# Post-COVID: risk factors and prevention to diagnostics and treatment

Date of publication: August 6<sup>th</sup> 2024
Deadline submitting project ideas: **October 8<sup>th</sup> 2024, 14.00 CEST**

This is an English translation of the original call for proposals. In the event of any ambiguities or inconsistencies, the original Dutch text shall prevail.

## Contents

# 1    Summary

**Who can Apply**
Private and public legal entities located in the Netherlands can apply for funding. It is important to involve different disciplines, patients and chain partners in the research. Relevant partners should be collaborated with as much as possible during the elaboration of the grant proposal.

**What for**
The aim of this call is to address research themes in the area of post-COVID that emerge from the Knowledge Agenda Post-COVID and research themes emerging from the post-COVID programme. The projects should join/connect with the research and expertise network post-COVID (Dutch name: Post-COVID Netwerk Nederland).

**What to request**
The total available grant budget in this funding round is €6.000.000 for a duration of up to 30 months. The project should start as soon as possible, but no later than 2 months after the grant decision.

**When**

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| Deadline submitting project ideas | October 8th 2024, 14.00 CEST |
| Receipt advice by advisory committee | First half December 2024 |
| Deadline for submitting detailed grant application | January 28th 2025, 14.00 CEST |
| Receipt of reviewers' reports | February 25th 2025 |
| Deadline submitting rebuttal | March 18th 2025 |
| Decision | End of June/Beginning of July 2025* |
| Latest start date | As soon as possible, no later than 2 months after granting |

*Decision depends on the committee meeting. This will be planned in April or May, depending on the availability of the committee and project group members during the holidays and may vacation.

An interview is part of the review process for your grant application. An audio recording will be made of the interview. At the end of the review process, the audio recording will be destroyed.

# 2    Aim of the call for grant applications

This call is part of the research programme post-COVID and the aim of this call is to address research themes emerging from the recently published 'Knowledge Agenda Post-COVID' of the Dutch Federation of Medical Specialists (Dutch abbreviation: FMS) and Dutch College of General Practitioners (Dutch abbreviation: NHG) and research themes as specified in the programme text of the post-COVID programme.

**Background**
Post-COVID syndrome, also referred to as long COVID or post-acute sequelae SARS-CoV-2 infection (PASC), refers to the persistent health problems that a proportion of people experience after infection with SARS-CoV-2, the virus that causes the disease COVID-19. These health problems can vary from mild to severe and may cover a broad range of persistent symptoms, including fatigue, shortness of breath and concentration problems, as well as longer term effects such as damage to the heart, lungs and brain.

There are still large knowledge gaps concerning the clinical picture, and there are currently no proven effective treatments available that can reduce or relieve (causes of) post-COVID complaints. An important cause of this is the limited information about the underlying disease processes and recovery-promoting factors. For example, the WHO has defined post-COVID as '*the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation*'.[1] Recently, the National Academies of Sciences, Engineering and Medicine (NASEM) published a new definition; '*Long COVID (LC) is an infection-associated chronic condition (IACC) that occurs after SARS-CoV-2 infection and is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state that affects*

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[1] https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition#:~:text=Definition,months%20with%20no%20other%20explanation

*one or more organ systems*'[2]. These definitions are broad, lack specificity and do not contribute to insights into the nature and scope of post-COVID.

**Post-COVID programme**
ZonMw has been commissioned by the Ministry of Health, Welfare and Sport (VWS) to realise a [post-COVID programme](link) to fund research into post-COVID, strengthen the knowledge infrastructure and establish a research and expertise network. The programme serves a societal interest: the development and application of practically relevant knowledge that contributes to preventing and reducing post-COVID problems and thus achieving as good a recovery as possible. The post-COVID programme aims to increase and disseminate knowledge and expertise about post-COVID for the diagnosis, treatment and optimisation of care. The research programme post-COVID is part of this overarching post-COVID programme.

