

# Clinical Management of COVID-19

## MANAGEMENT OF NEUROLOGICAL AND MENTAL MANIFESTATIONS ASSOCIATED WITH COVID-19

**PAHO**



Pan American  
Health  
Organization



World Health  
Organization  
REGIONAL OFFICE FOR THE  
Americas

# Learning objectives

## At the end of this lecture, you will be able to do the following:

- Recognize neurological and mental manifestations of COVID-19
- Prevent, recognize, and manage delirium in people with COVID-19
- Recognize & manage anxiety, depression, and sleep problems in people with COVID-19
- Understand how to assess for the risk of self-harm and suicide in people with COVID-19

# Reports of neurological manifestations in COVID-19

## Central nervous system:

- Headache
- Delirium/encephalopathy
- Ischemic, hemorrhagic strokes
- PRES (posterior reversible encephalopathy syndrome)
- Neuroleptic malignant syndrome
- Seizures
- Meningitis, encephalitis, myelitis
- Microangiopathy
- Para & post-infectious syndromes (e.g. Acute hemorrhagic necrotizing encephalitis, Acute disseminated encephalomyelitis)
- Cognitive changes (e.g. dysexecutive syndrome)

## Peripheral Nervous System:

- Anosmia, ageusia
- Guillain-Barré syndrome
- Miller Fischer syndrome
- Polyneuritis cranialis

## Musculoskeletal System:

- Myalgias
- Myoclonus
- Paresis
- Atonia

- What are the most common neurological manifestations in COVID-19 in the early stages of infection?
- What are the most common neurological manifestations that patients present at the Outpatient facilities as compared to inpatient facilities?

- **Perspective from the Field.**

# Mental health manifestations in COVID-19

- **Delirium**
- **Anxiety**
- **Depression**
- **Sleep problems**


# DELIRIUM

# Delirium: an acute neuropsychiatric emergency

## What is delirium?

Delirium is a state of altered consciousness characterized by fluctuating awareness, orientation, and attention in which a person may feel or appear to be:

- Drowsy (excessively sleepy) or agitated.
- Confused or disoriented to time, place, or persons.
- Inattentive, unable to communicate fully, or remember things.
- Experiencing disturbances in perception (e.g. hallucinations), emotions, or psychomotor functions.
- Experiencing disruptions of circadian rhythm and sensitivity to light or sound.

 **Caution: Delirium is an acute neuropsychiatric emergency.**

# What causes delirium in COVID-19?

In people with COVID-19, delirium may be due one or more of the following:

- **Severe, systemic inflammation** caused by the body's reaction to the virus. The extent to which SARS-CoV-2 is directly neuroinvasive is not known.
- **Low oxygenation status.**
- **Metabolic abnormalities** (present in severe dehydration or multiple organ failure).
- **Co-infections** and inflammation associated with them (e.g. UTIs or bacterial pneumonias).
- **Use of certain medications** or withdrawal from them, which may cause or worsen delirium.
- **Substance intoxication or withdrawal.**
- **Other neurological emergencies** (including stroke, intracranial bleeds, or seizure).

**Remember: Delirium in COVID-19 is associated with increased mortality.**



# When someone appears confused, agitated, or drowsy, consider the following questions (1/2):

## Could the person be experiencing an acute episode of psychosis?

- Psychosis may present with confusion, agitation, or hallucinations.
- Suspect delirium if someone experiences fluctuating awareness, disorientation, or problems with attention or short-term memory. Visual hallucinations are more common in delirium.

## Does the person have an underlying diagnosis of dementia?

- Dementia is typically slowly progressive and causes changes over months to years.
- Delirium is an acute state that develops over a short period of time (hours to days) and may change over the course of a day.

**Remember:** Someone with dementia may also experience delirium.

# When someone appears confused, agitated, or drowsy, consider the following questions (2/2):

## Could the person be acutely intoxicated or in withdrawal from substances?

- Intoxication or withdrawal can commonly present with drowsiness or agitation and in some cases, may also present with delirium.

## Does the person have acute signs and symptoms that may indicate other neurological emergencies?

- Be alert to signs of stroke, intracranial bleeds, or seizure (e.g., if the person has slurred speech without any evidence of intoxication; weakness/loss of sensation in face, arms or legs; blurred vision, abnormally reactive pupils; complaints of headache; visible signs of head trauma; witnessed convulsions, complaints of muscle aches or having lost control of bodily fluids).

