

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### Comparison of the effect of the integrated drug- incentive spirometry therapy with drug therapy alone on recovery and mortality of patients admitted to hospital with Covid 19

#### Protocol summary

##### Study aim

Evaluation of the effectiveness of integrated drug therapy and respiratory training with incentive spirometer on mortality and recovery rates of adult patients admitted to hospital with Covid 19.

##### Design

A clinical trial with the control group, with parallel groups, three-way blind, randomized, phase 3 on 160 patients. Randomization will be performed using the rand function of Excel software.

##### Settings and conduct

Participants are among 19 patients admitted to the non-intensive care unit of Imam Hussein Hospital in Tehran. Patients will be divided into intervention and control groups. Both study groups receive the same drug and non-drug treatments according to the latest published version of the national protocol. The case group will perform breathing exercises according to the study protocol. By assigning a dedicated code to participants, data collectors, treatment teams, patients, and analysts are blinded to group assignments.

##### Participants/Inclusion and exclusion criteria

Patients with definite Covid19, greater equal 18 years old with peripheral oxygen levels less than 94% who do not require intensive care, no pregnancy, and no history of chronic lung or heart disease.

##### Intervention groups

Eligible patients will be divided into two groups of 80, control and intervention. Both groups receive the same drug treatment according to the declared protocol. In addition, the intervention group was asked to perform breathing exercises with an encouraging spirometer on a daily basis.

##### Main outcome variables

-Clinical recovery rate -Severity Dyspnea based on Modified Borg 0-10 scale (MBS) -Blood pressure; Heart rate; Respiratory rate; Symptoms of respiratory distress

in the form of intercostal and sternal retraction and use of respiratory sub-muscles; O2 sat (pulse oximetry) in two modes with/without (oxygen therapy)

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20201012049010N2**

Registration date: **2022-03-04, 1400/12/13**

Registration timing: **retrospective**

Last update: **2022-03-04, 1400/12/13**

Update count: **0**

##### Registration date

2022-03-04, 1400/12/13

##### Registrant information

##### Name

Mohammad Bargahi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 6601 6580

##### Email address

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##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-08-16, 1400/05/25

##### Expected recruitment end date

2021-11-21, 1400/08/30

##### Actual recruitment start date

2021-08-19, 1400/05/28

**Actual recruitment end date**

2021-10-21, 1400/07/29

**Trial completion date**

2022-02-04, 1400/11/15

**Scientific title**

Comparison of the effect of the integrated drug-incentive spirometry therapy with drug therapy alone on recovery and mortality of patients admitted to hospital with Covid 19

**Public title**

Efficacy and Safety of Respiratory Exercises with Incentive Spirometry in Hospitalized Adult Patients with SARS-CoV-2

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Older age equals 18 years Patients with Covid 19 (based on diagnostic methods of the latest published version of the National Protocol) Need to be admitted to a non-intensive care unit Hospitalization in the last 6 hours

**Exclusion criteria:**

Any case of CNS disorder that interferes with patient communication and educability Need to be admitted to the intensive care unit at the time of enrollment history of lung disease sPo2<94% (at room air) Participation in any other clinical trial of an experimental treatment for COVID-19 pregnant woman or man who his spouse is pregnant history of CHF Requiring mechanical ventilation at screening Evidence of multi-organ failure Recent of ACS no willingness for enrollment

**Age**

From **18 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Care provider
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**

Target sample size: **160**

Actual sample size reached: **160**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

The sampling method in this study was based on Simple randomization (random numbers table). To create a random list in Excel software, 160 samples (two identical groups of 80) were considered in one column, then the RAND function was assigned. In the end, the samples were sorted from low to high. On a daily basis, eligible patients were assigned by the registrants based on the embedded list in two groups: A) control and B) intervention. Registrants, outcome assessors, and the relevant health care team were not aware of the randomization process.

**Blinding (investigator's opinion)**

Triple blinded

**Blinding description**

Eligible patients were divided into two groups by a two-person group of researchers based on a designed table. For one of the patients, a data collection form with a special code will be determined at the time of enrollment. The data were collected by a separate team of collectors on a daily basis and recorded in a designed online data sheet. Health care providers and the treatment team were also unaware of the allocation of patients to either group. The collected data will be statistically analyzed by the analysis group in groups A and B without group-specific labels.