**Drawing up the Knowledge Agenda Post-COVID**
At the start of 2024, the Expertise Team Post-COVID of the FMS and the NHG itemised where in daily practice there is a lack of scientific evidence (knowledge gaps) concerning the care for post-COVID patients. The Knowledge Agenda Post-COVID includes a top-5 of knowledge gaps in the area of 'risk factors and prevention', 'screening and diagnostics', and 'complications and risks'. In addition, a top-10 was produced for knowledge gaps in the area of treatment (primary care, hospital care and paramedical care).

The knowledge agenda is a living document, which means that it will be periodically updated. Knowledge gaps will be removed from the knowledge agenda when they have been answered by current research or when they cease to be relevant. At the same time, new knowledge gaps will be itemised and prioritised.

**Research themes relevant for this call**
Within this call for proposals, research into the themes emerging from the previously mentioned Knowledge Agenda Post-COVID is possible. [The complete knowledge agenda can be found on the ZonMw website](link) (only available in Dutch). Research themes that are part of this knowledge agenda are, for example, the treatment of post-COVID by means of pharmacological interventions, such as immune-modulating therapy, IDO-2 inhibition, selective serotonin reuptake inhibitors (SSRIs) and antihistamines. However, research into non-pharmacological interventions, such as hyperbaric oxygen therapy, heartbeat pacing, and the monitoring of heart rate variability can also be performed. In addition, it is possible to do research into risk factors, prevention and diagnostics of post-COVID, such as risks for other chronic conditions, identifying biological and clinical profiles, and using the PET-CT scan in diagnostics.

Care evaluation[3] is also part of the research themes. As described in the post-COVID programme, this theme offers room for the assessment of treatments by means of comparative research or research into the combination of treatments such as randomised controlled trials (RCTs) or platform studies. The last research theme is follow-up research, during which it is possible to expand an ongoing study with, for instance, a new patient category or a new intervention.

For all research themes, it is vital to take into account the different demographic patient categories such as children, teenagers, young adults, socioeconomic background, migration background and regional differences. Clinical patient categories should also be considered, such as patients with autonomic dysfunction, dysfunctional breathing, post-exertional malaise (PEM), postural orthostatic tachycardia syndrome (POTS), neurocognitive complaints, extreme fatigue and bedridden patients.

# 3 Conditions and obligations
You must take account of certain rights, conditions and obligations when applying for a ZonMw grant. The rights, conditions and obligations of a grant applicant are based upon the [Dutch General Administrative Law Act (Awb).](link) Article 4.2 of the Awb contains specific provisions applying to ZonMw grants. [General Terms and Conditions Governing Grants of ZonMw](link) also apply.

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[2] National Academies of Sciences, Engineering, and Medicine. 2024. A Long COVID Definition: A Chronic, Systemic Disease State with Profound Consequences. Washington, DC: The National Academies Press. https://doi.org/10.17226/27768

[3] Research on interventions that are standard care, but of which the effectiveness has not yet (sufficiently) been established.

## 3.1 Conditions

Your project idea and detailed grant application must comply to the conditions below in order to be processed.

Detailed grant applications will only be accepted from applicants who previously submitted project ideas in this funding round that were positively recommended for approval. Are you still considering submitting a grant application despite this negative advice? Then I kindly request you to contact us as soon as possible, but no later than 4 weeks after receipt of the advice, at covid19@zonmw.nl.

### 3.1.1. Who is eligible for a grant?

Private and public legal entities located in the Netherlands can apply for funding.

### 3.1.2. Avoiding State aid

No grants will be awarded by ZonMw if this would or could constitute unlawful state aid[4]. Therefore, the following state aid measure applies to this funding round:

**Exemption Decision for Services of General Economic Interest (SGEI)**

If ZonMw will consider a part of the proposed project activities as Services of General Economic Interest (SGEI), then this will mean that there are specific conditions for funding and rules for budgets. You can find out more about the SGEI Exemption Decision in Annex 1 – State aid – SGEI , as well as the requirements that have to be met under the SGEI Exemption Decision.

You can find more information about state aid on the ZonMw web page State aid exemption decrees.

### 3.1.3. Third-party collaboration and contributions

ZonMw encourages the participation of different partners in collaborative projects. Such projects will, however, not receive a grant if the agreements would or could lead to the provision of unlawful state aid or if ZonMw's General Terms and Conditions or the conditions of the call for grant applications cannot be met.

