

# Prednisolone for loss of smell after COVID-19 infection

<b>Submission date</b> 28/07/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 09/06/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 18/11/2022	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Loss of the sense of smell (anosmia) is common in COVID-19 infections. Most patients regain a normal sense of smell within 4 weeks, but in 6-8% the sense of smell does not fully recover. These persistent smell disorders greatly influence daily life. It is thought that COVID-19 causes disorders in smell due to inflammation around the olfactory nerve and in the olfactory pathways. Corticosteroids could reduce this local inflammatory response and improve the sense of smell. The aim of this study is to determine the effectiveness of a short high-dose treatment of oral prednisolone for persistent loss of sense of smell after COVID-19 infection.

### Who can participate?

Patients aged 18 years and over with a persistent loss of sense of smell (for over 1 month) within 3 months of a COVID-19 diagnosis

### What does the study involve?

Participants are randomly allocated to one of two groups. One group receives prednisolone daily for 10 days. The other group receives matching placebo (dummy drug) treatment. All patients will perform smell training. Participants' sense of smell and taste are assessed and they fill in questionnaires related to their smell and taste ability, quality of life and nasal symptoms.

### What are the possible benefits and risks of participating?

The potential benefit is an improvement in smell and a decrease in life-long disability. Treatment with prednisolone can have side effects. There is wide experience with this particular dose, which is generally well tolerated by patients. The main side effects include gastric problems, loss of sleep, mood swings, muscle cramps. Side effects stop after stopping the treatment. The researchers believe that the potential benefits are in proportion with the potential risks.

### Where is the study run from?

UMC Utrecht (Netherlands)

### When is the study starting and how long is it expected to run for?

February 2021 to March 2024

Who is funding the study?  
Netherlands Organisation for Health Research and Development (Netherlands)

Who is the main contact?  
Dr Digna Kamalski  
d.m.a.kamalski@umcutrecht.nl

## Contact information

**Type(s)**  
Public

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2021-004021-71

**ClinicalTrials.gov (NCT)**  
Nil known

**Protocol serial number**  
Nil known

## Study information

**Scientific Title**  
Corticosteroids for COVID-19 induced loss of Smell (COCOS trial)

**Acronym**  
COCOS

**Study objectives**  
Loss of smell (anosmia) is common in COVID-19 infections. Most patients regain normal smell within 4 weeks, but in 6-8% the smell does not fully recovery. These persistent smell disorders greatly influence daily life. It is thought that COVID-19 causes disorders in smell due to inflammation around the olfactory nerve and in olfactory pathways. Corticosteroids could reduce this local inflammatory response and improve smell.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 13/10/2021, METC.Utrecht (huispostnummer D01.343, Postbus 85500, 3508 GA Utrecht, The Netherlands; +31 (0)88-7556376; info@metcutrecht.nl), ref: 21-635

## **Study design**

Single-centre double-blind placebo-controlled randomized trial

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Persistent (>1 month) loss of smell within 3 months of COVID-19 (SARS-CoV-2 infection) diagnosis based on a positive test

## **Interventions**

The study will be double-blinded. Participants will be randomly allocated to one of the two groups. Both groups carry the same weight (1:1). Block groups will be 4. Blocks are used to minimise seasonal effects between the groups. The randomisation sequence list on which the patient's number is linked to the study medication is made by the pharmacy. Investigators and patients will be blinded to the randomisation sequence. After finishing all analyses the blinding of researchers and patients to the treatment allocation will be broken. If debinding is necessary this can be done by the pharmacy at any time

One group receives 40 mg of prednisolone daily for the duration of 10 days. The other group receives matching placebo treatment. All patients will perform smell training.

## **Intervention Type**

Drug

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

Prednisolone

## **Primary outcome(s)**

Objective olfactory function measured using Sniffin' Sticks at baseline, 12 weeks and 12 months

## **Key secondary outcome(s)**

1. Objective gustatory function measured using Taste Strips at baseline, 12 weeks and 12 months
2. Self-reported smell, taste, parosmia, trigeminal sensations measured using the visual analogue scale (VAS) at baseline, 12 weeks and 12 months
3. Quality of life measured using the questionnaire of olfactory disorders (QoD) at baseline, 12

weeks and 12 months

4. Nasal symptoms measured using Sino-Nasal Outcome Test (SNOT-22) at baseline, 12 weeks and 12 months

**Completion date**

01/03/2024

## Eligibility

**Key inclusion criteria**

1. Recent COVID-19 infection (<3 months), confirmed with a positive test
2. Persistent loss of smell after 1 month, objectified by threshold-discrimination-identification (TDI) <30.5 on Sniffin' Stick test
3. Age 18 years or older, capable of giving informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

115

**Key exclusion criteria**

1. Pre-existing olfactory disorders
2. Chronic rhinitis or rhinosinusitis (with or without nasal polyps)
3. Pregnancy
4. Corticosteroids (nasal, oral or intravenously) in last month
5. Contra-indications of steroid use:
  - 5.1. Insulin dependent diabetes mellitus
  - 5.2. Ulcus pepticum

**Date of first enrolment**

15/10/2021

**Date of final enrolment**

01/03/2022

## Locations

**Countries of recruitment**

Netherlands

**Study participating centre**

**UMC Utrecht**

Heidelberglaan 100

Utrecht

Netherlands

3584CX

## **Sponsor information**

**Organisation**

University Medical Center Utrecht

**ROR**

<https://ror.org/0575yy874>

## **Funder(s)**

**Funder type**

Research organisation

**Funder Name**

ZonMw

**Alternative Name(s)**

Netherlands Organisation for Health Research and Development

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

Netherlands

## **Results and Publications**

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from DHS-datamanagement@umcutrecht.nl or Dr Digna Kamalski (d.m.a. kamalski@umcutrecht.nl).

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		16/11/2022	18/11/2022	Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes