

# ASSESSING THE IMPACT OF COVID-19 ON THE MENTAL HEALTH OF SENIORS



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*I do not have any relationships with ineligible companies.*

# IOWA VETERANS HOME



# OBJECTIVES



- At the conclusion of this activity, participants should be able to:
  - Identify the psychological effects of the coronavirus pandemic with regard to older patients.
  - Discuss the neuropsychiatric sequelae of COVID-19 in the elderly.
  - Improve telepsychiatry services to geriatric patients.

# LIMITED DATA AVAILABLE



- Small observational studies (cohort, case series, case studies).
- Systemic reviews.
- Large surveys conducted online or by telephone.



# COVID-19 IN OLDER PATIENTS

➤ 90% of deaths in Italy and 80% in US were elderly.

➤ Elderly have higher risk of death (3X):

- Co-morbid conditions such as HTN, CVD, DM, COPD.
- Rationing of care?

▪ Grolli, 2020



# NEUROLOGICAL SEQUELAE OF COVID-19

- Significant number (1/3) have neurological symptoms:
  - Loss of taste/smell, headache, and delirium most common.
  - Also GB Syndrome, TG neuralgia, seizures, cerebrovascular events, meningitis/encephalitis.
- Neurological symptoms more common in severe cases.
- But not commonly the main cause of death (4.1%).

▪ Alonso-Lana, 2020

# POTENTIAL CAUSES OF NEUROLOGICAL SEQUELAE



## ➤ **Direct viral invasion of brain:**

- Cytokines may damage BBB
- Enter via peripheral nervous system
- Scant evidence

## ➤ **Immune reaction/inflammation:**

- Cytokine storm
- Hypercoagulation

## ➤ **Hypoxic brain damage:**

- Verified by post mortem studies

## ➤ **Long ICU stays:**

- Ventilation, drug use, organ dysfunction

▪ Ryoo, 2020

# NEUROPATHOLOGY



- Post-mortem histopathological analysis found no evidence of direct brain invasion; only hypoxic changes.
  - Ryoo, 2020
- Neuroimaging of living COVID-19 patients with neurological symptoms:
  - 34% had lesions.
  - Mostly diffuse subcortical or deep white matter abnormalities.
  - Some had hemorrhages and infarcts as well.
    - Egbert 2020



# CASE STUDY: SHARON



- 75 year old married female who was admitted to nursing home 3 years ago with husband, mainly due to his needs. Heavily invested in being a caregiver.
- She had an extensive history of mental illness, including depression and anxiety since childhood.
- Past history of self harm as well sexual and somatic preoccupations.
- Cognitive impairment, bipolar, OCD and borderline all mentioned in records.
- Father was mentally ill, sexually inappropriate and completed suicide.

# SHARON



- MOCA on admission was 23/30. But appeared to be functioning highly with no confusion observed. BIMS on admission was 15/15.
- Head CT prior to admission unremarkable apart from small vessel disease.
- Labs (CMP, CBC, TSH, B12, syphilis) unremarkable.
- Initial diagnoses: Generalized anxiety disorder, unspecified bipolar disorder, adjustment disorder, mild neurocognitive disorder.
- Deemed to have decisional capacity.

# SHARON



- Was very socially active and engaged in various activities.
- Challenging for staff: Demanding of their time and attention.
- Would often fret about husband and his care.
- Considered self an artist.
- Began psychotherapy immediately.
- Often ruminated about past sexual indiscretions.
- Had urges to scratch/injure self with pen or art tools.
- Soon after admission, added diagnosis of unspecified personality disorder with cluster B traits (borderline, histrionic, narcissistic).

# SHARON



- At various points, complained dramatically of insomnia, racing thoughts, difficulty concentrating.
- Also complained of medication side effects, especially dry mouth.
- Initially maintained on quetiapine and lorazepam.
- Trials of lurasidone, mirtazapine, oxcarbazepine not well tolerated or ineffective.
- Sent to UIHC for second opinion: Borderline PD thought to be primary diagnosis. DBT recommended.
- Bipolar diagnosis dropped and persistent depressive disorder added.

# NEUROPSYCHIATRIC SEQUELAE IN PAST CORONAVIRUS EPIDEMICS



## ➤ SARS-CoV, MERS

### ➤ PTSD most common psychiatric disorder, followed by anxiety and depression.

- Persisted for years in many.

