

Knowledge development post-COVID-19

Nordic Policy Paper

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Executive summary

The COVID-19 pandemic has emphasised the importance of new knowledge in dealing with sudden crises and the need for closer co-operation between the Nordic countries in order to improve preparedness and resilience for future health crises. In addition to research on acute health threats, there is an urgent need for more research knowledge on the post-COVID condition (PCC). PCC is a complex condition that affects multiple body systems and persists for months or even years after the initial phase of a SARS-CoV-2 infection with an estimated prevalence in the population of between 1% and 6%¹. In a Nordic context, data suggests that hundreds of thousands of individuals may have suffered PCC-related conditions in a clinically significant range. Consequently, PCC can have a significant effect on both afflicted patients and communities, as well as have far-reaching ramifications for health systems, national economies, and global health metrics.

Improving recovery from PCC is of the utmost importance and requires robust evidence on the effectiveness of rehabilitative interventions, including also patient perspectives. In addition to the impact that rehabilitation has on the daily lives and health outcomes of the individual PCC patient, it is also very important at the societal and organisational level. Moreover, there needs to be an emphasis on prevention as the risk for PCC increases with each SARS-CoV-2 re-infection², and more research is needed to understand how to best prevent PCC.

There are several important lessons to be learnt from the emergence of PCC. In future health crises, the potential long-term health consequences should be considered already in the acute phase of a pandemic. When encountering a new viral or pandemic disease, new knowledge should be derived from cross-sectoral and multidisciplinary research to make the most impact. Networks and platforms for such collaboration between experts in different areas should preferentially be in place already before a new pandemic emerges rather than established ad hoc as the situation develops.

The purpose of this policy paper is to summarise the key scientific findings on PCC and the relevant research needs that have been identified in the project "Knowledge development post-COVID" initiated by the Nordic Council of Ministers in accordance with the policy priorities of the Nordic Council. Knowledge gaps related to PCC and lessons learnt for developing preparedness for future pandemics and strengthening health resilience are discussed in a Nordic context. Nordic opportunities for collaboration within PCC research, research funding, and policy development are also highlighted.

1. Introduction

Strengthened Nordic collaboration for better crisis management is a priority of the Nordic Council. The COVID-19 pandemic has emphasised the importance of new knowledge in dealing with sudden health crises and the need for closer co-operation between the Nordic countries. In response to this, in 2022 the Nordic Committee of Senior Officials for Health and Social Affairs (EK-S), the operating body under the Nordic Council of Ministers for Social Affairs and Health, tasked NordForsk with co-ordinating a project on knowledge development post COVID-19. The project ran in 2023 and 2024.

Nordic Council

[The Nordic Council](#) is the official body for formal inter-parliamentary co-operation in the Nordic region. Formed in 1952, it has 87 members from the national parliaments of Denmark, Finland, Iceland, Norway, Sweden, the Faroe Islands, Greenland, and Åland.

The Nordic Council of Ministers

[The Nordic Council of Ministers](#) is the official body for inter-governmental co-operation in the Nordic Region. It consists of twelve individual councils of ministers and seeks common solutions wherever and whenever the countries can achieve more together than by working on their own.

Nordic Committee of Senior Officials for Health and Social Affairs

[The Nordic Committee of Senior Officials for Health and Social Affairs \(EK-S\)](#) consists of representatives from all five Nordic countries and the independent areas. It takes care of the practical work and preparations for meetings of the Nordic Council of Ministers for Health and Social Affairs (MR-S).

NordForsk

[NordForsk](#) is an organisation under the Nordic Council of Ministers that provides funding for and facilitates Nordic co-operation on research and research infrastructure.

The aim of the project was to establish a network for collaboration on new research questions born out of the pandemic, including knowledge sharing on examples of best practice and clinical guidelines for the treatment of patients suffering from post-COVID conditions (PCC). A further aim was to identify knowledge gaps that could be developed into Nordic clinical research initiatives.

NordForsk established a Nordic expert group responsible for the scientific and strategic design of the project. The expert group met a total of twelve times, and the conclusions of its work are presented in this policy paper. The group was supported by NordForsk's secretariat.