### **Remember:**

- Severe alcohol withdrawal can lead to delirium tremens, which is a life-threatening syndrome.
- Delirium is often a sign of underlying physical illness and may present with other neurological emergencies.

# Preventing delirium in COVID-19

## Strategies to prevent delirium in people with COVID-19 include:

- Monitor vital signs including oxygenation status closely.
- Monitor fluid status and avoid dehydration.
- Correct any metabolic or endocrine abnormalities as they arise.
- Stay vigilant for the risk of any co-infections.
- Minimize the use of medications that can cause or worsen delirium (including benzodiazepines, anticholinergic medicines, opioids).
- Minimize continuous or intermittent sedation for patients receiving invasive ventilation.
- Assess for the risk of severe substance use withdrawal.
- Maintain normal sleep/wake cycles as much as possible.

**For patients receiving invasive ventilation:** Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions, to reduce the risk of delirium.

# Management of delirium in COVID-19

**Strategies used to prevent delirium can also help you manage delirium in people with COVID-19. If you suspect delirium, do the following to address underlying causes:**

- Check the person's oxygen saturation and fluid status.
- Check the person's metabolic and endocrine function. Check electrolytes, renal function, and liver function. Are there any abnormalities?
- Is the person on any medications that can cause or worsen delirium?
- Is there a risk of co-infections? Check a urinalysis (and urine culture). Check blood culture if febrile.

**Caution:** For patients on invasive ventilation, some medications used for sedation such as propofol can cause agitation if withdrawn too quickly.

# Management of delirium with agitation in COVID-19

Delirium can be accompanied by agitation (restlessness, excessive motor activity, often with anxiety and distress)

## If a person is experiencing delirium with agitation, first do the following:

- Use calming communication strategies.
- Attempt to reorient the person.
- Continue to address underlying causes of delirium.
- Identify any triggers for the agitation.

**Note:** if the person is agitated despite the strategies described above and is experiencing severe distress, it may be necessary to use psychotropic medication.

## If a person is delirious and agitated:

Use calming communication strategies and continue to address underlying causes of delirium.

Look for triggers for agitation. Is there air hunger or pain?

If yes, address these immediately

If these strategies are ineffective, consider psychotropic medication.

# Management of delirium with agitation in COVID-19 (continued) 1/2

## If a medication for delirium with agitation is needed, consider haloperidol.

- Start with low-dose haloperidol (by mouth or IM injection).
- Carefully monitor for adverse effects such as ECG changes (QT-prolongation) or dystonic reactions.

## If haloperidol is contraindicated, another antipsychotic medication may be considered

- Contraindications to haloperidol include prolonged QT, recent heart attack, or sensitivity to strong dopamine blockades due to certain dementias.
- Other antipsychotic medications with safer cardiovascular profiles or lower risk of extrapyramidal symptoms (e.g., akathisia, dystonia) may be used after consideration of other risks (such as respiratory suppression or sedation).

### Clinical tips when using psychotropic medication:

- Consider any side effects that may worsen COVID-19 symptomatology.
- Use minimum effective doses (lowest frequency and shortest duration while still being effective).
- Start with lowest doses possible and titrate up as needed.
- Adjust doses for age, medical co-morbidities, and degree of distress.



Citation: NICE COVID-19 Rapid Guidelines, Managing anxiety, delirium, and agitation

# Management of delirium with agitation in COVID-19 (continued) 2/2

**If the person remains severely agitated, the addition of benzodiazepines can be considered.**

- Preference for benzodiazepines with shorter half-lives and lower risk of interactions (ex: lorazepam).
- Suggested dosing of lorazepam:
  - Start with 0.5-1.0 mg by mouth up to 4 times daily as needed (maximum daily dose 4 mg).
  - For older persons, start with lower doses (0.25-0.5 mg, with maximum daily dose 2 mg).
  - Tablets can also be used sublingually. IV administration should be avoided.