### ➤ Long-term cognitive impairment in many who were on ventilators:

- Attention, memory, verbal fluency, processing speed, executive function.
- 78% one year out, and 47% two years out.

- Alonso-Lana, 2020



# MENTAL HEALTH CONSIDERATIONS

- 20% of people >60 have a neuropsychiatric disorder (dementia, major depression and anxiety most prevalent).
- Chronic stress and depression is associated with activation of the HPA axis and in turn with neuroinflammation and inflammatory processes.
- Prolonged stress can increase corticosteroids causing increased susceptibility to viral infection.

• Grolli, 2020



# ACUTE NEUROPSYCHIATRIC SEQUELAE OF COVID-19

- Anxiety, insomnia, depression, PTSD, cognitive impairment all reported.
- Pre-existing neuropsychiatric condition increased risk.
- Overall in patients of all ages neuropsychiatric symptoms in 22.5% of patients.
- 31.2% of patients >60 had altered mental status.
- 69% of ICU admissions were agitated and 2/3 of them were cognitively impaired. Many required restraints and sedatives.



# ACUTE NEUROPSYCHIATRIC SEQUELAE OF COVID-19

- Systemic review of hospitalized patients.
- Mean ages in studies ranged from 61-69.
- 43.0-66.8% had cognitive impairment.
- **Delirium** was most common term. Also confusion, encephalopathy, encephalitis, altered mental status, and psychosis reported.
- Cytokine storm implicated.

• Ainefeesi, 2021





# NEW-ONSET PSYCHOSIS DURING PANDEMIC

- Associated with delirium or corticosteroid use.
    - Usually resolved after recovery.
  
  - Some cases also associated with quarantine stress:
    - Paranoia, fear, excessive/conflicting information.
- Fontes, 2020



# LONG TERM NEUROPSYCHIATRIC SEQUELAE OF COVID-19

- **VERY LITTLE IS KNOWN ABOUT THE LONG TERM NEUROPSYCHIATRIC EFFECTS OF COVID-19 ON THE ELDERLY.**

# LONG TERM NEUROPSYCHIATRIC SEQUELAE OF COVID-19



- Some recovered patients still have impaired memory, attention and processing speed.
- Anxiety and depression common after recovery.
- 1/3 of patients discharged from ICU had a dysexecutive syndrome with impaired attention, orientation and psychomotor function.
- 42% of hospitalized had delirium and then had reduced cognitive scores **4 weeks** after discharge.

▪ Alonso-Lana, 2020

# LONG TERM NEUROPSYCHIATRIC SEQUELAE OF COVID-19



- In one systemic review, the median age of survivors was 54.4 years old and 79.9% were hospitalized.
- 54% of them had symptoms beyond **6 months**.
- The most common persistent problems were pulmonary sequelae, neurologic syndromes, mental health disorders, functional mobility limitations and constitutional symptoms.
  - 37.5% with fatigue/weakness.
  - 29.6% with generalized anxiety
  - 23.8% difficulty concentrating

• Groff, 2021

# LONG TERM NEUROPSYCHIATRIC SEQUELAE OF COVID-19



- 740 patients followed for **several months**, including inpatient, ED, and outpatient cases.
- Assessing complaints of “brain fog.”
- Mean age 49.
- Neuropsychological testing performed. Deficits:
  - 24% memory encoding.
  - 23% memory recall.
  - 20% category fluency.
  - 18% processing speed.
  - 16% executive function.
  - 15% Phonemic fluency.

▪ Becker, 2021



# COVID-19 IN ELDERS WITH COGNITIVE IMPAIRMENT

- Confusion, disorientation, refusal of care, reduced appetite may be initial symptom.
- Abulia, alogia, rigidity, agitation may occur.
- Subtle behavioral changes may be initial symptoms and present even before fever or cough.

• Alonso-Lana, 2020



# COVID-19 IN ELDERS WITH COGNITIVE IMPAIRMENT

- Dementia increases risk of infection, severity of infection and mortality rate.
- Apolipoprotein E may increase risk of infection and death.
  - Known to be associated with dementia and inflammatory response.
- Delirium is common:
  - Hypoactive delirium more common than hyperactive.
  - Polypharmacy and catheter use increase risk.

