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INTERNAL MEMO

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To:	The Honorable Dr ZL Mkhize, Minister of Health	From:	Ministerial Advisory Committee (MAC) on Covid-19

LONG-COVID

Background

- The clinical spectrum of SARS-CoV-2 infection has been shown to range from asymptomatic infection to critical illness.
- Data have recently emerged that some patients continue to experience symptoms after the acute phase of infection.
- Long-Covid denotes those with symptoms lasting for > 28 days or developing after 28 days.

Problem Statement

Based on emerging and evolving evidence that patients who have tested Covid-19 positive are experiencing persistent symptoms 28 days or more after the initial infection, what is the spectrum of symptoms and signs associated with long-Covid and how should these patients be managed?

Evidence review

Definition

- Currently, there is no international consensus definition for long-Covid, but the phenomenon is generally defined as symptoms due to Covid-19 being present 28 days or longer after the initial infection.

Epidemiology

- A UK study reported that 13% of patients had symptoms at 1 month following initial infection, while 5% presented with symptoms at 2 months, and 2% at 3 months. Risk factors were more than 5 symptoms in the first week, older age and female gender. The model using these factors predicted long-Covid with an area under the curve of 76%.³
- The incidence of long-Covid is higher in women than in men, two-thirds of patients with mild or moderate Covid-19 were still symptomatic, with previously hospitalized patients being particularly affected ⁴

Clinical features

- The following clinical features have been reported:
- Fatigue, (98%) myalgias (64%);
- Respiratory tract symptoms (dyspnea (71%), persistent cough (69%), sore throat (67%), fever (63%);

- Anosmia (76%);
- Tinnitus and earache (4%),
- Cardiac symptoms (chest pain, tachycardia (6%) and palpitations (6%);
- Central nervous system symptoms (memory issues (4%), clouding of mentation, sleep disturbances, headaches (91%), peripheral neuropathy (2%);
- Gastro-intestinal symptoms (anorexia, nausea and diarrhea).
- Psychological (depression, anxiety and PTSD)
- Most symptoms reported for the first time 2-4 weeks after symptom onset.^{2,3,5,6, 7,8}

Pathogenesis

- The aetiology is likely to be multifactorial, with different causes in different patients.
- Post-infectious myocarditis was suggested by a study conducted by Puntmann et al, which found that 60% of patients assessed by cardiac MRI at a median of 10 weeks post diagnosis had evidence of ongoing myocarditis. Endomyocardial biopsy failed to show evidence of SARS-CoV-2.⁹
- Other possible causes that may apply in specific patients include prolonged viral shedding (perhaps localized to individual organs), anxiety following prolonged hospitalization, and post-traumatic stress disorder.¹⁰

Exclusion of other causes

- A thorough history and examination is recommended to exclude other causes or to make a differential diagnosis linked to long-Covid. Particular attention should be paid to excluding alternative causes in patients with unusual symptoms such as weight loss, and those with a history of cancer or other significant comorbidities, etc.
- Known sequelae of Covid-19 that warrant consideration include myocarditis, pulmonary embolism and stroke. However, these are not likely to be present in the most cases of Long-Covid.
- There is no role for routine investigations in Covid-19, other than those guided by the history and examination.
- Either a history of a positive SARS-CoV-2 PCR or a positive antibody test at the time of long-COVID symptoms would support the diagnosis of long-COVID. However, neither is a requirement for the diagnosis, given suboptimal test sensitivities.

Management

- Patients should be reassured that the majority of symptoms resolve with time. However, patients with troublesome symptoms or with symptoms that fail to resolve in 6-8 weeks should be advised to seek medical attention.
- There is no specific pharmacological therapy for long-Covid.
- Focus is on slow and stepwise rehabilitation and symptom alleviation.
- Most guidance at this stage is based on common-sense extrapolations from what is known about rehabilitation and symptom alleviation in other similar contexts. Robust evidence from patients with long-Covid specifically is eagerly awaited.
- An individualized approach is recommended, based on patient symptoms and goals, and taking into account patient comorbidities.
- The optimal rehabilitation strategy is likely to cut across several disciplines. A multidisciplinary team approach is likely to be most useful, with inclusion on doctors, physiotherapists, occupational therapists, and psychologists amongst others.
- Close attention should be paid to optimizing the management of any comorbidities, to ensure that these conditions are not contributing to the ongoing symptomatology.

- Despite their symptoms, patients with long-Covid do not need isolation, as they are not infectious.
- Fatigue and low energy levels may be helped by graded exercise programs, tailored towards the individual. Key features are careful pacing, prioritization and modest goal setting. Patients should engage in low intensity exercise initially, increasing gradually only if tolerated.^{8,10}
- Where available, respiratory or cardiac rehabilitation programs may be useful particularly for those patients who had severe Covid-19, and/or who had significant underlying cardiopulmonary comorbidities.¹⁰ A 6-week respiratory rehabilitation program significantly improves respiratory function, quality of life, and anxiety in older patients with Covid-19.
- Breathlessness and cough may respond to breathing control exercises.⁸
- Patients with long-Covid should be assessed for symptoms compatible with depression, anxiety or post-traumatic stress disorder. Stress reduction techniques, peer support, and, in a minority, referral to a psychologist or psychiatrist, may be required.⁸ COVID-19 may precipitate or unmask underlying psychiatric diseases.¹¹
- Patients with anosmia may benefit from olfactory training.¹²
- Patients with persistent fever may be treated with paracetamol.⁸
- Athletes or patients in physically demanding jobs who have confirmed Covid-19 myocarditis should ideally only resume high-intensity physical activity after a period of bed rest, and after their heart has been assessed as normal by echocardiography and ECG. Consultation with a cardiologist is advised.¹⁰

Recommendations

- A patient-centered rehabilitation approach, inclusive of respiratory, cardiac and musculoskeletal rehabilitation should be used to treat long-Covid patients.
- Resources should be made available at state sector level for the management of patients with long-Covid. These should include, but not be limited to, dedicated outpatient clinics staffed by a multidisciplinary team that includes doctors, occupational therapists, physiotherapists, rehabilitation specialists, and psychologists amongst others.
- Data should be formally collected on the incidence, symptomatology and outcomes of patients with long-Covid, given the considerable socioeconomic impact this condition may have.
- It is recommended that management of the long-Covid patient be included in the clinical management guideline.

Thank you for consideration of this request.

Kind regards,




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CO-CHAIRPERSONS: MINISTERIAL ADVISORY COMMITTEE ON COVID-19
DATE: 2 December 2020

CC:

- » **Dr S Buthelezi (Director-General: Health)**
- » **Dr T Pillay (Deputy Director-General)**
- » **Incident Management Team**