## Clinical tips when using psychotropic medication:

- Consider any side effects that may worsen COVID-19 symptomatology.
- Use minimum effective doses (lowest frequency and shortest duration while still being effective).
- Start with lowest doses possible and titrate up as needed.
- Adjust doses for age, medical co-morbidities, and degree of distress.



Citation: NICE COVID-19 Rapid Guidelines, Managing anxiety, delirium, and agitation

- The presentation mentioned that delirium can be accompanied by agitation (restlessness, excessive motor activity, often with anxiety and distress),
- What are the warning signs that require hospitalization?

- **Perspective from the Field.**



# ANXIETY

# Anxiety in people with COVID-19

## What is anxiety?

Anxiety is a feeling of unease such as worry or fear.

It can be mild or severe. Anxiety is a common reaction for people in the context of COVID-19 diagnosis and entirely normal.

However, interventions may be necessary when those symptoms are severe, persistent and prevent the person from functioning.

## Contributing factors for anxiety in COVID-19

Fear of sickness, risk of death

Fear of family/friends getting sick

Fear of hospitalisation

Fear of quarantine and social exclusion

Physical and social isolation

Loss of livelihood

Feelings of helplessness

# Recognizing anxiety in people with COVID-19

## Common symptoms of anxiety

- Excessive worry or intense fears
- Nervousness
- Irritability or feeling “on edge”
- Feeling restless
- Problems concentrating
- Problems sleeping

## Physical symptoms of anxiety may include:

- Headaches
- Muscle aches and tension
- Fast/irregular heartbeats
- Sweating
- Shortness of breath
- Nausea and stomach discomfort

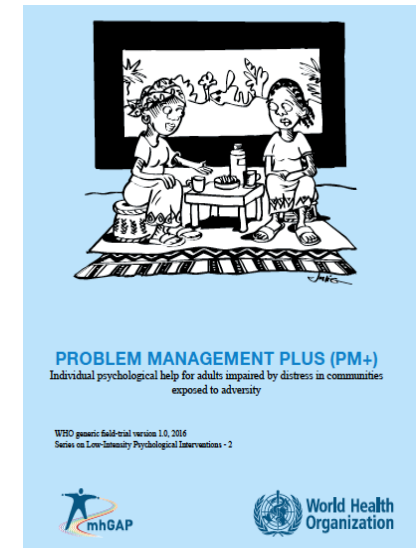
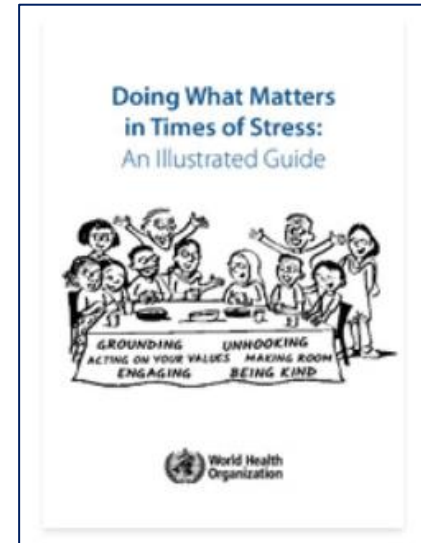
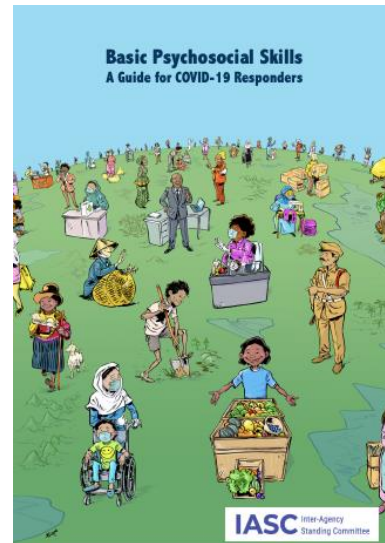
**Citations:** WHO ICD-11, WHO mhGAP-IG, 2.0

# Managing anxiety in people with COVID-19

Psychosocial support strategies should be the first-line intervention for treatment of anxiety.

