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Ayurveda for promoting recovery in long COVID

Submission date	Recruitment status	[X] Prospectively registered
03/08/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
15/08/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
20/06/2025	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is a double-blind randomised placebo-controlled trial aiming to evaluate the effectiveness of an Indian traditional herb, Ashwagandha, for promoting recovery in people experiencing ongoing symptoms of Long COVID.
'Ashwagandha' (Withania somnifera) has been used for centuries as part of the traditional Indian Ayurvedic system of medicine for promoting energy and vitality, reducing stress and boosting the immune system. Recently, a number of small and medium randomised trials in humans have demonstrated its potential effectiveness for reducing many of the symptoms characteristic of long COVID. Ashwagandha has a well accepted safety profile as is available over the counter as a herbal supplement in the UK.

Who can participate?
Adults over 18 years, diagnosed with long COVID.

What does the study involve?
Participants will be recruited through select recruiting GP practices based across the UK. They will take trial medication for 3 months which will be sent to their house via post.
Follow-up surveys to assess their functional status, quality of life, symptom burden and work status will be conducted by online or postal questionnaires. Clinical monitoring to assess safety will be conducted monthly and at the end of the trial, remotely or in-person, through participating GP practices.

What are the possible benefits and risks of participating?
The study may not benefit participants directly, but the information we get from the study will help our knowledge and understanding of how to treat long-term symptoms of COVID-19, for which there is currently no proven medical treatment or cure. Ashwagandha is considered a safe herbal medication which is widely used in India and globally. However as with all medications, there is a possibility that allergic reactions or side effects may occur. If participants experience any side effects or unusual symptoms they should let their study doctor know as soon as possible.

Where is the study run from?
London School of Hygiene & Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
July 2021 to June 2025

Who is funding the study?
Ministry of AYUSH, Government of India (through the All India Institute of Ayurveda (AIIA), an autonomous institution under the Ministry of AYUSH)

Who is the main contact?
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Study website
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Additional identifiers

EudraCT/CTIS number
2020-005789-33

IRAS number
293329

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 293329

Study information

Scientific Title
Clinical trial of Ashwagandha for promoting recovery from COVID-19 in the UK

Acronym
APRIL

Study objectives
Ashwagandha can improve functional status, quality of life and alleviate symptoms in UK adults suffering from long-term symptoms of Covid-19.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 25/07/2022, Wales Research Ethics Committee 3 (Health and Care Research Wales, Castle bridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2920 230457; Wales.REC3@wales.nhs.uk), ref: 22/WA/0157

Study design
Multicenter randomized double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Long COVID

Interventions
Trial design: Randomised double-blind placebo-controlled trial. Interested adults who are diagnosed with long COVID (defined as per NICE guidelines - NG188) that affect and limit their everyday activities will be randomised to take Ashwagandha or placebo for 3 months (delivered at home by post).
Participants will be recruited through participating GP practices based across the UK. Eligible participants will be approached by the participating GP's team and trial discussed in detail. Participant Information Sheet (PIS) will be emailed/posted to them or handed to them (if seen face-to-face) at least 1-2 days before signing the informed consent form (ICF). Participants will be able to go through the PIS and ask questions and discuss the trial information with research staff, their family and friends before taking a decision. Participants will be able to sign the ICF online or a paper copy will be posted to them. All ICFs will be verified and stored safely in the Investigator Site File (ISF) by the recruiting GP sites.

After signing ICF, participants will have a consultation with the recruiting doctor (study investigator) for clinical assessment and eligibility. This may be in-person or by phone/video call. Participants will have a blood test to assess their liver function at screening.
All WOCBP will have urine pregnancy done before taking trial medication to rule out pregnancy. All participants will follow contraception methods as described in the protocol. Once the participant is confirmed eligible, the trial team will formally enrol them into the study and baseline questionnaires will be sent out. On receiving completed baseline questionnaires, participants will be randomised in the trial.

Randomisation: Blinded computer-based randomisation in 1:1 ratio after baseline questionnaires are received. Block randomisation will be used to ensure balance across the study recruitment period.