During the development of the project idea and detailed grant application there should be as much cooperation as possible with relevant partners. It is also important to involve different disciplines, patients and chain partners in the research. If applicable, patient participation in the project group or consortium is required, as a partner from protocol development onwards.

The application and budget must make it clear:
- Which parties are participating. Describe how each party will be actively contributing to the project; these should in any case be parties who appear in the budget as a party intending to claim a portion of the grant. Also include parties that will be making an active contribution as partners in the collaborative project for their own account and at their own risk.
- With which party or parties a sponsorship agreement will be concluded and what their donation in kind or monetary contribution will be.
- Which parties will be hired, or, if this is not yet known, which activities are forecast as being performed by third parties, plus the related costs that will be incurred (including VAT). For more information and the conditions of hire/terms of contract, see the ZonMw web page.

Collaborations and sponsorship must be finalised before presenting the detailed grant application.

**Letters of Commitment**

Because ZonMw requires assurance that a project party or sponsor will be legally bound to provide the agreed amounts, each project party or sponsor must provide a Letter of Commitment, which is to be submitted together with the detailed grant application. Please use the template letter which you can find on the ZonMw web page Grants and collaborations/contributions from third parties.

**Collaboration and sponsorship agreement**

You can find more information about the various types of collaboration and contributions (sponsoring/assignment) with sample agreements on the ZonMw web page Grants and collaborations/contributions from third parties as an aid to drafting the relevant agreement; the

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[4] Section 107 of the Treaty on the Functioning of the EU (TFEU).

accompanying explanation contains the conditions the agreement must meet. The conditions specified on this web page and in the explanation form an integral part of this call for grant applications. Where ZonMw requests draft collaboration and/or sponsorship agreements, it awards the grant on the condition that the agreements are found to be acceptable..

### 3.1.4. What is the amount of the grant I can apply for?

The total available grant budget for this funding round is €6.000.000. There are no limitations to the amount of the grant you can apply for. The aim is to grant projects focused on, one or more of, the various research themes as described in the Post-COVID Knowledge Agenda and the post-COVID programme.

- The maximum duration of the project is 30 months.
- The budget must be realistic and well-substantiated. You are urged to draw up a budget that is appropriate to the scope of the proposed research. Co-financing is possible and desirable in certain types of projects.
- Reserve 10% of your project budget for communications and implementation. Include this amount in the budget of the detailed grant application.
- Costs for datamanagement, including the deployment of data steward and additional activities and/or services for FAIR data management. Provide a realistic budget or use approximately 3-5% of the research budget as a guideline.
- Include a compensation for patient participation in the budget of the detailed grant application.
- For projects of €125,000 or more, auditing costs (max €3,500) may be included in the budget. The amendment to the General Terms and Conditions Governing Grants of ZonMw as of 1 April 2022 means that after completion of a project of €125,000 or more, an auditor's report must be provided in addition to the final report and financial accounts. Universities and university medical centres may not include auditing costs in the budget. Separate agreements have been made with these institutions regarding the required auditor's report. Please contact your financial department for more information.
- If you publish according to the full golden Open Access route, you may include the cost of Open Access publications in the project budget. The maximum amount of this allowance is €5,000. Please include 'Open Access' as a separate line in your budget. For more information about Open Access, see Section 3 and the ZonMw web page Open Access.

### 3.1.5. Practical conditions

**Project idea**
- Write your project idea in English.
- Your project idea will also be evaluated by a post-COVID patient panel. Therefore it is important to clearly describe the following subjects in the application form under patient participation: relevance of the research for post-COVID patients, feasibility of the project from the patient perspective and how patient participation is integrated in the research.
- The total requested budget in the detailed grant application cannot be more than 15% higher than the amount you presented in the project idea.
- Together with the project idea only the following optional annex may be added: Maximum 1 sheet of A4 size with figures and tables.