- Offer basic psychosocial support (BPS)
- Stress management
- Brief psychological interventions based on the principles of cognitive behavioural therapy

Relevant resources include:



# Managing anxiety in people with COVID-19 (1/2)

If the person has severe anxiety and does not improve with psychosocial support strategies, you may consider benzodiazepines (specifically in the hospital setting):

- **Benzodiazepines should only be used with extreme caution as they carry risks in people with COVID-19 including:**
  - Risk of confusion and respiratory suppression
  - Risk of producing tolerance and dependence

**Caution: Benzodiazepines are often used indiscriminately in emergencies and may actually worsen traumatic stress reactions.**

# Managing anxiety in people with COVID-19 (2/2)

- **If benzodiazepines are used, there should be preference for those with shorter half-lives and lower risk of drug-drug interactions (ex: lorazepam).**
  - Minimally effective doses should be used. Suggested dosing of lorazepam below:
    - Start with 0.5-1.0 mg up to 4 times daily as needed (maximum daily dose 4 mg).
    - For older persons, start with lower doses (0.25-0.5 mg, with maximum daily dose 2 mg).
    - Tablets can be used sublingually. IV administration should be avoided.

# Follow-up and referral for anxiety in people with COVID-19

**If symptoms of anxiety persist beyond recovery from COVID-19 and/or discharge from the hospital, an anxiety disorder may be suspected.**

- Arrange follow-up and referral to a mental health professional, if available.

- While COVID may affect one person, the associated anxiety could affect everybody around.
- What support could be provided to family to reduce the effects of anxiety with family member?

- **Perspective from the Field.**



# DEPRESSION

# Depressive symptoms in people with COVID-19

## What is depression?

Many people are likely to experience periods of low mood as a normal and transient reaction to COVID-19, however when these symptoms persist or affect their ability to function, depression may be suspected. Depression is characterised by **persistent depressed mood** and **markedly diminished interest in or pleasure from activities**.

## Contributing factors for depression in COVID-19 include:

- Loneliness from physical and social isolation
- Loss of loved ones
- Loss of livelihood
- Feelings of helplessness

# Recognizing depression

## Signs of depression may include the following:

- Persistent sadness or low mood
- Irritability
- Feelings of emptiness
- Loss of interest or pleasure in activities
- Low energy, tiredness
- Psychomotor changes (moving too much or difficulty moving)
- Changes in appetite or sleep
- Problems with concentration
- Feelings of worthlessness
- Excessive guilt
- Hopelessness
- Recurrent thoughts of dying or suicide

**Note:** some symptoms of depression may overlap with those of COVID-19 such as tiredness, loss of appetite, and problems with sleep.

**Citations:** WHO ICD-11,  
WHO mhGAP-IG, 2.0

# Managing depressive symptoms in people with COVID-19 who do not meet the criteria for depressive disorder

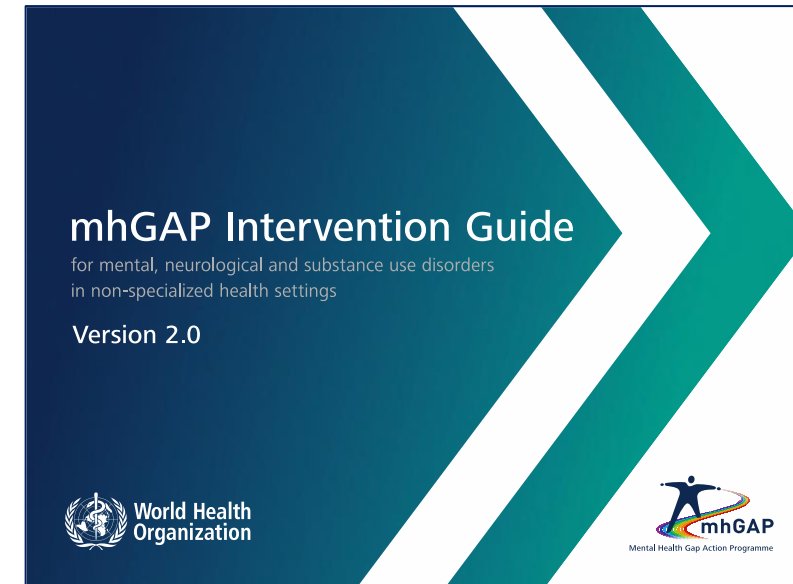
## Treatments for depression

- Cognitive behavioural therapy
- Problem solving treatments
- Interpersonal psychotherapy
- Stress management and relaxation training (adjunctive treatments)