Nordic expert group

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The expert group arranged a workshop in Stockholm, Sweden, on 20 November 2023 (Appendix) to establish a Nordic forum and gather broader expertise in order to anchor the project's aims. The aims of the workshop were to:

- share knowledge about ongoing Nordic PCC research projects;
- identify knowledge gaps and emerging research questions related to PCC;
- identify Nordic opportunities for research collaboration on PCC; and
- discuss and compare national guidelines for the treatment and rehabilitation of patients with PCC from a research perspective

The workshop was attended by 25 invited Nordic experts, including researchers working on PCC and representatives of health boards (or similar). The programme included presentations on ongoing PCC research both in the Nordic countries and internationally, as well as comments from the patients' organisation Svenska Covidföreningen. Much of the workshop was dedicated to discussions in smaller groups on questions raised by the attendants.

The feedback from the participants of the workshop was predominantly positive. Many pointed out that there is an urgent need for more research knowledge around PCC and that they had lacked a forum for discussing and sharing knowledge around emerging challenges and practices. Contacts formed at the workshop have been maintained afterwards and the outcome of the discussions at the workshop were carefully analysed by the expert group when producing this policy paper. Based on the discussions in the first workshop, a draft for this Nordic policy paper on the post-COVID condition was prepared. A second workshop was arranged on 11 November 2024 to include a wider group of Nordic experts in developing the policy paper and anchoring its recommendations among these experts before publication (Appendix). The workshop was attended by 34 Nordic experts, including many attendees from the first workshop as well as new collaborators and research contacts formed since then. NordForsk also launched a [call for funding for Nordic network activities on post-COVID](#) in line with the recommendations in this policy paper.

The aim of this policy paper is to summarise the key scientific questions and knowledge gaps related to PCC that have been identified during the project. Lessons learnt for developing preparedness for future pandemics and strengthening health resilience are discussed in a Nordic context.

The expert group has identified Nordic opportunities for collaboration within PCC research, research funding, and policy development. These have been formulated into recommendations directed towards the Nordic policy level and funders of national research. It is hoped that these recommendations will lead to support for new Nordic research initiatives and collaboration networks that may help to bridge the key knowledge gaps around PCC, improve the wellbeing of those affected, and strengthen Nordic preparedness for post-viral conditions in the future.

The sole responsibility for the content of the policy paper lies with the Nordic expert group and does not necessarily reflect the opinion of NordForsk. NordForsk is not responsible for any use of the information contained in the Nordic Policy Paper on knowledge development post-COVID.

2. Key scientific questions and knowledge gaps

2.1 Understanding the post-COVID-19 condition

Post-COVID condition (PCC), also referred to as Long COVID, is a complex condition that affects multiple body systems and persists for months or even years after the initial phase of a SARS-CoV-2 infection.³ The World Health Organization (WHO) states that PCC typically emerges in individuals who have had a probable or confirmed SARS-CoV-2 infection, often appearing within three months of recovering from COVID-19.⁴ Symptoms persist for at least two months with no clear explanation from an alternative diagnosis. This condition can impact the respiratory, cardiovascular, neurological, and gastrointestinal systems resulting in diverse symptoms.

Definitions of PCC

World Health Organization WHO (adults)⁴:

Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time.

World Health Organization WHO (children and adolescents)⁵:

Post COVID-19 condition in children and adolescents occurs in individuals with a history of confirmed or probable SARS-CoV-2 infection, when experiencing symptoms lasting at least 2 months which initially occurred within 3 months of acute COVID-19. Current evidence suggests that symptoms more frequently reported in children and adolescents with post-COVID-19 condition compared with controls are fatigue, altered smell/anosmia and anxiety. Other symptoms have also been reported. Symptoms generally have an impact on everyday functioning such as changes in eating habits, physical activity, behaviour, academic performance, social functions (interactions with friends, peers, family) and developmental milestones. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. They may also fluctuate or relapse over time. Workup may reveal additional diagnoses, but this does not exclude the diagnosis of post COVID-19 condition. This can be applied to children of all ages, with age-specific symptoms and impact on everyday function taken into consideration.