**Placebo**

Not used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Research Ethics Committee of Shahid Beheshti University of Medical Sciences

**Street address**

Imam Hussein Hosp, Shahid Madani St, Teharan

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**Province**

Tehran

**Postal code**

1617763141

**Approval date**

2021-10-31, 1400/08/09

**Ethics committee reference number**

IR.SBMU.RETECH.REC.1400.519

**Health conditions studied****1****Description of health condition studied**

Covid19

**ICD-10 code**

U07.1 + J1

**ICD-10 code description**

مواردتائید شده کووید 19 با بیماری تنفسی (پنومونی ویروسی) و/یا (علایم و نشانه های بیماری تنفسی) تنگی نفس ، سرفه

**Primary outcomes****1****Description**

Clinical recovery rate

**Timepoint**

Daily until discharge from the hospital

**Method of measurement**

No shortness of breath (by patients) + Larger SpO<sub>2</sub> equal to 93 (no oxygen uptake) + lower temperature equal to 37.5 ° C for 48 hours.

**2**

**Description**

Respiratory rate

**Timepoint**

The first day before the intervention and daily for 5 days or until discharge, whichever is earlier

**Method of measurement**

Number of breaths per 1 minute

**3**

**Description**

Peripheral blood oxygen saturation in oxygen therapy

**Timepoint**

The first day before the intervention and daily for 5 days or discharge, whichever is earlier

**Method of measurement**

Percentage of oxygen after 2 minutes with finger pulse oximeter in 5 minutes apart from oxygen while sitting on the bed

**4**

**Description**

Percentage of peripheral blood oxygen saturation in the absence of oxygen therapy

**Timepoint**

The first day before the intervention and daily for 5 days or discharge, whichever is earlier

**Method of measurement**

Percentage of oxygen after 2 minutes with a finger pulse oximeter while sitting on the bed

**5**

**Description**

Intravenous carbon dioxide content

**Timepoint**

The first day of hospitalization and the fifth day or time of discharge, whichever is earlier

**Method of measurement**

According to the VBG report

**6**

**Description**

Intravenous oxygen level

**Timepoint**

The first day of hospitalization and the fifth day or time of discharge, whichever is earlier

**Method of measurement**

According to the VBG report

**7**

**Description**

Intravenous bicarbonate

**Timepoint**

The first day of hospitalization and the fifth day or time of discharge, whichever is earlier

**Method of measurement**

According to the VBG report

**8**

**Description**

Intravenous blood pH

**Timepoint**

The first day of hospitalization and the fifth day or time of discharge, whichever is earlier

**Method of measurement**

According to the VBG report

**9**

**Description**

Severity of dyspnea

**Timepoint**

The first day before the intervention and daily for 5 days or discharge, whichever is earlier

**Method of measurement**

Based on Modified Borg Standard Questionnaire 0-10 scale (MBS)

**10**

**Description**

Blood pressure

**Timepoint**

The first day before the intervention and daily for 5 days or discharge, whichever is earlier

**Method of measurement**

With the same standard sphygmomanometer cuff while the patient is sitting on the bed for 10 minutes

**11**

**Description**

Sex

**Timepoint**

the first day

**Method of measurement**

Being male or female

**12**

**Description**

Stress level

**Timepoint**

The first day before the intervention and daily for 5 days or discharge, whichever is earlier

**Method of measurement**

Based on the standard Zung Self-Rating Anxiety Scale (SAS)

## **13**

### **Description**

Duration of hospitalization

### **Timepoint**

From the first day of hospitalization until discharge

### **Method of measurement**

Number of days elapsed until discharge

## **Secondary outcomes**

## **1**

### **Description**

One-month mortality rate for any reason

### **Timepoint**

One month after enrollment

### **Method of measurement**

telephone follow-up

## **2**

### **Description**

3-month mortality rate for any reason

### **Timepoint**

3 months after enrollment

### **Method of measurement**

telephone follow-up

## **3**

### **Description**

The need for intubation

### **Timepoint**

Until discharge from the hospital

### **Method of measurement**

Number of intubated patients based on the opinion of the relevant treatment team

## **4**

### **Description**

The need for hospitalization in the intensive care unit

### **Timepoint**

Until discharge from the hospital

### **Method of measurement**

Number of patients admitted to the intensive care unit based on the opinion of the relevant treatment team