▪ Manca, 2020

# COVID-19 AND ALZHEIMER'S



- Many COVID-19 patients had elevated biomarkers similar to patients who have Alzheimer's disease (especially those with neurologic sequelae).
- Suggestive of inflammation and neuronal injury.
- Toxic metabolic encephalopathy (due to sepsis, hypoxia or multiple) was most common neurologic event.
- These patients had more cognitive and functional impairment.
- Could COVID-19 increase risk for dementia or worsen pre-existing dementia?

• Frontera, 2021



# PSYCHOLOGICAL IMPACT OF ISOLATION



- **Social isolation (objective) versus loneliness (subjective):**
  - Both can increase mortality (immune/inflammation).
  - Both can increase risk of dementia.
  - Isolation tends to worsen anxiety, depression, sleep, physical activity.
  - Can be lonely even if not isolated (perception).
  - Before pandemic, about  $\frac{1}{4}$  of elderly reported loneliness.

▪ Roy, 2020



# COPING ABILITIES OF SENIORS

- Older adults tend to have lower stress reactivity and better emotional regulation.
- “Successful aging” improves coping abilities and optimism.
- Negative views of aging tend to correlate with increased loneliness.
- Close meaningful relationships are more important than frequent interactions.

• Vahia, 2020



# EFFECTS OF CORONAVIRUS QUARANTINE ON COGNITIVELY INTACT ELDERLY

- Many experienced anxiety, depression, sleep disruption or reduced physical activity.
  - Excessive information could cause emotional instability or paranoia.
  - If a close relative was affected, this could increase depression.
  - Apprehension about safety/security could increase anxiety/panic.
  - Grolli, 2020
  
- Worse for elders who felt older than actual age or had pre-existing neuropsychiatric conditions.
  
- May be dependent on number of people in household and size of social network.
  - Manca, 2020



# SURVEY OF PSYCHOLOGICAL SYMPTOMS DURING PANDEMIC

- JAMA reported a survey of 933 community dwelling subjects >65 who were **cognitively intact**:
  - Trauma/stress 9.2%
  - Anxiety 6.2%
  - Depression 5.8%
  
- Younger age groups had much higher rates:
  - 45-64 **2X**, 25-44 **5X**, 18-24 **8X**.
  - Vahia, 2020



# ARE OLDER ADULTS MORE RESILIENT?

- Several studies in multiple countries confirmed that older adults were experiencing fewer pandemic related psychological symptoms (anxiety, depression, stress) than younger adults.
- Thought to have more “wisdom”:
  - Compassion, empathy, emotional regulation, self reflection, decisiveness, social advising, spirituality, acceptance of uncertainty, tolerance of diverse perspectives, social connectedness.
  - Vahia, 2020



# EFFECTS OF CORONAVIRUS QUARANTINE ON COGNITIVELY IMPAIRED ELDERERS

- Multiple studies confirm increased rates of behavioral and psychological symptoms in those with subjective cognitive impairment, mild cognitive impairment and dementia including:
  - Apathy, agitation, aggression, irritability, depression, sleep disturbance.
- Cognitive decline, language problems and aberrant motor activity also reported.

▪ Alonso, 2020



# INDIRECT EFFECTS OF CORONAVIRUS QUARANTINE ON COGNITIVELY IMPAIRED ELDERS

- Less access to memory clinics, home care, outpatient care, senior centers, family contact, etc.
  - Resulting in less medical care, socialization and exercise.
- Manca, 2020

# STRATEGIES FOR MENTAL WELLNESS DURING QUARANTINE



- Encourage family/friends to connect any way possible:
  - Video, phone call, Email, writing, packages, etc.
- Reduce exposure to “news”.
- Regular physical activity.
- Stay on a schedule (esp. sleeping and eating).
- Online classes and groups.
- Spiritual activities.
- **BE CREATIVE!**
  - Example: Program to pair student volunteers with nursing home residents to visit by phone.