National Academies of Sciences, Engineering, and Medicine (NASEM)⁶:

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 one or more organ systems. LC manifests in multiple ways. A complete enumeration of possible signs, symptoms, and diagnosable conditions of LC would have hundreds of entries. Any organ system can be involved, and LC patients can present with

- single or multiple symptoms, such as shortness of breath, cough, persistent fatigue, post-exertional malaise, difficulty concentrating, memory changes, recurring headache, light-headedness, fast heart rate, sleep disturbance, problems with taste or smell, bloating, constipation, and diarrhoea.
- single or multiple diagnosable conditions, such as interstitial lung disease and hypoxemia, cardiovascular disease and arrhythmias, cognitive impairment, mood disorders, anxiety, migraine, stroke, blood clots, chronic kidney disease, postural orthostatic tachycardia syndrome (POTS) and other forms of dysautonomia, myalgia encephalomyelitis/chronic fatigue syndrome (ME/CFS), mast cell activation syndrome (MCAS), fibromyalgia, connective tissue diseases, hyperlipidaemia, diabetes, and autoimmune disorders such as lupus, rheumatoid arthritis, and Sjogren's syndrome.

National Institute for Health and Care Excellence (NICE)¹⁸:

Signs and symptoms that develop during or after an infection consistent with COVID-19, 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. Post-COVID-19 syndrome may be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed.

In addition to the clinical case definitions, the term 'long COVID' is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).

Mechanisms

Although the mechanisms behind PCC are not yet fully understood, various theories have been put forward:

- **Viral persistence.**^{7,8} Some research indicates that remnants of the SARS-CoV-2 virus or its genetic material may linger in tissues sparking prolonged responses. Viral RNA is reported within enterocytes, pneumocytes and other cell types.^{9,10} Viral RNA in recovered patients has been found to be significantly associated with the development of PCC symptoms, with a higher likelihood of developing PCC symptoms in individuals with a higher viral load.⁸
- **Immune system imbalance.**¹¹ Long-term activation and irregularities in the immune system are believed to play roles in causing PCC. Prolonged immune responses such as the continued activation of immune cells, presence of autoantibodies, and dysregulation of cytokines could result in inflammation and damage to tissues.
- **Endothelial dysfunction and blood clots.**¹² Some patients with PCC have been found to have endothelial dysfunction and microclots in their blood, which may contribute to the vascular symptoms and chronic fatigue associated with this condition. Studies with data from 2020-21 have found that COVID-19 is a risk equivalent for coronary artery disease and stroke^{13,14} as well as microvascular dysfunction.^{15,16}
- **Problems with mitochondrial function.**¹⁷ Impaired mitochondrial function that impacts energy production has been suggested as a mechanism leading to fatigue and muscle weakness in PCC patients.

- **Autoimmunity.**¹⁹ Several studies find signs that autoimmunity may play a role in PCC. Furthermore, a recent meta-analysis of genome-wide association studies (GWAS) of PCC has found that variants in the HLA region, genes essential for T cell target detection, and the ABO locus, earlier found to be associated with COVID-19 severity, are associated with PCC.²⁰

Consequently, there are several hypotheses behind this complex condition, which could in turn explain the multiple conditions under the PCC umbrella. PCC has similarities with symptoms occurring after other infections such as post-viral infection fatigue syndrome and post-viral meningitis symptoms²¹ (see below).

Bases for diagnosing PCC in clinical practice

Diagnosing PCC remains difficult due to its broad range of presentations and the lack of specific biomarkers. The diagnostic criteria typically involve:

- History of a confirmed or probable SARS-CoV-2 infection.
- Duration of symptoms. Symptoms that persist for a minimum of two months significantly affecting activities and not attributable to other medical issues.
- Symptoms involving multiple body systems, such as fatigue, difficulty breathing, chest discomfort, cognitive challenges (referred to as "brain fog") disruptions in sleep patterns, irregular heartbeat, and digestive problems. Problems with the nervous system, such as post-exertional malaise (PEM) and postural orthostatic tachycardia syndrome (POTS) are also commonly seen in individuals with PCC.²²

Among the wide range of symptoms associated with PCC²³, cognitive symptoms, dyspnoea, fatigue, and loss of smell and taste have been found to be most specific for PCC.²⁴ Nordic general population studies have provided important evidence for which symptoms are overrepresented from several months to 2-3 years following a SARS-CoV-2 infection, namely: reduced memory, concentration problems, shortness of breath, chest pain, dizziness, fainting spells, heart palpitations, headaches, and fatigue^{25,26,27}. Compromised cognitive function stands out as one of the most consistent findings.²⁸ The likelihood of suffering persistence in most of these symptoms largely depends on the severity of the acute COVID-19 illness, i.e. being hospitalised or extended time spent bedridden (at home) in the acute phase.²⁹ Nevertheless, due to the very large number of people suffering from mild COVID-19, the majority of people suffering from PCC have had a mild COVID-19 disease.