Interventions: The intervention arm will receive Ashwagandha (aqueous root extract) at a daily dose of 1000mg in tablet form, taken twice daily (morning and evening) for 3 months (2x (2x250mg) tablets). The control arm will receive placebo tablet indistinguishable from Ashwagandha in appearance, to be taken as per the same regimen. Trial medication will be sent monthly by post with tracked delivery. The courier will confirm that the products were delivered to a member of the correct household and take the name and signature of the recipient. Receipt of the products by trial participant will be confirmed via text and/or phone call from the study team within 2 days.

Follow-up: Participants will be followed-up monthly for 3 months. Each month clinical monitoring and safety assessment will be done by the recruiting doctor's team. All participants will have a blood test to assess their liver function after one month of trial medication and at the end of 3 months (end of the trial). All adverse events (AEs), serious adverse events (SAEs) will be promptly reported to the trials unit as described in the protocol. Patients will be further investigated and treated if required and if required medication will be discontinued or stopped as per clinical assessment and participant safety. All WOCBP will repeat a urine pregnancy test at the end of each month for 3 months to rule out pregnancy. If pregnant while on trial treatment they will discontinue trial treatment and report to their doctor immediately.

For outcome assessment, participants will be asked to complete monthly online questionnaires for physical functioning, quality of life and symptoms. These will be sent to participants at the end of the first month, end of the second month, end of the third month. Automated email or text reminders will be sent as per participant preference. In case participants are unable or unwilling to complete surveys online, paper questionnaires in pre-paid return envelopes will be posted each month along with the trial medication packages. If participants fail to respond two months in a row, a follow-up call will be made to them. If they fail to respond then a phone call will be made to their nominated next of kin only to ascertain participant's wellbeing.
Analysis: At the end of the trial, the results will be analysed according to a pre-specified analysis plan, comparing whether people in the Ashwagandha or Placebo group had better functional status after 3 months.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ashwagandha (Withania Somnifera root extract)

Primary outcome measure
Self-reported functional status measured using the Post-COVID-19 Functional Status Scale (PCFS), at 3 months

Secondary outcome measures
Measured at baseline, 1 month, 2 months and 3 months
1. Quality of life by PROMIS 29+2 summary score

2. Self-reported fatigue, pain, sleep, anxiety, depression and social, physical and cognitive function by PROMIS 29+2 individual dimensions
3. Self-reported breathlessness by modified MRC Dyspnoea Scale
4. Health utility by EQ 5D-5L utility score
5. Self-reported work status and productivity
6. Other self-reported symptoms
7. Number of adverse events (3 months)

Overall study start date
26/07/2021

Completion date
18/06/2025

Eligibility

Key inclusion criteria
1. Adults (18 years or older) with the capacity to provide informed consent, and
2. Have been diagnosed with Long COVID as per the NICE Guidelines (NG188) – that is, either one of “Ongoing symptomatic COVID-19; signs and symptoms of COVID19 from 4 weeks up to 12 weeks”, or “Post-COVID-19 syndrome; Signs and symptoms that develop during or after an infection consistent with COVID19, continue for more than 12 weeks and are not explained by an alternative diagnosis. It usually presents with clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body. PostCOVID19 syndrome may be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed”. The diagnosis will be confirmed by the participant’s GP and/or
3. medical records.
4. Report that their Long COVID has reduced their ability to carry out day-to-day activities compared with the time before they had COVID-19.
5. Willing and able to complete the study protocols (take trial medication regularly for 3 months, complete online telephone or postal surveys monthly, and participate in clinical monitoring assessment monthly)
6. Not taking any other herbal medicines, or willing to stop taking any such medicines for the duration of the trial. Herbal medicine is defined as a plant or plant part, or mixture or extract of these, which is taken in medicinal form to improve health, prevent disease, or treat illness