# Follow-up and referral for depression in people with COVID-19

**If symptoms of depression persist for at least two weeks (and/or beyond recovery from COVID-19 or discharge from the hospital), a depressive disorder may be suspected.**

- Arrange follow-up and referral to a mental health professional, if available.
- The mhGAP Intervention Guide, version 2.0 (WHO, 2016) provides algorithms for the assessment and management of depressive disorder.
- Brief psychological treatments including cognitive behavioural therapy (CBT), interpersonal therapy (IPT), behaviour activation and problem solving may be considered. Antidepressants may also be considered.



<https://www.who.int/publications-detail/mhgap-intervention-guide---version-2.0>

- When patient are discharged, they get a prescription for physical management of Covid, but they do not receive guidance on the symptoms and signs of depression and how to manage their wellness.
- How do health care providers help patients and their family cope with the mental health effects of COVID-19?

**Remember:**

- **Perspective from the Field.**

# SELF-HARM/SUICIDE

# Assessing risk for self-harm/suicide in people with COVID-19 (1/2)

**Most people with COVID-19 will experience higher stress than usual. Some people may be at risk of self-harm and suicide, due to the following:**

- Sense of isolation
- Loss of loved ones
- Job insecurity, financial loss, and inequalities
- Feelings of hopelessness

**Note:** Warning signs and risk factors do not predict who will die by suicide. Suicidal behaviour must be assessed individually.

**Remember:** It is important to ask about thoughts or acts of self-harm when someone expresses extreme distress or a history of suicide/self-harm, particularly during COVID-19.

**Note:** Chronic pain and certain mental, neurological, and substance use conditions are additional risk factors for self-harm and suicide.



# Assessing risk for self-harm/suicide in people with COVID-19 (2/2)

**If a person you are caring for expresses or is experiencing the following, you should assess for the risk of self-harm or suicide.**

- Extreme hopelessness, emotional distress, or despair
- Current thoughts, plans or acts of self-harm/suicide
- History of thoughts or actions of self-harm
- Worsening of underlying mental, neurological, or substance use conditions

**Remember:** It is important to ask about thoughts or acts of self-harm when someone expresses extreme distress or a history of suicide/self-harm, particularly during COVID-19.

**Note:** Chronic pain and certain mental, neurological, and substance use conditions are additional risk factors for self-harm and suicide.

# How to determine if there is imminent risk of self-harm/suicide

The following is a general guide to inform clinicians about assessing imminent risk of self-harm/suicide. A person is in imminent risk of self-harm/suicide:

If a person reports either:

- Current thoughts of suicide (for example, thinking “I want to kill myself today”)
- A current plan of self-harm/suicide

**OR**

A person reports extreme emotional distressed **AND** any one of the following:

- Recent thoughts of suicide in the past month (e.g., having thoughts like “I can’t live like this anymore, I need to die soon”)
- A plan to self-harm in the past month (e.g., having planned to drink pesticide prior to your current contact with them; they may or may not have acted on this plan)
- A recent act of self-harm in the past year (e.g., ingesting pesticide prior to your current contact with them)

# How to ask about self-harm/suicide (1/2)

**Try to establish a relationship with the person and create an open, non-judgmental environment before asking questions about self-harm or suicide.** It is important to express that you understand that the person is going through a difficult time and that you want to help. You might consider saying:

- I can see that you are going through a difficult time. In your situation many people feel would feel distressed. I want to be helpful and I want to understand how you are feeling. Sometimes, when people face challenges and feelings like you have described to me, they think about hurting themselves or taking their own life. Have you ever had thoughts of harming yourself or taking your own life?

**Remember:** Do not be afraid to ask directly about self-harm or suicide. Asking about self-harm or suicide does not provoke it. It often reduces anxiety associated with thoughts or acts of self-harm and helps the person feel understood.

# How to ask about self-harm/suicide (2/2)

**If the person answers yes to your initial question, you should further explore thoughts and plans of self-harm or suicide:**

- What are some of the aspects in your life that make you feel it is not worth living?
- Have you been thinking about ways you would harm yourself? What would you do?

