COVID-19 Infection in Persons Living With Dementia

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Disclosures

- Consulting fees from Biogen and Alnylam Pharmaceuticals
- Royalties from UpToDate
- Not an infectious disease expert

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Outline

- What is COVID-19?
- Clinical symptoms and course
- Effects on the brain
- Ethics of the response to the pandemic

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What is COVID-19?

- Coronavirus Disease 2019.
- New human disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).

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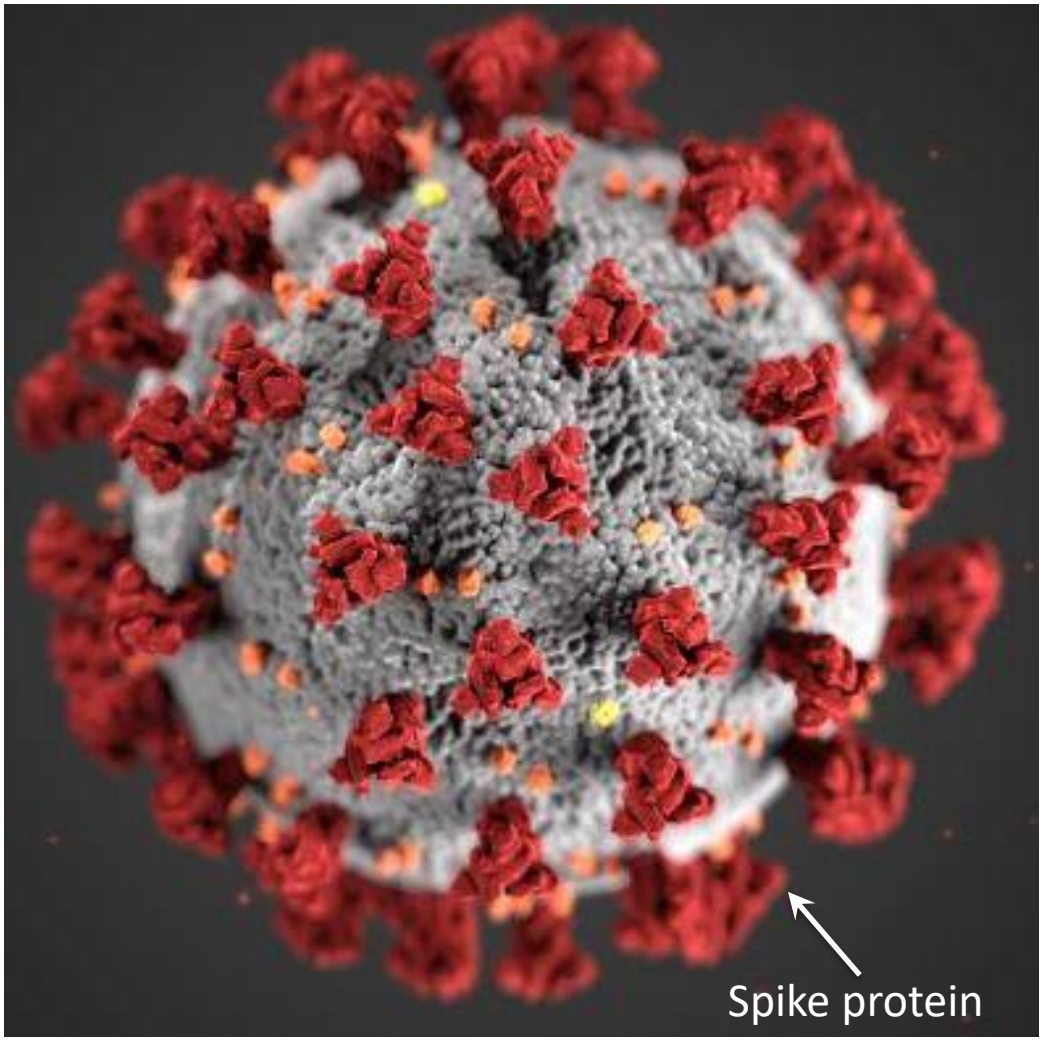
SARS-CoV-2



- Single strand RNA virus
- Encodes 27 proteins
- Coronavirus
- Spike protein binds to human cells by ACE-2 receptors

