intensive care unit follow-up clinic. During this visit, you and an ICU nurse and/or doctor will review your stay in the intensive care unit. They will see if you need help from other healthcare providers, such as a physiotherapist or psychologist, and you can ask questions about your intensive care unit stay. Prior to this visit you will be asked to complete questionnaires, which will be sent to you by e-mail or postal mail.

Step 6: Questionnaires

All participants will be asked to complete questionnaires on 5 time points during the study. You will receive the first questionnaire immediately after signing the consent form, as described in 'Step 2'. In addition, you will be asked to complete questionnaires 1 month, 3 months (before the visit to the aftercare outpatient clinic), 6 months and 12 months after your discharge from the intensive care unit. The length of the questionnaires varies per follow-up time point. Completing the questionnaires will take approximately 30 to 45 minutes per questionnaire.

5. What commitments do you make when participating?

We would like this study to be conducted as intended. Therefore, we ask you to honour the following commitments:

- If you are in a group receiving ICU-VR, you are willing to watch ICU-VR and you will try to watch the entire film. Of course, you can stop if you want to, for example if it gets too intense or you have nausea symptoms.
- During this study, you will not also participate in other medical scientific research without discussing this with the investigator. He/she can determine whether or not you can simultaneously participate in the other study.
- You visit the intensive care unit follow-up clinic when you are invited. If you are unable to attend on the proposed date, please try to find another date for this appointment.
- You complete the questionnaires at the requested time points. The investigator will also send you reminders. If you are unable to complete the questionnaires yourself, ask a family member/friend/girlfriend to help you with this.
- You contact the investigator in these situations:
    - You will be re-admitted to the hospital or the intensive care unit.
    - You no longer wish to participate in the study.
    - Your contact details, such as your telephone number, address or e-mail address, change.

6. What side effects, adverse effects or inconveniences may you experience?

We have shown in previous studies that the use of ICU-VR for patients is safe. There were no serious or long-lasting side effects. However, virtual reality can cause short-term complaints that resemble motion sickness. Think of nausea or dizziness, both during the film and just after the film. These complaints are usually mild in nature, last a few minutes and go away on their own. If the complaints persist for longer, you can contact someone from the study team. Their contact details are listed in **Appendix A.**

7. What are the advantages and disadvantages of participating in the study?

Participating in the study may have advantages and disadvantages. We list them below. Consider these when considering participation, and talk about them with others.

A possible advantage of participating in this study is that it may lead to a better psychological recovery and a better quality of life after your intensive care unit stay. However, this is **not certain and is being investigated in this study.** In addition, this only applies to patients who have been randomized to the early or late ICU-VR group and who have received ICU-VR.

A disadvantage is that it takes time to complete the questionnaires. In addition, you must adhere to the commitments as discussed in section 5. Also, if you are randomized to the early or late ICU-VR group, you may experience side effects as described in section 6.

Don't want to participate?

You are the one to decide whether or not you want to participate. Do you not want to participate? This is no problem, and nothing will change with regard to how you are treated.

8. When will the study end?

The investigator will let you know if there is new information about the study that is important for you as participant. The investigator will then ask you whether you want to continue your participation.

In these situations, the study will stop for you:

- You completed the last questionnaire 12 months after you were discharged from the intensive care unit.
- You decide that you no longer wished to participate. You can always terminate your participation. We ask you to immediately inform the investigator if you wish to no longer participate. You don't have to give a reason why you wish to no longer participate. Discontinuation of your participation will never have consequences for your treatment.
- The investigator thinks it's better for you to stop.
- One of the following authorities decides that the study should be terminated:
    - The sponsor,
    - the government, or
    - the medical ethics committee that assesses the research.

What happens if you stop the study?

The investigators may use your data which is collected until the moment you decide to discontinue your participation. If you want, data that is collected from you can be deleted. You can request this by the investigator.

The entire study will be ended if all participants have completed their last questionnaire.

9. What happens after the study?

Within twelve months after you completed the last questionnaire, the investigator will contact you to ask if you would like to be informed about the most important findings of the study.

10. What do we do with your data?

Are you participating in the research? Then you also give permission to collect, use and store your data.

What data do we keep?

We keep this data:

- your name
- your gender
- your (e-mail) address
- your date of birth
- information about your treatment in the intensive care unit
- data that we collect during the research, such as the outcomes of the questionnaires

Why do we collect, use and store your data?

We collect, use and store your data to answer the questions of this study. And to be able to publish the results.

How do we protect your privacy?

To protect your privacy, a code will be assigned to all your data. This code will be the only identifier for your data. The key, which makes it possible to link the code with you, will be stored in a safe place in the intensive care unit where you were treated. When we process your data, we will only use this code. In reports or publications about the study, we will ensure no participants can be identified based on the data provided.

Who has access to your data?

There are persons can be given permission to access the data without codes. These are persons who monitor whether the study is conducted properly and reliably, and according to all regulations.

Persons who will be given permission are:

- A monitor who is an employee of the Erasmus MC
- National supervisory authorities.

These persons will treat you data confidentially. By consenting to participate in this study, you also give permission that your data can be monitored by these.

How long do we keep your data?

We store your data for 15 years in the hospital where you were treated, or in a secured online database.