PCC can also manifest as organ dysfunction or damage from SARS-CoV-2, with symptoms from nearly any organ system reportedly affected by the virus.^{30,31,32,33} Organ damage has also been linked to immune system response and disease severity in PCC.³⁴ Despite this, evident organ damage is rarely observed in clinical practice, as some of this damage has only been found using examination methods with increased sensitivity³⁵ that are not in common use and whose clinical validation and relevance often remain uncertain.

Consequently, patients suffering from health problems after infection with the SARS-CoV-2 virus may present with a wide range of symptoms including anything from light symptoms of dyspnoea, fatigue, or forgetfulness to extreme debilitation from the same symptoms and may need assistance from a broad range of healthcare professionals and medical specialists. Individualised assessment and follow-up are therefore crucial, and PCC-related variables should be included in national registers both as a primary diagnosis and as a side diagnosis to facilitate research and medical follow-up.

Association with other conditions following infections

PCC displays resemblances to other known conditions arising after infections.²¹ One example is myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Both disorders exhibit fatigue, cognitive impairment, and worsening symptoms after activity. The shared symptoms suggest pathways involving immune system imbalance and mitochondrial issues.

Another example is post-Ebola syndrome. Individuals who survive Ebola often endure prolonged symptoms such as joint and muscle pain, fatigue, and cognitive issues similar to those observed in PCC. Similar conditions are also seen following other infections, such as post-polio syndrome, post-Dengue fatigue syndrome, post-SARS syndrome, and symptoms following *Giardia lamblia* infections. Viruses such as Epstein Barr and influenza can also result in prolonged fatigue and other symptoms even after the infection has passed, demonstrating that lingering symptoms post infection are not exclusive to SARS-CoV-2.

New-onset disease as a consequence of COVID-19

COVID-19 is a multi-organ, systemic disease. Consequently, SARS-CoV-2 infections are also suggested to be associated with a long-term increased risk of several other conditions, such as diabetes in adults and children³⁶, cardiovascular diseases³⁷, neurological diseases³⁸, infectious diseases³⁹, and many others. A study of electronic health records found associated increased mortality persisted for one year, and even longer for hospitalised individuals, after COVID-19.⁴⁰ These associations add to the problem of quantifying the long-term consequences following SARS-CoV-2 infection and may increase the burden on healthcare and welfare systems from causes not categorised as COVID-19-related. This further highlights the need for a better understanding of the mechanisms and consequences of SARS-CoV-2 infection to mitigate future impacts.

Protective effect of vaccines on PCC

When comparing vaccinated and unvaccinated individuals, vaccines have been found to be safe^{41,42} and to give partial protection against PCC symptoms.^{43,44} A large Swedish population-based study showed that the protective effect increases with each dose⁴⁵, but few studies have yet studied the effect of 4+ doses. The vaccines have also been shown to have a protective effect against cardiovascular complications post COVID-19.⁴⁶ Post-vaccination myocarditis is a rare but serious side effect from the mRNA COVID vaccines. However, the risk of myocarditis is higher after COVID-19 than vaccination, and the prognosis is poorer.⁴⁷

In summary, PCC is a condition with multiple aspects and an intricate pathophysiology that is not completely understood. Understanding the mechanisms behind PCC and establishing guidelines are essential for developing effective management and treatment approaches. More generally, various neurological consequences of different historical pandemics and epidemics are common, which emphasises that short and long-term effects of infections on the nervous system are under-recognised.⁴⁸

2.2 Prevalence in the population

A major obstacle to the appropriate allocation of Nordic resources for the treatment and rehabilitation of patients with PCC is the absence of reliable data on the prevalence and natural history of the condition in the general population.

The complexity and extensive array of symptoms associated with PCC has complicated formulating consensus on diagnostic criteria and the corresponding development of validated measurement tools which, along with a dramatic post-pandemic decline in PCR testing, presents major challenges in studying the changing prevalence of PCC. *Consequently, major research efforts are needed to establish clear diagnostic criteria, severity classification of the condition, and clinical assessment tools that can (also) be used to study the prevalence and natural history of the condition.*