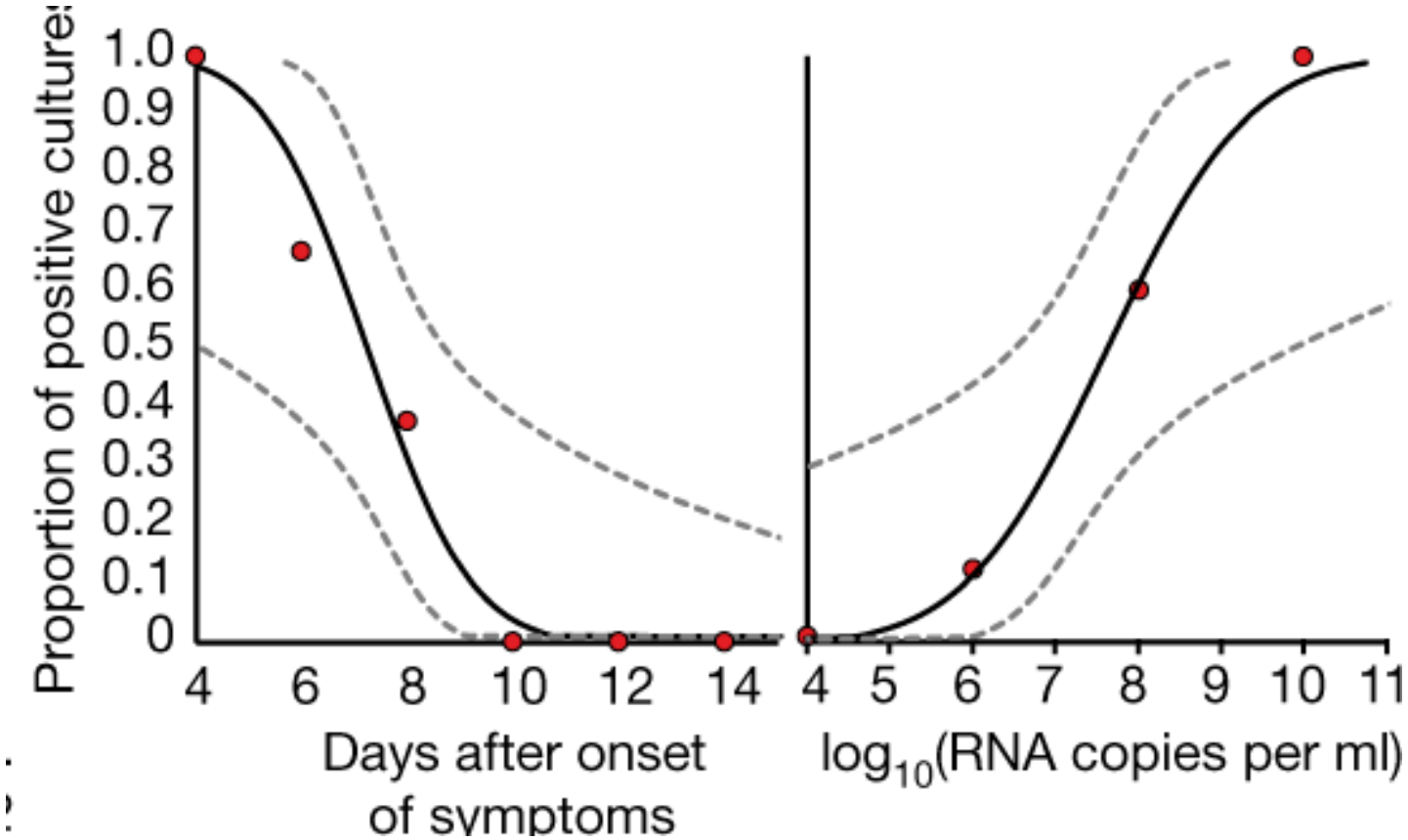
Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020;382:727-733.

SARS, MERS, and COVID-19

Virus	Disease	Cases	Case Fatality	R_0
SARS-CoV-1	SARS		9.5%	1.7
MERS-CoV	MERS		34.4%	0.7
SARS-CoV-2	COVID-19	10,168,657	4.9% (0.5-1.0%?)	2-2.5

Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E. COVID-19, SARS and MERS: are they closely related? Clin Microbiol Infect 2020;26:729-734.
https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (accessed June 29)