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
2500

Total final enrolment
105

Key exclusion criteria
1. Self-diagnosed Long COVID in the absence of a clinical diagnosis as per the NICE Guidelines
2. Any medical condition or suspected medical condition which, in the opinion of the Investigator may present an unreasonable risk to the study participant as a result of his/her participation in this clinical study (this may involve conduct of any clinical assessment deemed necessary by the study investigator to confirm that this criterion is met, such as (but not limited to) validated psychiatric scales, ECGs, and laboratory tests for clinical chemistry, haematology, urinalysis, kidney function, etc).
3. Previous clinical diagnosis of severe psychiatric disorders
4. Abnormal liver function test results, as indicated by alanine aminotransferase or aspartate aminotransferase or total bilirubin >2 x ULN, either measured as part of routine care within past 3 months or conducted for the purposes of the clinical trial (if a recent test result is not available).
5. Previous clinical diagnosis of chronic kidney disease or other medical condition associated with impaired kidney function
6. Previous clinical diagnosis of heart disease or other cardiac problems
7. Use of any investigational products within 5 elimination half-lives after the last dose or at screening
8. History of malignancy unless resolved by adequate treatment with no evidence of recurrence
9. Hypersensitivity to the active substance or to any of the excipients
10. Women breastfeeding or with a positive urine pregnancy test at screening
11. Women planning to become pregnant for the duration of the participation in the study
12. Men and women of childbearing potential unwilling to adhere to the relevant contraception requirements for the duration of the study (until at least 24 hours after the final dose of trial medication is taken). Women of childbearing potential (WOCBP) are defined as all women who are: “fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, confirmation with more than one FSH measurement is required.” Acceptable contraception methods for WOCBP in this trial include: combined hormonal contraception, progestogen-only hormonal contraception, intrauterine device, intrauterine hormone-releasing system, bilateral tubal occlusion, vasectomised partner, sexual abstinence, or condom use. Sexual abstinence is defined as: “refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject”. Male participants are required to use condoms. All participants are required to inform investigator immediately if these contraception requirements are not met or if pregnancy is suspected.
13. Participants taking benzodiazepines, anticonvulsants, barbiturates or any other CNS depressants

Date of first enrolment
14/11/2022

Date of final enrolment

31/08/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Hockley Farm Medical Practice
39 Hockley Farm Road
Leicester
United Kingdom
LE3 1HN

Study participating centre
Bay Medical Group
York Bridge Surgery
5 James Street
Morecambe
United Kingdom
LA4 5TE

Study participating centre
Highcliff Medical Centre
Heila House
Lymington Road
Highcliffe
Christchurch
United Kingdom
BH23 5ET

Study participating centre
Oaks Healthcare
26 – 30 London Road
Cowplain
Waterlooville
United Kingdom
PO8 8DL

Study participating centre
Whaddon Healthcare
25 Witham Court
Bletchley
Milton Keynes
United Kingdom
MK3 7QU

Study participating centre
Finchampstead Surgery
474 Finchampstead Road
Finchampstead
Wokingham
United Kingdom
RG40 3RG

Study participating centre
Hedena Health
207 London Road
Headington
Oxford
United Kingdom
OX3 9JA

Study participating centre
St. Clements Surgery
39 Temple Street
Oxford
United Kingdom
OX4 1JS

Study participating centre
Kes@northgate
Northgate Health Centre
15 Market Street
Oxford
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OX1 3EF

Study participating centre

Melrose Surgery
73 London Road
Reading
United Kingdom
RG1 5BS

Study participating centre
Lancaster Medical Practice
20-21 Leinster Terrace
London
United Kingdom
W2 3ET

Study participating centre
Penicuik Medical Practice
The Health Centre
37 Imrie PLACE
Penicuik
United Kingdom
EH26 8LF

Study participating centre
Blackpool Teaching Hospitals NHS Foundation Trust
Victoria Hospital
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ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Government

Funder Name
Ministry of AYUSH, Government of India (through the All India Institute of Ayurveda (AIIA), an autonomous institution under the Ministry of AYUSH)

Results and Publications

Publication and dissemination plan
Primary study results will be dissemination via a peer-reviewed publication in an open-access high-impact journal, as soon as possible after trial databases are locked. Following this, press releases and other public statements may be made. Additional publications arising from the trial (secondary analyses etc) will also be published in peer-reviewed journals.

Intention to publish date
18/06/2026

Individual participant data (IPD) sharing plan
We will be asking consent from participants to put their de-identified data onto a public data repository. For patients who consent to this, we will review the data after databases are locked to ensure that confidentiality would be maintained, and put an appropriate data extract onto a public repository within 1 year of database lockdown.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3	05/07/2022	15/11/2022	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 4	01/03/2023	20/02/2024	No	No
Protocol article		25/04/2025	28/04/2025	Yes	No
Protocol file	version 4.1	25/03/2025	20/06/2025	No	No