A 2022 meta-analysis of data from 1.2 million individuals infected with SARS-CoV-2 worldwide in 2020-21, including from some Nordic countries⁴⁹, suggests a prevalence of 6.2% of at least one of three symptom clusters (persistent fatigue with bodily pain or mood swings; cognitive problems; or ongoing respiratory problems) present at three months after infection. Prevalence was somewhat higher among women (10.6% vs. 5.4% among men) and considerably higher among hospitalised (27.8%-43.1%) vs. non-hospitalised individuals (5.7%).⁴⁹

One year after infection, the overall prevalence of a probable PCC was 0.9% of infected individuals, remaining at 11.1%-20.5 % among hospitalised individuals.⁴⁹ Similar results on the prevalence of post-COVID symptoms persisting three months after infection (6.9%) were more recently reported in a nationwide US sample of individuals infected up to 2023⁵⁰ and in a nationwide Scottish study.⁵¹ Importantly, the prevalence of PCC is considerably lower among vaccinated than unvaccinated individuals.

However, only a fraction of individuals with symptoms indicative of PCC are captured by the health-care system. The UK Office of National Statistics has reported the prevalence of ongoing self-reported PCC symptoms as around 3%⁵², while preliminary registry data from Finland suggests a PCC diagnosis prevalence close to 1% (unpublished registry-based data). In Denmark, by September 2022, 0.25% of all diagnosed SARS-CoV-2 infections had a diagnosis of PCC requiring tertiary care.⁵³ In Sweden, a registry-based study of 40% of the general population found a cumulative incidence of diagnosed PCC in primary and secondary care among patients with documented COVID-19 of 2% by 15 February 2022.⁵⁴

Prevalence of PCC in children

Research into prevalence of PCC in children has encountered even greater methodological challenges. Publications with data from 2020 and 2021 have reported a wide range of prevalence estimates of between 10% and 25%, some considerably lower.⁵⁵ A more recent Swedish study suggests a PCC prevalence of 0.2% among children.⁵⁶ Although research efforts are ongoing, there is an urgent need to understand more about this complex and sometimes debilitating condition in children and adolescents.⁵⁷ Furthermore, as discussed above, many studies report an increased long-term risk of being diagnosed with other, non-COVID illnesses after a SARS-CoV-2 infection.

2.3 Treatment, rehabilitation, and patient engagement in post-COVID conditions

Although long-term rehabilitation is essential in managing PCC, the effectiveness of various rehabilitative interventions remains uncertain.⁵⁸ High-quality, long-term rehabilitation programmes, in particular individualised and targeted exercise interventions, are crucial for optimal patient outcomes.^{59,60} In addition to the impact that rehabilitation has on the health outcomes of PCC patients at the individual level, rehabilitation is crucial at the societal and organisational level.^{3,61,62}

Studies on rehabilitation have included different interventions such as pacing strategies, fatigue management, breathing exercises, psychological support, physical exercise, and cognitive rehabilitation. However, due to the complexity and heterogeneity of PCC, individually tailored interventions are essential.^{3,61,62} Studies have shown that rehabilitation interventions have an impact on functional exercise capacity, dyspnoea, and quality of life, compared to standard care.³ Diagnostics before starting rehabilitation are also important for identifying red flags such as desaturation, post-exertional malaise/post-exertional exacerbation (PEM/PESE), and orthostatic intolerance⁶⁰ (WHO clinical guidelines). Since most of the patients with PCC have fatigue and a subgroup suffers from PEM/PESE, it is a challenge to prescribe the optimal interventions to avoid symptom exacerbation.

Medical treatments are based on evidence of treating similar symptomatology in other conditions. The primary focus has been on symptom management. The early use of oral antiviral drugs has been suggested to potentially reduce the risk of PCC in non-hospitalised COVID-19 patients.⁶³

However, with current knowledge, antiviral treatment should be guided by existing clinical guidelines as its role in PCC prevention in the general population is still under investigation and further research is needed to provide stronger evidence to inform future recommendations and potentially expand their use.^{3,62,64,65}

In addition to evaluating the effect of rehabilitative interventions, it is important to incorporate process evaluation and stakeholder perspectives (i.e. experiences of individuals living with a condition) to enhance the understanding of rehabilitation and enable the development of future rehabilitative interventions.

A fundamental aspect of research involves the engagement of patients throughout the entirety of the research process. Moreover, in the context of an emerging disease such as PCC, it is imperative to develop strategies for meaningful engagement that are tailored to the specific population. The involvement of patients early in the process through a co-design method can contribute to more personalised interventions and patient-centred care.^{66,67}

In conclusion, as PCC can affect various body functions, physical activity, return to work, health-related quality of life (HRQoL) etc., there is a need for effective and tailored interventions in this population. Therefore, to enhance recovery in PCC, it is important to improve evidence regarding treatment and rehabilitation.