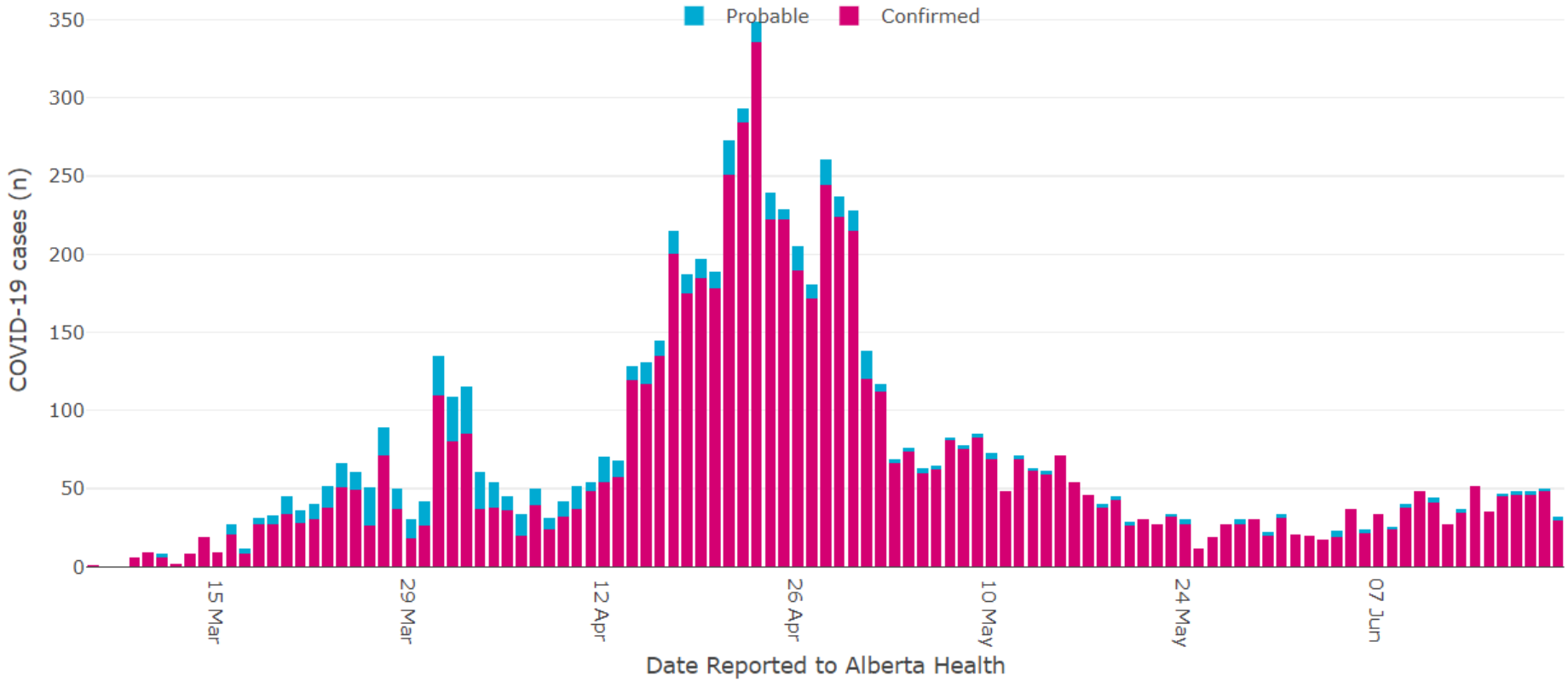
Transmission of SARS-CoV-2



Wolfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581:465-469.

Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med 2020;382:2081-2090.

New Cases in Alberta



https://www.alberta.ca/stats/covid-19-alberta-statistics.htm

Public Health Measures to Control COVID-19

- Hand hygiene
- Physical distancing
- Wearing masks in public
- Working remotely
- No large gatherings

Impact of Measures on Persons Living with Dementia and Care Partners

- Disruptions to medical care.
- Difficulty adhering to hygienic measures.
- Loss of formal and informal care support.
- Anxiety and burn out among care partners.
- Accelerated cognitive decline due to social isolation.

Roach P, Zwiers A,…**Smith EE**. Understanding the impact of the COVID-19 pandemic on well-being and virtual care for people living with dementia and care partners living in the community. medRxiv 2020:2020.2006.2004.20122192

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Clinical Symptoms

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Possible Symptoms (Not Exhaustive)

- Fever or chills (83-99%)
- Cough (59-82%)
- Shortness of breath or difficulty breathing (31-40%)
- Fatigue (44-70%)
- Muscle or body aches (11-35%)
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html

Severity

Mild	Cough, fever, dyspnea, or asymptomatic; outpatient management	81%
Moderate	Dyspnea, hypoxia; hospital care	14%
Critical	Respiratory failure, cardiac, neurological, renal; intensive care	5%