Can you withdraw your consent to the use of your data?

You can always withdraw your consent for the use of you data. However, if you withdraw your consent, and the investigators have already collected data for the study, the investigator is allowed to use the data collected until the consent was withdrawn.

Would you like to know more about your privacy?

- Do you want to know more about your rights with regard to the use of your data? You can take a look at www.autoriteitpersoonsgegevens.nl.
- Do you have any questions about your right? Or do you have complaints about the use of your data? You may contact the person who is responsible to the collection of your data. For this study, this will be the principle investigator, of whom the contact details can be found in **Appendix A of this letter**.
- If you have complaints about the use of your data, we would recommend to first discuss these with the investigators of the study. You can also contact the Data Protection Officer of the hospital where you relative was treated. Their contact details are stated below. You can also file a complaint by the Authority of Personal Data.

Where can you find more information about the study?

On the website www.trialregister.nl you will find more information about the study. After the study, the website may display a summary of the findings of this survey. You can find the study by searching for 'ICU-VR for patients in the ICU' (number: NL78555.100.078)

11. Will you be financially compensated when you participate in the study?

Participation in this study is free of charge. You will neither receive any compensation for participation in this study, also no travel or expense reimbursement.

12. Are you insured during the study?

You are not extra insured for this research, because participating in the research has no additional risks. Therefore, the investigators do not need to purchase additional insurance from the United Medical Ethics Committee, the medical ethics review committee that approved this study.

13. Do we inform your GP?

As participation to this study is not expected to have any negative consequences for your health, or the health of your family members/relatives, we will not inform you general practitioner about your participation in this study. You are however free to tell your general practitioner yourself, and he/she can contact the study team for questions.

14. Do you have questions?

Questions about the study can be asked to the study team. The contact details of the study team are stated in **Appendix A**. Would you like to be advised by someone who is not involved in the study team? You can then contact dr. [redacted], his contact details are in **Appendix A.** He is an independent expert of the study, and has thereby the knowledge to answer your questions and give you advice, but is not involved in the study.

Do you have a complaint? Then discuss this with the investigator or the doctor who is treating you. Do you prefer to talk to somebody else? You may contact the complaints officer or complaints committee of your hospital, or the Authority of Personal Data. **Appendix A** shows where you can find them.

15. How do you give consent for the study?

You should first think about participating in this study. Therefore, you should tell the investigator whether you have understood the provided information and whether or not you would like to participate. If you want to participate, you will be asked to fill out and sign the informed consent form on the last page of this letter. Both you as the investigator will receive a copy of the signed version of the informed consent form.

Thank you for your time.

16. Attachments to this information

A. Contact Details

B. Consent Form

Appendix A: Contact Details

Research team:

[redacted], executive investigator, first contact person

Mail: [redacted]
Telephone: [redacted]
Accessibility: Working days between 09.00 and 18.00

[redacted], coordinating investigator

Mail: [redacted]
Telephone: [redacted]
Accessibility: Working days between 09.00 and 18.00

[redacted], principal investigator

Mail: [redacted]
Telephone:
Intensive Care: [redacted]
Hospital: 010 704 07 04
Accessibility: Working days between 09.00 and 18.00

Independent physician:

[redacted]
Mail: [redacted]
Telephone:
Intensive Care: [redacted]
Hospital: [redacted]
Accessibility: Working days between 09.00 and 18.00

Complaints:

Do you have a complaint? Then discuss this with the researcher or the doctor who is treating you. Would you rather not? Then go to the complaints officer or complaints committee of your hospital ([redacted]). You can submit your complaint digitally ([redacted]), by mail ([redacted]), by post ([redacted]) or by telephone ([redacted]).

Erasmus MC Data Protection Officer:

Mail: [redacted]
Phone number: [redacted]

For more information about your rights, please contact Hans Vlake. He is responsible for the processing of your personal data.

Participant Information
Virtual Reality for patients in the Intensive Care Unit

Appendix B. Informed Consent Form

Related to to: 'The effect of Intensive Care-specific Virtual Reality (ICU-VR) on psychological complaints after Intensive Care treatment.'

- I have read the information letter. I have been given the opportunity to ask additional questions, and my questions are answered sufficiently. I have had enough time to consider participation.
- I know that participation is on a voluntary basis. I also know that I can always decide to not participate or to stop participation. I do not have to give any reason if I decide not to participate or to stop participation.
- I give consent to the investigators to collect and use my data. The investigators will only collect and use data to answer the research question of the study.
- I am aware that there are persons who can be granted permission to access my data to monitor the study. I give consent to these persons to access my data.
- I give permission to collect, store and use my data to answer the research question: ☐**YES / ☐ NO**
- I give permission to contact me after this study to ask if I am interested to participate in another, related study: ☐**YES / ☐ NO**
- I want to participate in this research.

My name is (participant): ……..

Signature: …… Date : __ / __ / __

I declare that I have fully informed this subject about the said study.

If new insights will be obtained about the study, which could influence the participant's decision to participate in the current study, I will timely inform the participant.

Name of investigator (or its representative):……..

Signature:…… Date: __ / __ / __

The participant will receive a complete copy of the information letter, including a (copy of the) signed version of the informed consent form.