**Detailed grant application**
- Write your detailed grant application in English.
- You are required to include a budget with your detailed grant application, use the DAEB budget format. The total amount cannot be more than 15% higher than the amount you presented in the project idea.
- Reserve 10% of your project budget for communications and implementation.
- Costs for datamanagement, including the deployment of data steward and additional activities and/or services for FAIR data management. Provide a realistic budget or use approximately 3-5% of the research budget as a guideline.
- The following annexes are mandatory:
  - If the project involves collaboration and/or sponsorship: a Letter of Commitment per collaborating party.
- The following optional annexes may be added: Maximum 2 sheets of A4 size with figures and tables.

If an annex is not mandatory, it will not be included in the assessment of your application. The exception is the optional annex presenting figures and/or tables. This annex will also be included in the assessment.

## 3.2 Obligations
**General Terms and Conditions Governing Grants of ZonMw**
In addition to the General Terms and Conditions Governing Grants of ZonMw, the following conditions also apply:

– **Open Access**
All publications resulting from scientific research fully or partially funded by ZonMw must be made available in Open Access, in accordance with the ZonMw Open Access policy. ZonMw accepts various Open Access routes. In addition to articles, ZonMw encourages researchers to make their results available in other formats via Open Access, such as monographs, books, conference proceedings and grey literature, but also research data and knowledge products for practice-oriented research, such as models, protocols, prototypes, digital tools and demonstrations.
For more information about the ZonMw Open Access policy, conditions and opportunities, please visit our website.

– **Conditions for valorisation**
As ZonMw is committed to making the projects it funds widely accessible, the ten principles of Socially Responsible Licensing (SRL) should be applied to the licensing of results. Please describe, where applicable, how intellectual property rights will be arranged with partners and any third parties. Also indicate how these parties will comply with the ten principles.

# 4 Assessment criteria

## 4.1 Assessment procedure
For the procedures on how to assess grant applications, please refer to the infographic 'applying for a grant in 10 steps'.

This grant call consists of 2 phases: a project idea phase and a detailed application phase. During the project idea phase, the project ideas will be assessed by the advisory committee for relevance and generally for quality, with relevance weighing more heavily. The relevance from the patient perspective will be assessed by a post-COVID patient panel. Only the most relevant and most promising project ideas will receive positive advice to elaborate the project idea into a detailed grant application.

During the detailed grant application phase, reviewers will assess the quality of your application. The reviewers who assess your grant application are experts in the field and not involved in your application. You will receive the reviewers' quality assessments in anonymised form. In addition, the relevance of your application is assessed by the post-COVID patient panel, who specifically assess your application from the patient perspective. You will also receive this assessment in an anonymized form. You will then be invited to respond in writing (rebuttal). Finally, you will be invited to participate in an interview with the assessment committee.

The assessment committee assesses the relevance, quality and budget of all applications using your application, the assessments by the reviewers and the patient panel, the interview and the rebuttal. The committee will use the criteria as stated in this call text. The applicable relevance and quality criteria are given below.

## 4.2 Relevance criteria
– **Diversity**
Consider how attention is given to diversity and target group differentiation by characteristics such as sex and gender, age, socioeconomic situation, educational level, migratory and cultural backgrounds, and sexual inclination, inasmuch as these are relevant to the theme of the project..

– **Participation of patients and/or end users**
Describe how you will involve stakeholders in the project. Stakeholders include the ultimate target group or end users, whose knowledge is based on practical, personal experience. By 'involve' we

mean consulting, asking for advice, collaborating with and/or involving end users in project decisions.

– **Access to data**
ZonMw promotes the optimal use of data. In your detailed grant application, describe the possibilities of making use of existing data files and substantiate any stated need for new data collection. Also indicate your plans regarding sharing and making your future results FAIR. When planning your project and its budget, take into account the opportunities and requirements set out at [FAIR data & data management](). If you do not intend to collect any data, please mention this in your grant application. The basic principle is that you use existing databases where possible. If you are going to collect new data, you must comply as much as possible to existing standards, models, terminologies (etc.) that are used in (post-)COVID research. For projects in the post-COVID programme it is mandatory to produce FAIR metadata with the [COVID-19 specific metadata schemes](). The metadata about your project and dataset will then be made available via Health-RI's [COVID-19 data portal](). We recommend that you involve your data steward/expert in your application at an early stage.