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

Lung Involvement

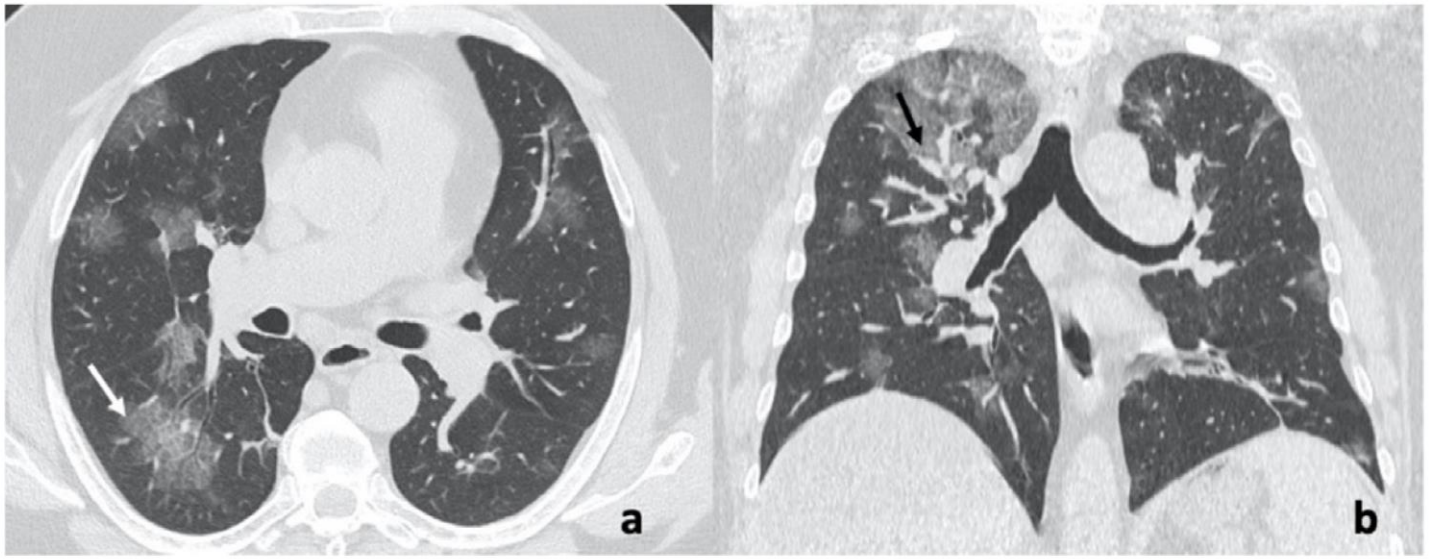

Figure 3: Axial and coronal thin-section unenhanced CT scan of 55-year-old man with history of recent travel to Milan who presented with fever and dyspnea. (a) Scan shows bilateral ground-glass opacities with rounded morphology (white arrow) in both upper and lower lobes, and interlobular/intralobular septal thickening (crazy paving).

(b) Scan shows predominantly apical ground-glass opacities with tubular size increase of segmental and subsegmental vessels (black arrow).

Caruso D, Zerunian M, Polici M, et al. Chest CT Features of COVID-19 in Rome, Italy. Radiology 2020:201237.

Critical Illness

- Often about 1 week after symptoms; cytokine storm.
- Most (75%) require intubation with mechanical ventilation for acute respiratory distress syndrome, and pressors.
- Mortality approaches 50%.
- Long length of stay (median stay 14 days)
- Life threatening complications
  - Hypotension
  - Prothrombotic state
  - Heart failure with reduced ejection fraction.
  - Renal failure

Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region — Case Series. New England Journal of Medicine 2020: publshed online before print March 30, 2020.

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Case Fatality Rate by Age

Age group (yrs) (no. of cases)	%		
	Hospitalization	ICU admission	Case-fatality
0–19 (123)	1.6	0	0
20–44 (705)	14.3	2.0	0.1
45–54 (429)	21.2	5.4	0.5
55–64 (429)	20.5	4.7	1.4
65–74 (409)	28.6	8.1	2.7
75–84 (210)	30.5	10.5	4.3
≥85 (144)	31.3	6.3	10.4
Total (2,449)	**20.7**	**4.9**	**1.8**

Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep 2020;69:343-346.

Treatments

- Remdesivir
  - Antiviral, adenosine analog.
  - Shortened time to recovery by 4 days in hospitalized patients; but not effective if started in ventilated/ECMO.[1]
  - Smaller trial of hospitalized patients showed trend to improvement if started early.[2]
- Dexamethasone
  - Glucocorticoid anti-inflammatory
  - Reduced deaths by one third in ventilated patients and one fifth (RR 0.80) in patients on oxygen.[3]

[1] Beigel JH, Tomashek KM, Dodd LE, et al. N Engl J Med 2020.
[2] Wang Y, Zhang D, Du G, et al. Lancet 2020;395:1569-157
[3] https://www.recoverytrial.net/results

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Effects on the Brain

Neurological Symptoms and Signs in Hospitalized Patients

- First retrospective cohort: 78/214 (36.4%) had documented neurologic symptoms/signs.

Symptom	%
Dizziness	16.8
Headache	13.1
CK elevation	10.7
Impaired consciousness	7.5
Anosmia	5.1
Acute cerebrovascular	2.8
Painful neuropathy	2.3
Ataxia	0.5
Seizure	0.5