## **5**

### **Description**

Maximum exhaled exhaust air pressure in the first second

### **Timepoint**

3 months after the time of enrollment

### **Method of measurement**

According to spirometry reports

## **6**

### **Description**

Maximum amount of exhaust air

## **Timepoint**

3 months after the time of enrollment

## **Method of measurement**

According to spirometry reports

## **7**

### **Description**

Ratio of exhaust air loss from the first second to the total

### **Timepoint**

3 months after the time of enrollment

### **Method of measurement**

According to spirometry reports

## **8**

### **Description**

Overall carbon monoxide emission capacity

### **Timepoint**

3 months after the time of enrollment

### **Method of measurement**

According to spirometry reports

## **9**

### **Description**

Mileage in 3 minutes

### **Timepoint**

3 months after the time of enrollment

### **Method of measurement**

Based on standard 3-minute walk distance test (6MWD)

## **Intervention groups**

## **1**

### **Description**

Intervention group: Patients in this group (from the day of admission to the study) were given the same in addition to pharmacological and non-pharmacological treatments. After each training session, the patients in the intervention group were asked to intervene after a deep breath for 2 to 5 seconds and confinement. Breathe for 1 second, begin to exhale deeply in the spirometer, encourage each time they can take action, then wait for rest until the patient feels the need, then repeat this breathing exercise 4 more times with the same quality. Will repeat. If the patient receives oxygen through the mouth mask, he or she will receive oxygen through the nasal mask during breathing exercises. This group was also asked to continue the same treatment for the given exercise in case of discharge from the hospital for up to 3 months.

### **Category**

Treatment - Devices

## **2**

### **Description**

Control group: Patients in this group did not receive any additional intervention and received the same drug and non-drug treatments as the intervention group, based on the opinion of the relevant treatment team according to

the latest published version of the national protocol.

**Category**

N/A

**Recruitment centers**

**1**

**Recruitment center**

**Name of recruitment center**

Imam Hussein Hospital

**Full name of responsible person**

Naser Parvaei

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Imam Hussein Hosp, Shaid Madani St, Tehran

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**Sponsors / Funding sources**

**1**

**Sponsor**

**Name of organization / entity**

Shahid Beheshti University of Medical Sciences

**Full name of responsible person**

Dr. Afshin Zaraghi

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Shahryari Sq, Evin, Tehran

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**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Shahid Beheshti University of Medical Sciences

**Proportion provided by this source**

100

**Public or private sector**

Public

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

*empty*

**Country of origin**

**Type of organization providing the funding**

Academic

**Person responsible for general inquiries**

**Contact**

**Name of organization / entity**

Shahid Beheshti University of Medical Sciences

**Full name of responsible person**

Mohammad Bargahi

**Position**

General practitioner

**Latest degree**

Medical doctor

**Other areas of specialty/work**

General Practitioner

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**Person responsible for scientific inquiries**

**Contact**

**Name of organization / entity**

Shahid Beheshti University of Medical Sciences

**Full name of responsible person**

Mostafa Alavi Moghadam

**Position**

Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Immunology

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## Person responsible for updating data

### Contact

**Name of organization / entity**

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**Position**

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**Latest degree**

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

Yes - There is a plan to make this available

**Study Protocol**

Yes - There is a plan to make this available

**Statistical Analysis Plan**

Yes - There is a plan to make this available

**Informed Consent Form**

Yes - There is a plan to make this available

**Clinical Study Report**

Yes - There is a plan to make this available

**Analytic Code**

Yes - There is a plan to make this available

**Data Dictionary**

Yes - There is a plan to make this available

**Title and more details about the data/document**

All collected data can be subscribed in CSV format after identifying the participants. And videos taken from patients during breathing exercises can also be shared if they are satisfied.

**When the data will become available and for how long**

Immediately after publishing the article

**To whom data/document is available**

All researchers and individuals working in academic and scientific institutions

**Under which criteria data/document could be used**

For all scientific and therapeutic uses

**From where data/document is obtainable**

Email the corresponding author and the first author of the relevant article

**What processes are involved for a request to access data/document**

After receiving the email, the request will be answered in coordination with the responsible team, and mentioning the source is mandatory

**Comments**