**If the person HAS a plan, you should ask about access to means of suicide:**

- You mentioned you have considered ending your life by drinking pesticides, do you have access to that pesticide now? Have you made a plan to obtain these?

**If the person DOES NOT HAVE a plan, ask about previous attempts of self-harm/suicide:**

- Have you ever tried to harm yourself or tried end your own life?

**For more information, see the WHO mhGAP Training Manuals (2017).**

**If the person is at imminent risk of self-harm/suicide, do not leave them alone.**

**Offer continued support until you can refer the person to (or consult) a mental health professional.**

# Managing the risks of self-harm/suicide in people with COVID-19 (1/3)

## Interventions for self-harm/suicide include:

- Do not leave the person alone.
- Refer the person to (or consult) a mental health professional.
- Advise the person and/or carers to remove any possible means of self-harm.
- Focus on protective factors and activate psychosocial support for the person.
- Explore the persons reasons and ways to stay alive (see following slide).
- Focus on the person's strengths by encouraging them to talk about how earlier problems have been resolved.
- Attempt to understand the concerns and identify potential solutions through basic problem-solving.
- Offer psychoeducation to help the person understand it is best to talk about these feelings and identify people whom they can turn to when they feel this way.

# Managing the risks of self-harm/suicide in people with COVID-19 (2/3)

**It is also important to ask about aspects in the person's life that can protect them from self-harm/suicide.**

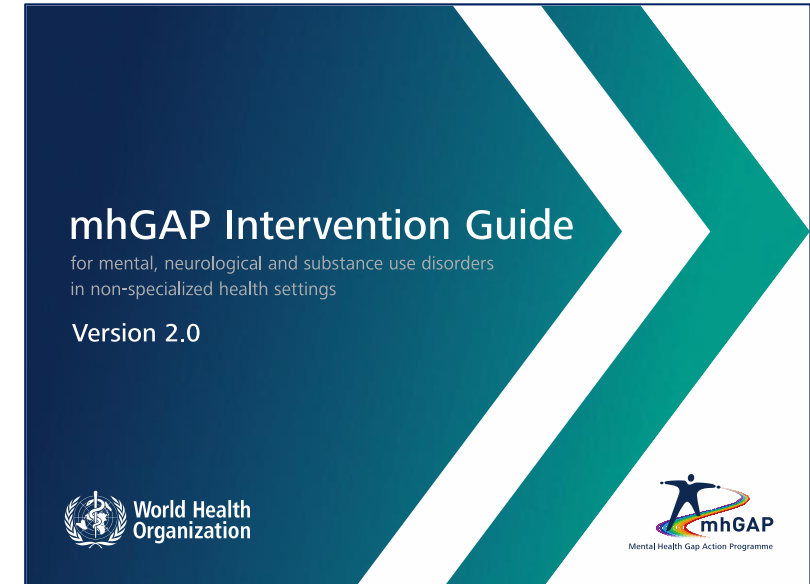
Questions to explore protective factors include:

- What are some of the aspects of your life that make it worth living?
- How have you coped before when you were under stress? What has helped you in the past?
- Who can you turn to for help? Who can you speak to? Who do you feel supported by?
- What changes in your circumstances will change your mind about harming yourself?

# Managing the risks of self-harm/suicide in people with COVID-19 (3/3)

## Interventions for self-harm/suicide include:

- Manage concurrent mental, neurological or substance use conditions (e.g. depression, or substance use disorder) if present.
- Arrange for close follow-up for the person and maintain regular contact for the first 2 months.
- **The mhGAP Intervention Guide, version 2.0 (WHO, 2016) provides algorithms for the assessment and management of self-harm/suicide.**



**Citation:** WHO mhGAP Intervention Guide, version 2.0 (2016)

<https://www.who.int/publications-detail/mhgap-intervention-guide---version-2.0>

# SLEEP PROBLEMS



# Sleep problems in COVID-19

**People with COVID-19 may experience problems with sleep.**

This may be caused by the body's reaction to the illness itself; it may be a response to acute stress; or it may be related to delirium, anxiety, or depression.