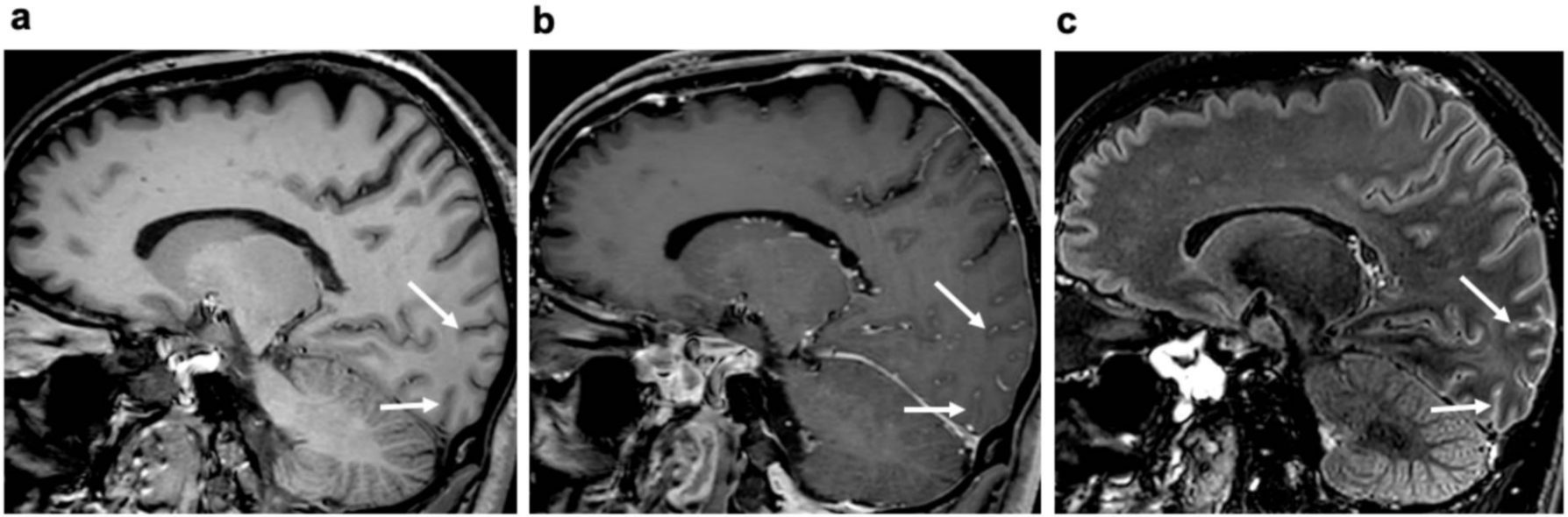
Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurology 2020.

Neurological Signs in Critically Ill COVID-19

- 58/64 consecutive patients from 2 hospitals in France.
- Most had confusion.
- Enhanced tendon reflexes, clonus.
- CSF: 2/7 oligoclonal bands, 0/7 rt-PCR negative.
- MRI: often leptomeningeal enhancement, sometimes small infarcts.
- 1/3 had “dysexecutive syndrome” at time of ICU discharge.

Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Fafi-Kremer S, Ohana M, Anheim M, Meziani F. Neurologic Features in Severe SARS-CoV-2 Infection. N. Engl. J. Med. 2020;382:2268-2270. DOI 10.1056/NEJMc2008597.