# EFFECTS OF CORONAVIRUS QUARANTINE ON CAREGIVERS

- Pre-pandemic, dementia caregivers reported anxiety (43.6%) and depressive (34%) symptoms.
  - Altieri, 2020
  
- Stress symptoms in 2/3 of caregivers during pandemic.
  - Many caregivers working from home and schooling children.
  - Iodice, 2020
  
- Increased rates of caregiver anxiety associated with:
  - Female, pre-existing psychiatric problems, contact with COVID-19, or lack access to information.
  - Li, 2021



# EFFECTS OF CORONAVIRUS QUARANTINE ON CAREGIVERS

## ➤ Dependent adult abuse:

- One study reported increase of 83.6% during quarantine.
  - 1/5 seniors reported caregiver abuse.
- Increased risk: Financial strain, close proximity, lacking a sense of community.

• Chang, 2021

# PROLONGED GRIEF DISORDER



- New Diagnosis for ICD-11 and DSM-5.
- Persistent and pervasive yearning, longing, pre-occupying thoughts and memories of the deceased lasting at least 6 months.
- Complicated by the pandemic:
  - Dying alone.
  - Rapid unexpected death.
  - Bereavement rituals (e.g., funerals).
  - Less social support.
  - Changes in hospice or palliative care.
  - Guilt related to circumstances.

# SHARON



- Approximately two years after admission, COVID-19 restrictions are implemented at her facility.
- She struggles with the changes and initially violates infection control rules.
- Complains bitterly of being “trapped” and “imprisoned.”
- She and her husband both test positive for SARS-Cov2 and develop symptoms of COVID-19. They are both moved to the COVID unit for several days.
- She seems to enjoy the extra attention received in the COVID unit and begs to stay there.
- She and husband both have mild cases of COVID and move back to home unit after a short stay on COVID unit.

# SHARON



- After returning to home unit, behavior changes are noted.
- Becomes obsessive and compulsive about cleaning vaginal and anal areas.
- Uses large quantities of cleaning supplies and worries constantly about running out.
- Fixated on losing weight (due to fibromyalgia).
- Obsessive about bowels making multiple requests for laxatives and for nurses to “dig me out”.
- Obsessive about urinary incontinence and pull-ups.
- Insists that clothes are wet and puts them in dryer compulsively.
- OCD added to list of diagnoses.

# SHARON



- Watches the same TV show obsessively and claims that actors have changed.
- Pries bridgework out of mouth with a tweezer causing bleeding and injury. Wanted all remaining teeth pulled out “so I could have a full set in the morning.”
- Scrapes lips with fingernails causing bleeding. Was trying to achieve “the perfect lips.”
- Never appears delirious.
- Trials of risperidone and ziprasidone not tolerated or beneficial.
- Unspecified psychotic disorder (brief vs bipolar) added.

# SHARON



- SLUMS test 17/30
- Decisional capacity doubted.
- Moved to memory care unit.
- Becomes frantic and very depressed (mainly due to limited access to hygienic supplies).
- Neuropsychological assessment performed at UIHC:
  - Impaired cognitive processing speed, learning, memory, executive function and visual/spatial.
  - Language and attention intact.
  - Major neurocognitive disorder likely due to vascular disease, medication and mental illness. Cannot rule out COVID.
  - Lacks decisional capacity for complex decisions.
- Upset about testing results (doctor said she was “stupid” and “very bad person”).
- Donepezil started.

# SHARON TODAY



- Quetiapine, lorazepam, sertraline, donepezil.
- Mood stable, non-psychotic, BIMS 15/15.
- Continues to challenge staff.
- Back to baseline behaviorally?
- Will her neuropsychological testing improve?
- Will she return to an open unit?



# SHARON'S TIMELINE



Timeline	Admission 2 years before COVID Dx	2 months before COVID	1 month after COVID	4 months after COVID	7 months after COVID	10 months after COVID	15 months after COVID
BIMS	15/15	13	13	12	9	14	15/15
PHQ-9	8/27	16	13	18	1	6	6/27





# TELEPSYCHIATRY

- Has been utilized for many years by the VA, rural communities, prisons and in many LTC facilities.
- COVID-19 brought an unprecedented expansion.
- 75% of nursing home residents benefitted from psychology services via telehealth during pandemic.
  - Renzi, 2020



# TELEPSYCHIATRY BARRIERS FOR THE ELDERLY

- Sensory deficits
- Speech/language impairment
- Cognitive impairment
- Access to and familiarity with technology
- Preference to see providers in person
- Irritates some dementia patients
- Limitations of LTC staff



# TELEPSYCHIATRY TIPS

- Ask family members to assist if at home.
- Be attentive to lighting.
- Turn off other devices and shut doors.
- Set up on stationary surface.
- Headphones if appropriate.
- Long-term care facilities:
  - Staff education.
  - Designate staff to assist (repeat questions, visual scan).
  - Ask facility to upgrade WiFi/equipment.