2.4 Randomised controlled trials in PCC research

Randomised controlled trials (RCTs) are the golden standard in medical research for evaluating the effectiveness of a new intervention or treatment on a given condition.⁶⁸ Randomisation is an important tool for reducing bias and improving the possibility to prove causality between intervention and outcome. Although there has been a lack of RCTs into PCC, several studies are underway.

Challenges: The key challenge for RCTs in PCC research is that PCC remains poorly defined, while any intervention trial needs clear endpoints. The three key PCC symptoms of cognitive difficulties, dyspnoea, and fatigue defined in the initial WHO clinical case definition should be applied. Since dyspnoea is related to severe COVID-19 and as such is not new after severe lung infections, this may not be a relevant endpoint to focus on. Moreover, fatigue is unspecific, and it might be difficult to disentangle fatigue caused by the infection from fatigue caused by other factors. New-onset cognitive difficulties after COVID-19 might be the most attractive target/endpoint.

Opportunities: The heterogeneity of the pandemic response in the Nordic countries is an opportunity for collaboration because we have large populations with COVID-19 both before and after vaccination as well as differences in which viral strain was predominant when most of the population was infected. Several large cohorts exist in the Nordic countries that may facilitate RCTs.

Criteria: A key criterion for any RCT is that the research question is of sufficient importance to defend the high cost of an RCT. Of course, the proposed intervention must also be likely to succeed and viable to implement. These criteria point towards preventive interventions (ventilation, air purifiers, medications taken during disease, masking etc.) but do not exclude promising drug interventions based on hypothetical underlying disease mechanisms. Interventions such as rehabilitation programmes should also be pursued to enhance the recovery of PCC patients.

Outcomes: Challenges: Beyond the symptoms reported by patients, newer literature suggests that immunology or imaging-based endpoints might be relevant. Measurements of daily functioning, such as being able to work, study, care for others, and other daily tasks should also be considered. Research has shown that PCC consists of several different conditions, probably with different causes, which need different kinds of interventions.⁶⁹ RCTs should focus on mechanisms directly associated with the viral infection and the specific consequences of this infection.

3. Conclusions and lessons learnt from PCC of importance for other new or pandemic diseases

Rehabilitation and prevention of PCC

The COVID-19 pandemic and the following outbreak of PCC has generated new knowledge and lessons learnt of importance for the preparedness for handling future new or pandemic diseases. Up to 6% of the population may have suffered from PCC symptoms and at least 1% with a symptom burden that has led them to seek healthcare assistance and receive a clinically confirmed diagnosis of PCC.⁵¹ In a Nordic context, data suggests that several hundred thousand individuals may have suffered PCC-related conditions in a clinically significant range.^{70,71} Yet the complexity of the condition and absence of validated measurement tools is hampering research on prevalence and prognosis.

From both an individual and societal perspective, PCC has severe negative implications on the health-related quality of life of those affected as well as on health systems, national economies, and global health metrics.⁶⁵ Therefore, in addition to the impact that rehabilitation has on the daily lives and health outcomes of PCC patients at the individual level, **rehabilitation** is crucial at the societal and organisational level. To further research on PCC, the Nordic expert group concludes that:

- Concise criteria as well as subjective and objective assessment tools for diagnosing PCC are needed to enable the establishment of valid estimates of prevalence.
- Knowledge, experiences, and examples of best practice need to be shared to identify the best support for individualised, targeted interventions for the treatment and rehabilitation of those affected with PCC. Cross-sectoral co-operation is essential for the holistic evaluation of the impact of any intervention.
- Robust evidence on treatment and rehabilitative interventions, encompassing both evaluations of their effectiveness and patient perspectives, are needed to improve recovery from PCC.
- Several studies show that re-infection increases the risk of PCC.^{72,73} Means of reducing spread and the viral load through improving indoor air quality⁷⁴, self-isolating when infectious, or masking when needed⁷⁵, are still relevant and important in the prevention of PCC. However, drawing on lessons from both the overreactions and underreactions observed during the previous pandemic, it is evident that further multidisciplinary research is needed on the overall benefits and drawbacks of implementing restrictions aimed at preventing COVID-19 and PCC. These disciplines include, but are not limited to, clinical medicine, sociology, psychology, health and population economics, epidemiology, environmental science, behavioural science, and public policy analysis. This is crucial also in preparing for future health crises.