Leptomeningal Enhancement

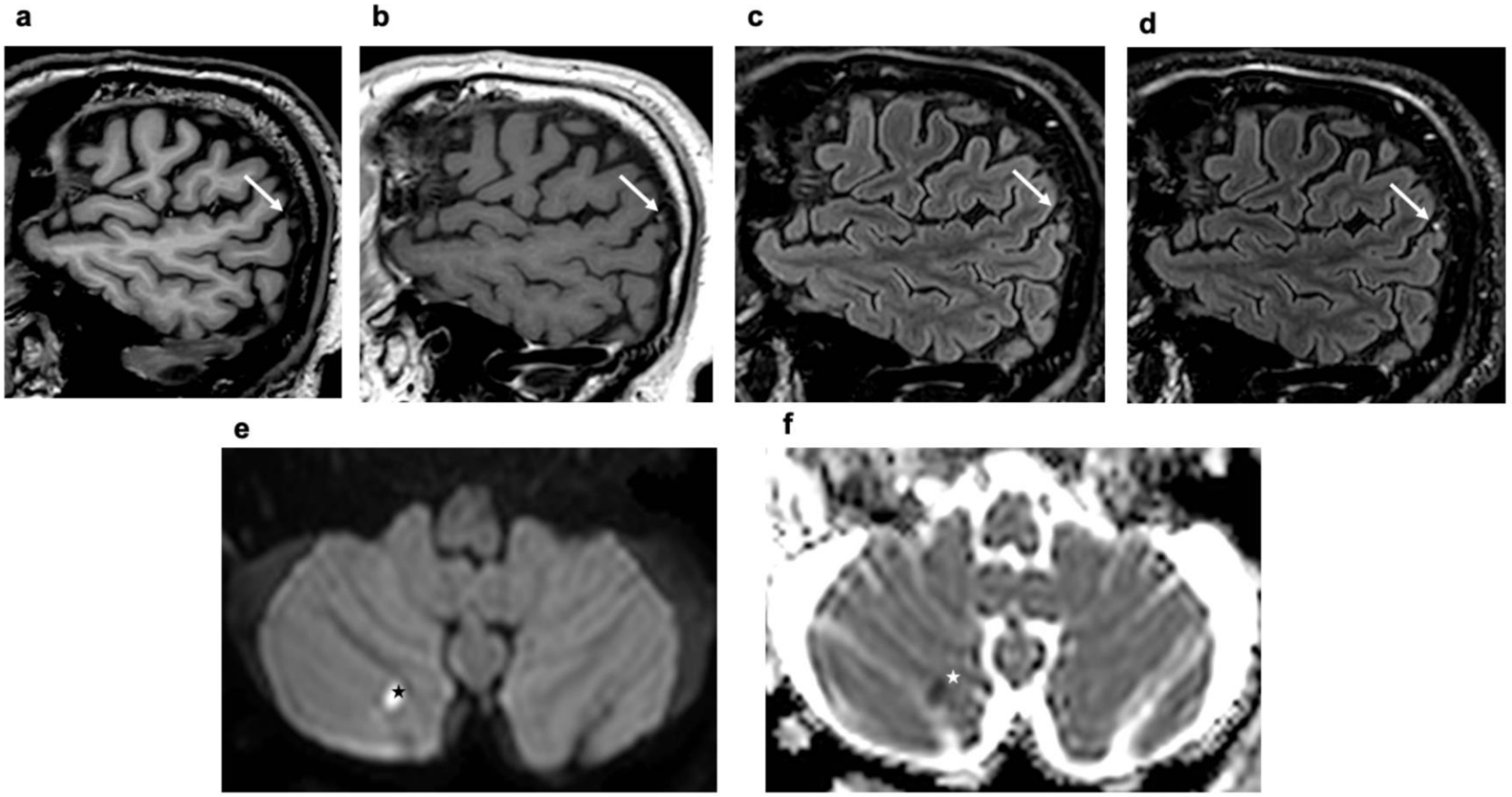


T1 T1 with contrast FLAIR

Leptomeningeal enhancement in 8/13.

Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Fafi-Kremer S, Ohana M, Anheim M, Meziani F. Neurologic Features in Severe SARS-CoV-2 Infection. N. Engl. J. Med. 2020;382:2268-2270. DOI 10.1056/NEJMc2008597.