– **Implementation and impact**
Describe how you expect to achieve and demonstrate impact. Projects funded by the ZonMw must have impact. New knowledge and expertise must be used in practice, policy, education and/or further research. On our website we explain what impact is, how we work to achieve and demonstrate it and what we expect from project managers. You can find more information on the ZonMw web page [Implementation]().

– **Call specific criteria**
  - The subject fits within the framework of the post-COVID programme and fits the goal of this grant call as described in section 2.
  - Patient participation is an essential component and a requirement in the project, as a partner from protocol development onwards. There is a clear plan for involving stakeholders and end-users in the project. The application describes how they will be consulted, collaborated with, and/or engaged throughout the duration of the project.
  - The proposed research takes into account the recommendations from the patient perspective, if applicable to the research, as described in the [published stakeholder consultation]() (only available in Dutch).
  - There is a clearly substantiated plan on how to connect to the [Post-COVID Network Netherlands]() (only available in Dutch). It is also clearly described how the infrastructure of this network will be utilized. The project plan of PCNN is available via the application form.
  - The research project (also) addresses or includes children experiencing post-COVID conditions, deviating from this criterium can only be justified if there is convincing substantiation.
  - In case of follow-up research; promising pilot data are described in the application, convincing the committee of the relevance of the follow-up research.
  - The research is not already being conducted (inter)nationally (applicant must convincingly substantiate this), or the applicant must convincingly substantiate that research in the Netherlands is necessary in addition to international research. The committee will take into account the current calls for proposals within the post-COVID programme: 'Biomedical Knowledge gaps Post-COVID' and 'Clinnical Research Post-COVID – patient questions'.
  - Connection is made with ongoing (inter)national research as much as possible.
  - There is a clear plan for the dissemination and implementation of the research findings towards clinical practice.

## 4.3  Quality criteria

– **Objective and research question/mission statement**
Describe the objective and research question or remit. In your outline, pay attention to clarity, scope and originality.

– **Action plan**
Describe the chosen methods and analyses, including theoretical and/or empirical support.

– **Feasibility**
Make it plausible that the objective of the grant application can be achieved within the established timeframe and with the expertise, staffing, facilities and resources available.

- **Project group or person**
  Describe how the composition of the project group/consortium will contribute to the quality of your research or project. Preferably, this concerns a multidisciplinary composition, all relevant disciplines are represented in the project group/consortium.

You can find more information about these criteria on the ZonMw webpage Assessment.

## 4.4 Prioritisation

During the assessment of the detailed grant applications, the committee weighs relevance and quality using the matrix below. In the matrix, relevance is given more weight than quality. A grant application must at least be of good quality to be considered for funding.

| Quality \ Relevance | Highly relevant | Relevant | Low relevance |
|---|---|---|---|
| **Very good** | 1 | 3 | Reject |
| **Good** | 2 | 4 | Reject |
| **Sufficient** | Reject | Reject | Reject |
| **Poor** | Reject | Reject | Reject |
| **Insufficient** | Reject | Reject | Reject |

Grant applications will be eligible for funding in the order of priority 1 to 4. The applications that fall in the non-numbered cells will not qualify for funding in any circumstance. If after applying the prioritisation matrix the number of eligible applications exceeds the available budget, the committee will deploy the following additional grounds of evaluation:

- A proposal eligible for funding that focuses on treatment possibilities for children with post-COVID will be given priority over a higher-ranked proposal aimed at treatment possibilities for adults if, within the available budget, no proposal centred on children has been prioritised for funding.
- A proposal eligible for funding concerning bedridden patients will be given priority over a higher-ranked proposal targeted at non-bedridden patients if, within the available budget, a proposal aimed at bedridden patients has not been prioritised for funding.
- The committee may choose to fund the next application that fits into the call budget instead of a the application with higher priority that exceeds the call budget.