Preparedness

In the Nordics, we need to strengthen our **preparedness** for future pandemic diseases and other health crises by drawing on our experience and the lessons learnt from the COVID-19 pandemic. We have learnt that long-term consequences were not easy to predict or measure using conventional biomarkers, although the severity of the initial illness has consistently been associated with increased risk of PCC-related symptoms.³⁶ The Nordic expert group therefore concludes that:

- When encountering a new viral or pandemic disease, possible long-term consequences need to be considered already in the acute phase.
- The systematic follow-up of patients should be a priority from the onset of any emerging infection. This should include long-term cohort or registry-based follow-ups of infected populations across the spectrum of severity, assessing symptoms, function, and the ability to work compared to pre-infection. The comprehensive and unbiased assessment of cohorts of patients, including patient-reported outcomes, observations, and biomedical assessments should be pursued from the outset. Research studies should be planned to allow for a large number of patients and non-infected controls to be included as new hypotheses emerge. Valuable opportunities for learning and knowledge development will be lost if such planning is not executed.
- When encountering a new viral or pandemic disease, new knowledge should be derived from cross-sectoral and multidisciplinary research in order to make the most impact. As discussed above, research should not only encompass the medical sciences and professions, but also other research areas and include patients and their carers/relatives/significant others as valuable partners.
- Nordic networks and platforms for multidisciplinary and cross-sectoral collaboration should be in place already before a new pandemic emerges, not only established ad hoc as the situation develops. Significant added value can be achieved through Nordic co-operation, networking, and strategic co-ordination to strengthen our resilience and preparedness for future public health threats and challenges.

4. Nordic opportunities

The Nordic countries have a great opportunity to leverage their strong tradition of collaboration to address emerging challenges such as post-COVID condition (PCC). There are several ways in which Nordic co-operation can add significant value also in a global context, particularly in terms of research, policy development, and funding initiatives.

- **Opportunities for research collaboration:** The complexity of PCC presents significant knowledge gaps, particularly in understanding its mechanisms, prevalence, and treatment options. The Nordic countries, with their shared healthcare values and robust research infrastructures, are well-suited to conducting **joint studies** that address these gaps. Collaborating on longitudinal studies, clinical trials, and biobanking could help accelerate discoveries related to PCC and other post-viral syndromes. High-quality health registers, similar cultures in the practice of medicine, and general trust in scientists and healthcare professionals strengthen this collaboration. By pooling resources, including access to national health registers and population-based cohorts, the Nordic countries can enhance the scientific understanding of PCC while providing comparative data across different national healthcare systems.
- **Development of policy and guidelines:** Joint efforts in the development of policy and guidelines can help harmonise approaches to the diagnosis and treatment of PCC across the region. This could include developing common diagnostic criteria, clinical protocols, and rehabilitation strategies tailored to the diverse manifestations of the condition. Shared policy frameworks would streamline healthcare delivery, ensuring that all patients, regardless of their country of residence, have access to uniform, high-quality care, treatment, and rehabilitation.
- **Research funding and infrastructure:** Co-ordinated funding efforts are key to unlocking the full potential of Nordic collaboration. Leveraging national research investments through NordForsk's funding programmes, for example, along with co-ordinated applications for EU research grants, would enable larger-scale projects with more diverse participant cohorts. Co-funding initiatives through national research councils, combined with NordForsk's support, could establish a robust infrastructure for PCC research. Additionally, establishing Nordic collaboration and platforms for exchanging knowledge, such as research networks and workshops, would facilitate knowledge exchange and capacity building, fostering an interdisciplinary approach to addressing PCC.

5. Recommendations

In the Nordic countries, **research policy should support** multidisciplinary research on PCC, including research on the causes, diagnosis, monitoring, treatment, and rehabilitation of the condition. Research on the long-term consequences of PCC and other post-viral conditions on both public health and health economics in a Nordic context should also be supported. **National research funding agencies and NordForsk should support:**

- opportunities for setting up and co-funding Nordic PCC research programmes where there is clear added value in conducting research at the Nordic level and clear Nordic strengths are addressed. The wider international context should also be considered in connection with EU and other international funding opportunities, among others.
- the establishment of cross-disciplinary and cross-sectoral Nordic PCC research collaborations to increase the impact of ongoing research.
- the establishment of Nordic PCC-co-operation platforms, e.g. networks for researchers, clinicians, and/or cross-sectoral co-operation between medical expertise, public-private partnerships, key opinion leaders, and patient organisations. with the aim of using lessons learnt from the COVID-19 pandemic to strengthen Nordic preparedness for future crises.
- the engagement of patients and their carers/relatives/significant others as valuable partners throughout the entirety of the research and policy process to strengthen the feasibility and impact of PCC research.