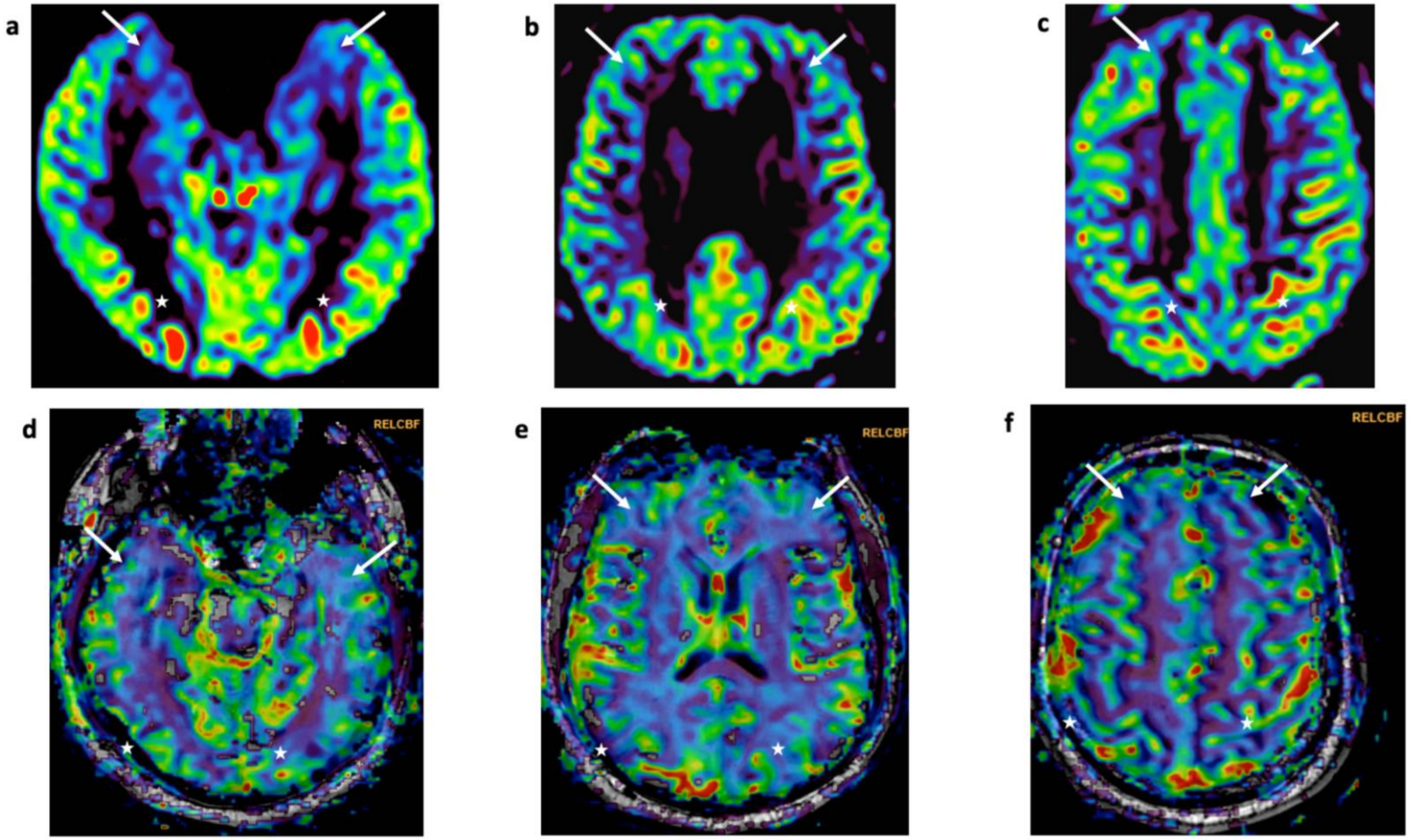
Small Brain Infarcts



Small infarcts in 2/13; all had encephalopathy with no focal neurological signs

Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Fafi-Kremer S, Ohana M, Anheim M, Meziani F. Neurologic Features in Severe SARS-CoV-2 Infection. N. Engl. J. Med. 2020;382:2268-2270. DOI 10.1056/NEJMc2008597.

Frontal Hypoperfusion



Hypoperfusion seen in 11/11

Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Fafi-Kremer S, Ohana M, Anheim M, Meziani F. Neurologic Features in Severe SARS-CoV-2 Infection. N. Engl. J. Med. 2020;382:2268-2270. DOI 10.1056/NEJMc2008597.

Neuropathology of COVID-19

- 18 autopsies of patients who died of COVID-19 at an American teaching hospital.
- All had confusion or decreased arousal.
- Hypoxic changes.
- qRT-PCR detected low levels of viral RNA in 17/18
  - Mostly about a million-fold lower than lung
- No viral staining on immunohistochemistry.
- Suggests either low level of viral infection or contamination from blood viremia.

Solomon IH, Normandin E, Bhattacharyya S, Mukerji SS, Keller K, Ali AS, Adams G, Hornick JL, Padera RF, Sabeti P. Neuropathological Features of Covid-19. N. Engl. J. Med. 2020. DOI 10.1056/NEJMc2019373.

COVID-19 in Persons with Dementia

- 82/627 admitted patients had history of dementia.
- Mortality higher in persons with dementia: 62.2% vs. 26.2%.
  - Varied by stage: CDR 1.0 41.7%, CDR 2.0 66.7%, CDR 3.0 83.9%
- Most frequently presented with delirium (67.1%) and/or functional decline (56.1%) rather than fever (47.6%) or cough (13.4%).

Bianchetti A, Rozzini R, Guerini F, et al. Clinical Presentation of COVID19 in Dementia Patients. J Nutr Health Aging 2020:1-3

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Unanswered Questions about Brain Involvement

- Effects on non-hospitalized patients?
- Source of viral RNA found in the brain?
- Is virus replicating in brain endothelium and is this related to the small infarcts that can be seen?
- What is the stroke risk following COVID-19 infection?
- Are there long term neurological impairments?
- How does COVID-19 interact with pre-existing conditions such as dementia to affect clinical course and outcomes?

Summary of COVID-19 Clinical Features

- Causes respiratory illness, ranging from mild to severe, with highest impact in the elderly.
- Effects on other organs, either primary or secondary, are just beginning to be understood.
- Critical illness in only 5% but is severe with prolonged intensive care stay and uncertain prognosis (about 50% will die, neurological prognosis in survivors is unclear).
  - Potential to overwhelm existing intensive care resources, leading to difficult decisions when the number of patients needing intensive care exceeds bed spaces and equipment (e.g. mechanical ventilators).

COVID-19: Difficult Decisions

- 4 patients, 2 ventilators: who would you treat?

82 years old History of dementia Severe COVID-19	35 years old No comorbidities Severe COVID-19
82 years old History of dementia Trauma	82 years old History of stage IV cancer Severe COVID-19

Truog RD, Mitchell C, Daley GQ. The Toughest Triage - Allocating Ventilators in a Pandemic. N Engl J Med 2020;382:1973-1975.

Principles for resource planning

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Director, Neuroscience, Engagement & Smart Tech (NEST) Lab

NEUROETHICS CANADA

BRAIN HEALTH HUMAN VALUES

BC Children's Hospital

UBC

Acknowledgements

- Dr. John Fisk
- Dr. Eric Smith
- Dr. Serge Gauthier
- Alzheimer Society of Canada

CCNA Canadian Consortium on Neurodegeneration in Aging

AGEWELL Canada's technology and aging network

Alzheimer Society BRITISH COLUMBIA

SSHRC CRSH Social Sciences and Humanities Research Council of Canada Conseil de recherches en sciences humaines du Canada

alzheimer's association

Overview of ethical issues

- Harms related to limited visits to hospitals and long-term care
- Demand for medically-assisted death due to COVID-19
- Development of unhealthy coping habits in isolation

- Immunity passports
- Perceptions about long-term care

- Interventions without informed consent
- Pandemic exceptionalism
- Fair profit from vaccine/therapies
- Ethical comparators for vaccine trials

- Harms related to the use of at-home technology
- Experimental drug access
- Resource allocation and triage