**Note:** Insomnia may be a presentation of acute stress (within one month of the stressful experience or event).

# Addressing sleep problems in COVID-19 (1/2)

## Try to identify any underlying causes of sleep problems.

- Is the person experiencing delirium, agitation, pain, discomfort, or air hunger? If so, address these symptoms immediately.
- Manage external/environmental factors (such as excessive light or noise at night).
- Explain to the person that insomnia is a common problem in situations of extreme stress.
- Ask the person for their own explanation of why they can't sleep. Are they experiencing excessive worries or feelings of sadness? (If so, refer to anxiety and depression sections.)

**Remember: Underlying causes of insomnia should be addressed first.**



# Addressing sleep problems in COVID-19 (2/2)

## After addressing underlying causes, consider psychosocial support strategies.

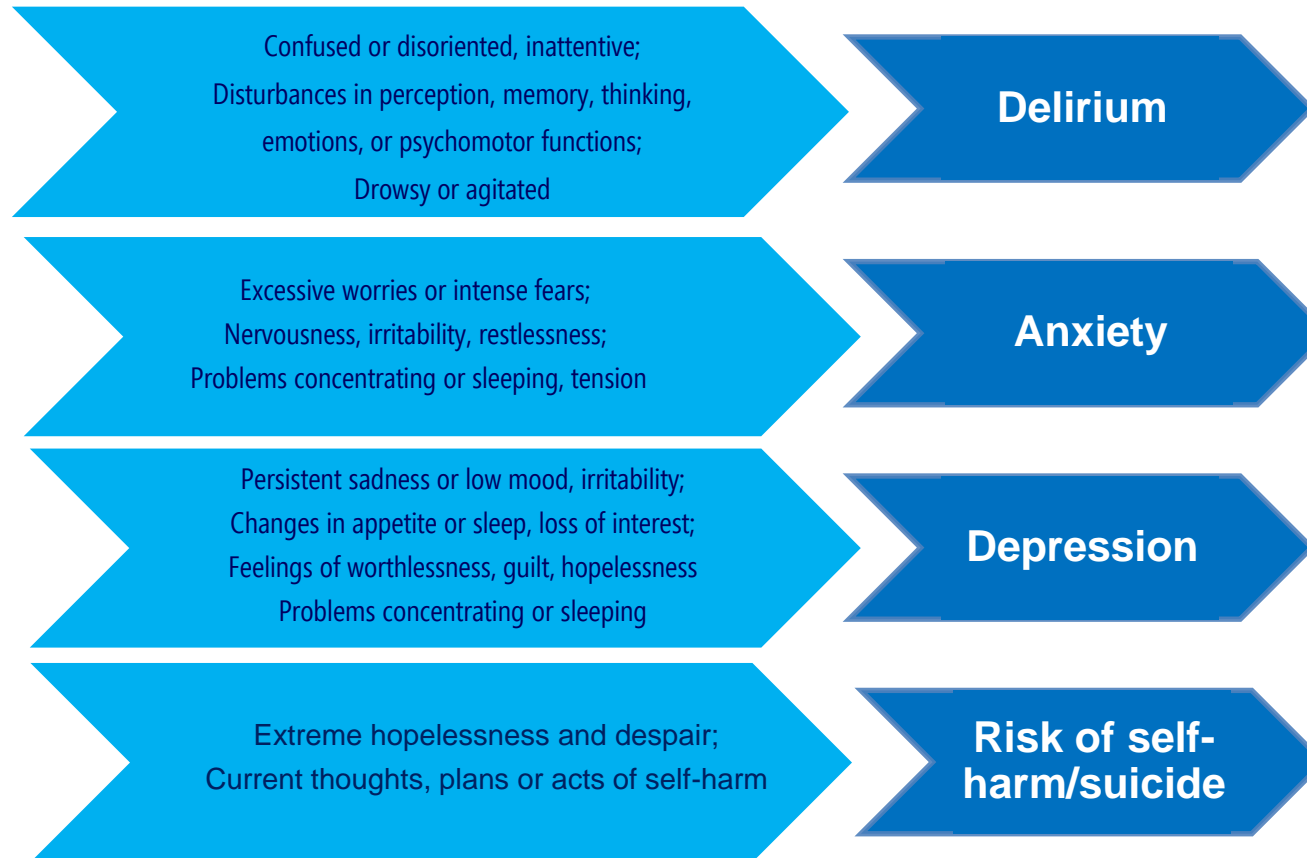
- In adolescents and adults, consider relaxation techniques and advice about sleep hygiene (e.g. regular bed times, avoiding caffeine and alcohol).
- If the problem persists after one month, re-assess for and treat any concurrent mental or physical health conditions.