To support high-quality science on the long-term effects of pandemics, **the healthcare system of the Nordic countries should advocate:**

- the monitoring, surveillance, and evaluation of diagnostics, treatments, and rehabilitation processes effective for PCC, e.g. in national expertise centres that encompass research and clinical expertise, as well as support education. Testing for SARS-CoV-2 infection and other epidemic pathogens should be available in the clinical setting.
- professional training of healthcare personnel and medical students in the causes and treatments of PCC.
- the inclusion of PCC-related variables in national registers both as a primary diagnosis and as a side diagnosis to facilitate research and medical follow-up.
- the establishment of platforms for Nordic PCC networks as mentioned above.
- encouraging international and cross-sectoral co-operation also during health crises in order to foster both knowledge and impact.
- tailored public health communication for better awareness and understanding of PCC.
- continuing to stress the importance of prevention of COVID-19 as a means of preventing PCC, however, drawing on lessons learnt so far.

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Appendix: Workshop programmes

Nordic workshop on post-COVID

Date: 20 November 2023

Venue: Radisson Blu Royal Viking Hotel, Stockholm

09.30 – 10.00 Coffee

10.00 Opening of the workshop, Markus Perola

10.15 Keynote 1: Long-COVID Studies Within the RECOVER Platform [online]

Professor Upinder Singh, MD Stanford University School of Medicine

10.35 Discussion

10.45 – 12.00 Ongoing Nordic research projects on post-COVID

One 15-minute presentation from each country, including a short discussion

1. Jane Agergaard, Aarhus University Hospital, Denmark
2. Unnur A. Valdimarsdottir, University of Iceland
3. Anna-Marie Fors-Connolly, University of Umeå, Sweden
4. Nina Langeland, University of Bergen, Norway
5. Markus Perola, Finnish Institute of Health and Welfare

12.00 Lunch

12.45 Keynote 2: What research questions would the patients prioritise? [online]

Tove Lundberg, Svenska Covidföreningen

13.00 Discussion

13.15 – 14.45 Thematic discussions in smaller groups

Group 1: Research evidence for current clinical practice in post-COVID rehabilitation

Group 2: Post-COVID RCTs and other clinical trials.

Group 3: The definition of post-COVID-19

14.45 Coffee break

15.00 Summaries from the groups, discussion on recommendations

16.00 End of workshop

Second Nordic workshop on post-COVID

Date: 11 November 2024

Venue: Radisson Blu Royal Viking Hotel, Stockholm

09.30 – 10.00 Coffee

10.00 Opening of the workshop, Markus Perola

10.10 Ongoing Nordic research projects on post-COVID

imPROving Quality of LIFe In the Long COVID Patient (PROLIFIC), Judith Bruchfeld [online] and Malin Nygren-Bonnier, Karolinska Institutet

Mental Morbidity trajectories in COVID-19 - COVIDMENT, Unnur A. Valdimarsdottir, University of Iceland

LongCovid – Decision support for prediction and management of LCS, Helena Liira, Helsinki University Central Hospital

11.10 Presentation of the policy paper and the network call, discussion

The Nordic expert group and the executive team

12.00 Lunch

12.45 Commentary 1

Niklas Arnberg, Virus- och pandemifonden

13.00 Commentary 2

Cecilia Meldahl and Lisa Norén, Svenska Covidföreningen

13.15 Thematic discussions in smaller groups

Group 1: Key scientific questions and knowledge gaps that need to be addressed by new research

Group 2: Lessons learnt from PCC of importance for other new or pandemic diseases

Group 3: Nordic opportunities for collaboration in research and policy

14.30 Conclusions from the group discussions, way forwards

15.00 Keynote: Long COVID science, research and policy

Dr. Ziad Al-Aly, Washington University School of Medicine, St. Louis, MO, USA. [online]

15.45 Closing of the workshop, next steps



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