# BENEFITS OF TELEPSYCHIATRY IN LTC



- Safe for patients and providers.
- More efficient and less travel time.
- Can utilize volume controls and headphones.
- LTC facility can capture reimbursement for providing assistance.
- Easy to include learners and family members.



# ELECTRONIC COGNITIVE ASSESSMENT INSTRUMENTS

<b>Video Only:</b>	MOCA telehealth	MMSE		
<b>Telephone or Video:</b>	MOCA telephone	Brief Test of Adult Cognition	Cognitive Telephone Screening Instrument	Telephone Interview for Cognitive Status

Hantke, 2020



# ETHICAL DILEMMAS

- Ageism
- Rationing of care (acute and maintenance)
- “Being Mortal” by Atul Gawande.

# SUMMARY



- Significant numbers of COVID-19 patients have neurological sequelae, although these symptoms may be mild and rarely cause death.
- Both social isolation and COVID-19 can exacerbate pre-existing neuropsychiatric disorders.
- Social isolation often causes increased rates of anxiety, depression, and stress/trauma symptoms, but higher functioning older adults may be less affected than younger adults are.
- Cognitively impaired patients infected with SARS-CoV2 often initially present with subtle behavior changes.
- Very little is known about the long-term neuropsychiatric effects of COVID-19 on the elderly.
- Lifestyle, technology and behavioral interventions are important to offset the adverse effects of quarantine.