**Remember:** Identifying and promptly addressing underlying causes should be prioritized before using any pharmacological sleep aids.



# Summary

It is important to recognize neurological and mental manifestations of COVID-19:



- Insomnia is a common problem in situations of extreme stress, often this can be associated with excessive worries or feelings of sadness, therefore sleep hygiene is essential.
- How do you address insomnia without providing benzodiazepines?

- **Perspective from the Field.**

# Summary (continued)

- Delirium is common people with COVID-19; there are multiple strategies to prevent delirium; and if delirium occurs, it should be promptly addressed.
- All people with COVID-19 should receive basic psychosocial support
- Many people with COVID-19 will experience anxiety, depression, and sleep problems, and these symptoms should be addressed with psychosocial and psychological support interventions first before resorting to medications.
- It is important to assess for the risk of self-harm and suicide in people with COVID-19.

## : Dr. Julia Dornik –McGill University

- Finally, the issue of stigma. Which is very concerning, stigma harms people's health and well-being in many ways.
- Stigma can make people feel isolated and even abandoned. They may feel depressed, hurt and angry when friends and others in their community avoid them for fear of getting COVID-19.
- From your experience, what are specific strategies that you recommend to health care providers in the fight against stigma ?

- **Perspective from the Field.**

# Acknowledgements

## Contributors

**WHO HQ:** Tarun Dua, Neerja Chowdhary, Fahmy Hanna, Mark van Ommeren, Kavitha Kolappa, Alison Schafer, Nicoline Schiess, Alessandro Massazza, Katrin Seeher, Stéphanie Freel, Inka Weissbecker, Alexandra Fleischmann, Brandon Gray, Yuka Sumi, Dévora Kestel

**WHO Regional Advisors:**, Nazneen Anwar, Florence Baingana, Andrea Bruni, Dan Chisholm, Carmen Martinez, Khalid Saeed, Renato Souza, Martin Vandendyck

**Expert Working Group:** Jose Luis Ayuso (University of Madrid, Spain); Corrado Barbui (University of Verona, Italy); Shi Chuan (Peking University, China); Rabih El Chammy (Ministry of Health, Lebanon); Oye Gureje (Department of Psychiatry, University College Hospital, Nigeria); Mario Maj (Department of Psychiatry, University of Naples, Italy); Farrah Mateen (Department of Neurology, Harvard Medical School, USA); Pratima Murthy (National Institute of Mental Health and Neuro-Sciences, India); Felicia Smith (Massachusetts General Hospital, Department of Psychiatry, Harvard Medical School, USA); Graham Thornicroft (King's College London, Institute of Psychiatry, Psychology & Neuroscience, UK); Peter Ventevogel (UNHCR, Switzerland)

**Neurology & COVID-19 Global Forum Members:** Foad Abd-Allah (Cairo University, African Academy of Neurology, Egypt); Albert Akpalu (University of Ghana, The West African College of Physicians); Sherry Chou (University of Pittsburgh School of Medicine, USA); Maria Lucia Brito Ferreira (Department of Neurology, Hospital da Restauração, Brazil); Ericka Fink (Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, USA); Fan Kee Hoo (Universiti Putra Malaysia); Benedict Michael (Institute of Infection and Global Health, University of Liverpool, UK); Alessandro Padovani (Neurology, Public Health, Disability Unit & Coma Research Centre, Italy); Kameshwar Prasad (Department of Neurology, All India Institute of Medical Sciences, India); Erich Schmutzhard (Medical University of Innsbruck, Austria); Tom Solomon (National Institute for Health Protection Health Protection Research Unit in Emerging and Zoonotic Infections, Department of Neurology, University of Liverpool, UK); Kiran Thakur (Department of Neurology, Columbia University, USA); Thirugnanam Umapathi (National Neuroscience Institute, Singapore); Andrea Winkler (Department of Neurology, Center for Global Health, Technical University of Munich, Germany)