Shifting ethical frameworks

During normal times:
Biomedical ethics

- Autonomy
- Beneficence
- Non-maleficence
- Justice

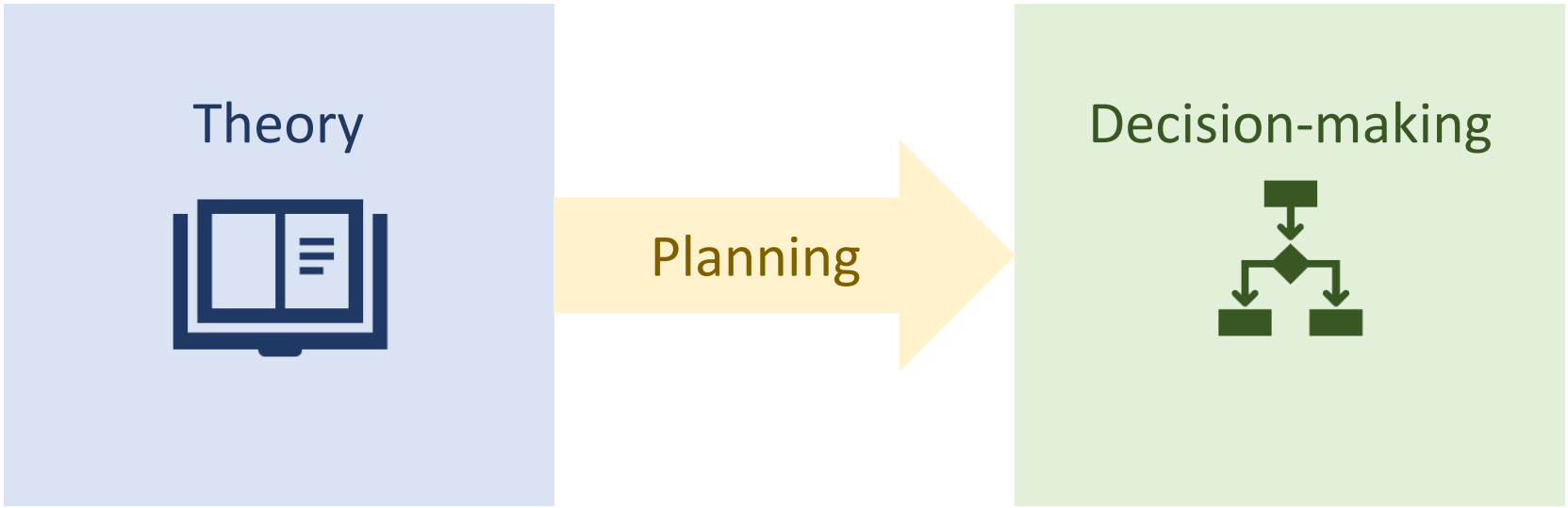
During a public health crisis:
Public health ethics

- Population benefit
- Collective good
- Efficiency
- Equity

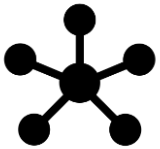
Allocating scare resources during the covid-19 pandemic

"Before anything else, preparation is the key to success"

- Alexander Graham Bell, maybe



1 Decisions on access to lifesaving resources for persons with dementia should be individualized



Dementia is a heterogenous syndrome with varying individual trajectories

Blanket restrictions on lifesaving care for persons with dementia are not appropriate

2

Persons with dementia should be provided the opportunity to indicate their wishes regarding goals of care

Ideally carried out ahead of time

Every effort should be made to engaged persons directly

3

Decisions on resource allocation should respect the personhood of people with dementia

Reduce stigma and promote equity by defining guiding principles in advance

Engage persons with lived experience in developing protocols

4

Decisions on access to resources should be based on expected survival, not presumptions about quality of life

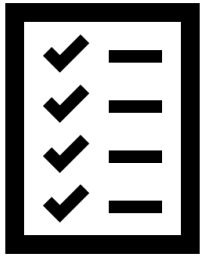
Primary objective:

Maximizing survival

Predicting future quality of life

5 Prognostications should be based on an objective, validated assessment

Examples:



- Clinical Frailty Scale
- Mortality risk models for persons with dementia
- Dementia functional stage

6

The presence of MCI should not be used as a criterion for assessing suitability for lifesaving care

MCI is a risk factor for developing dementia, BUT:

- Many remain stable or improve over time
- MCI does not imply disability
- Can live independently

7

Persons with dementia who are denied lifesaving care are entitled to an explanation and best alternative care

Transparency ➡ trust

Alternative care includes access to palliative care as appropriate

Moving forward

Dissemination and awareness

- Synopsis available at the website for the **Alzheimer Society COVID-19 and Dementia Taskforce***
- Academic publication in Canadian Geriatrics Journal in September

Feedback and engagement

* https://alzheimer.ca/en/Home/Living-with-dementia/managing-through-covid-19/covid-19-and-dementia-task-force

Contact

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