# REFERENCES



- Ainefeesi, Y, et al. Impact of SARS-CoV-2 Infection on Cognitive Function: A Systemic Review. *Frontiers in Psychiatry*. Feb 2021, Vol 11, Art 621773.
- Alonso-Lana S, Marquié M, Ruiz A, Boada M. Cognitive and Neuropsychiatric Manifestations of COVID-19 and Effects on Elderly Individuals With Dementia. *Front Aging Neurosci*. 2020 Oct 26;12:588872.
- Altieri M, Santangelo G. The Psychological Impact of COVID-19 Pandemic and Lockdown on Caregivers of People With Dementia. *Am J Geriatr Psychiatry*. 2021 Jan;29(1):27-34.
- Bailey L, Ward M, DiCosimo A, Baunta S, Cunningham C, Romero-Ortuno R, Kenny RA, Purcell R, Lannon R, McCarroll K, Nee R, Robinson D, Lavan A, Briggs R. Physical and Mental Health of Older People while Cocooning during the COVID-19 Pandemic. *QJM*. 2021 Jan 20.
- Beaud V, Crottaz-Herbette S, Dunet V, Vaucher J, Bernard-Valnet R, Du Pasquier R, Bart PA, Clarke S. Pattern of cognitive deficits in severe COVID-19. *J Neurol Neurosurg Psychiatry*. 2021 May;92(5):567-568.
- Becker, J, et al. Assessment of Cognitive Function in Patients After COVID-19 Infection. *JAMA Network Open*. Oct 22, 2021; 4(10): e2130645,
- Chang ES, Levy BR. High Prevalence of Elder Abuse During the COVID-19 Pandemic: Risk and Resilience Factors. *Am J Geriatr Psychiatry*. 2021 Jan 19.
- Egbert AR, Cankurtaran S, Karpiak S. Brain abnormalities in COVID-19 acute/subacute phase: A rapid systematic review. *Brain Behav Immun*. 2020 Oct;89:543-554.
- Fernández RS, Crivelli L, Guimet NM, Allegri RF, Pedreira ME. Psychological distress associated with COVID-19 quarantine: Latent profile analysis, outcome prediction and mediation analysis. *J Affect Disord*. 2020 Dec 1;277:75-84.
- Fontes WHA, Gonçalves Júnior J, de Vasconcelos CAC, da Silva CGL, Gadelha MSV. Impacts of the SARS-CoV-2 Pandemic on the Mental Health of the Elderly. *Front Psychiatry*. 2020 Aug 17;11:841.
- Frontera, J., et al. Elevation of Neurodegenerative Serum Biomarkers among Hospitalized COVID-19 Patients. *MedRxiv preprint doi: <https://doi.org/10.1101/2021.09.01.21262985>.*
- Goveas J., et al. Grief and the COVID-19 Pandemic in Older Adults. *Am J Geriatr Psychiatry*. 2020 Oct;28(10):1119-1125.
- Groff, D. et al, Short Term and Long Term Rates of Post acute Sequelae of SARS-CoV-2 Infection: A Systemic Review. *JAMA Network Open*, 2021; 4(10).
- Grolli RE, Mingoti MED, Bertollo AG, Luzardo AR, Quevedo J, Réus GZ, Ignácio ZM. Impact of COVID-19 in the Mental Health in Elderly: Psychological and Biological Updates. *Mol Neurobiol*. 2021 May;58(5):1905-1916.
- Hantke NC, Gould C. Examining Older Adult Cognitive Status in the Time of COVID-19. *J Am Geriatr Soc*. 2020 Jul;68(7):1387-1389.
- Iodice F, Cassano V, Rossini PM. Direct and indirect neurological, cognitive, and behavioral effects of COVID-19 on the healthy elderly, mild-cognitive-impairment, and Alzheimer's disease populations. *Neural Sci*. 2021 Feb;42(2):455-465.
- Ismail II, Kamel WA, Al-Hashel JY. Association of COVID-19 Pandemic and Rate of Cognitive Decline in Patients with Dementia and Mild Cognitive Impairment: A Cross-sectional Study. *Gerontol Geriatr Med*. 2021 Mar 23;7:23337214211005223.
- Li Q, Zhang H, Zhang M, Li T, Ma W, An C, Chen Y, Liu S, Kuang W, Yu X, Wang H. Mental Health Multimorbidity among Caregivers of Older Adults During the COVID-19 Epidemic. *Am J Geriatr Psychiatry*. 2021 Jan 19. pii: S1064-7481(21)00017-8.
- Manca R, De Marco M, Venneri A. The Impact of COVID-19 Infection and Enforced Prolonged Social Isolation on Neuropsychiatric Symptoms in Older Adults With and Without Dementia: A Review. *Front Psychiatry*. 2020 Oct 22;11:585540.
- Renzi A, Verrusio W, Messina M, Gaj F. Psychological intervention with elderly people during the COVID-19 pandemic: the experience of a nursing home in Italy. *Psychogeriatrics*. 2020 Nov;20(6):918-919.
- Roy J, Jain R, Golamari R, Vunnam R, Sahu N. COVID-19 in the geriatric population. *Int J Geriatr Psychiatry*. 2020 Dec;35(12):1437-1441.
- Ryou N, Pyun JM, Baek MJ, Suh J, Kang MJ, Wang MJ, Youn YC, Yang DW, Kim SY, ParkYH, Kim S. Coping with Dementia in the Middle of the COVID-19 Pandemic. *J Korean Med Sci*. 2020 Nov 2;35(42):e383.
- Sardella A, Lenzo V, Bonanno GA, Basile G, Quattropani MC. Expressive Flexibility and Dispositional Optimism Contribute to the Elderly's Resilience and Health-Related Quality of Life during the COVID-19 Pandemic. *Int J Environ Res Public Health*. 2021 Feb 10;18(4).
- Sepúlveda-Loyola W, Rodríguez-Sánchez I, Pérez-Rodríguez P, Ganz F, Torralba R, Oliveira DV, Rodríguez-Mañás L. Impact of Social Isolation Due to COVID-19 on Health in Older People: Mental and Physical Effects and Recommendations. *J Nutr Health Aging*. 2020;24(9):938-947.
- Vahia IV, Jeste DV, Reynolds CF 3rd. Older Adults and the Mental Health Effects of COVID-19. *JAMA*. 2020 Dec 8;324(22):2253-2254.
- van Dyck LJ, Wilkins KM, Ouellet J, Ouellet GM, Conroy ML. Combating Heightened Social Isolation of Nursing Home Elders: The Telephone Outreach in the COVID-19 Outbreak Program. *Am J Geriatr Psychiatry*. 2020 Sep;28(9):989-992.
- Yeung DY, Chung EKH, Lam AHK, Ho AKK. Effects of subjective successful aging on emotional and coping responses to the COVID-19 pandemic. *BMC Geriatr*. 2021 Feb 17;21(1):128.