# 5 Submitting your application

## 5.1 Submission through Mijn ZonMw

Project ideas can only be submitted by the main applicant in ZonMw's online submission system (Mijn ZonMw). The closing date for submitting a project idea is October 8th 2024, at 14.00 CEST

## 5.2 Tips

- ZonMw now uses a different online application system. If you have not worked with Mijn ZonMw before, you must first register as a 'New user'.
- For further information, see the Mijn ZonMw manual.

We advise you to print out a Word version of your application (via Mijn ZonMw) and carefully review it for errors before you submit it digitally. This is especially important if you have created your application in Word and then copied it to Mijn ZonMw, as some characters (such as quotes) may not be converted correctly. You can correct this yourself in Mijn ZonMw.

## 5.3 Statement of agreement for submission of detailed grant application

The 'Statement of agreement for submission of detailed grant application' must be signed by the individual with administrative responsibility and the main applicant. The signed declaration can be added to the application in Mijn ZonMw or sent to ZonMw by email at covid@zonmw.nl. The declaration must have been received no later than one week after submission of the application.

## 5.4    Substantive questions

For questions regarding the contents of the application, please contact: Myrthe Naber, 070 515 03 13 or covid19@zonmw.nl.

## 5.5    Technical questions

If you have any technical questions about using ZonMw's online application system, please contact the Service Desk from Monday to Friday between 8.00 and 17.00 070 349 51 78, servicedesk@zonmw.nl). Please include your telephone number in your email so that we can call you back if necessary.

## 5.6    Downloads and links

- General Terms and Conditions Governing Grants of ZonMw
- Applying for funding in 10 steps
- What must I submit?
- Conditions and obligations
- The assessment
- Grants and collaborative third-party contributions
- State support exemption
- Datamanagement and FAIR data
- Open Access
- Implementation and impact
- Mijn ZonMw manuals
- Statement of approval for submission of a detailed grant application
- Programme page Post-COVID (Dutch)
- Programme Post-COVID (Dutch)
- Stakeholder consultation (Dutch)
- Post-COVID Knowledge Agenda (Dutch)

# 6. Annexes

- Annex 1 – State aid – SGEI

# Annex 1 – State aid – SGEI

If an undertaking applies for a grant in this funding round, ZonMw will provide the grant under the SGEI Exemption Decision[5], provided a number of conditions have been met. You can find these conditions below.

ZonMw has designated the activities referred to under the heading 'aim of the call for grant applications' as economic activities of general interest. Before allocating the grant, ZonMw will, by means of a decision, charge the grant recipient or recipients of the activities described above with the administration of a Service of General Economic Interest (SGEI).

The SGEI consists of implementing (a part of )the activities described in the project proposal. The grant recipient(s) are obligated on the grounds of Article 5(2) of the SGEI Exemption Decision to list revenue and expenditure associated with activities in the service of general economic interest separately from revenue and expenditure for other activities that do not fall within the SGEI.

Project funding will not exceed the maximum duration of the project. In line with the SGEI Exemption Decision, the maximum duration of a project is 10 years.

The grant amount applied for may not exceed the net cost of the planned project activities. The parameters for calculating the compensation for each project are included in the budget documents of ZonMw. The calculation methods included in the submitted budget are in accordance with Article 4 of the SGEI Exemption Decision.
ZonMw will recover any proven overcompensation on the basis of Article 6(2) of the SGEI Exemption Decision. If the project duration exceeds 3 years, ZonMw will perform an interim check to establish whether there has been any overcompensation.

If there is a consortium and at the time of application, it is still unclear which parties are participating in the consortium, it is possible to add these parties to the consortium at a later stage. If a new party is added to the consortium, please notify ZonMw of this in writing. The new party will only be included in the consortium if ZonMw has approved this. All parties must individually meet all the conditions of the SGEI Exemption Decision.

If the project activities are shown not to have been carried out, or not to have been carried out in full, or if the obligations attached to the grant have not been fulfilled, ZonMw may set the grant at a lower amount and recover all or part of any advance payments made.

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[5] Commission Decision of 20 December 2011 on the application of Article 106(2) of the TFEU on state aid in the form of public service compensation granted to certain undertakings entrusted with the operation of services of general economic interest, 2012/21/EU, OJ EU 2012 L7/3.