มหาวิทยาลัยมหิดล
คณะแพทยศาสตร์ศิริราชพยาบาล

Siriraj Hospital

การดูแลผู้ป่วยโรคสมองเสื่อม ในช่วงสถานการณ์การระบาดโรค COVID-19

รองศาสตราจารย์แพทย์หญิงวรพรรณ เสนาณรงค์ วทบ พบ, DTM&H(London), FRCP(London)

ความซับซ้อนของการป้องกันและจัดการการติดเชื้อCOVID19 นั้นส่งผลทวีคูณในผู้ที่มีภาวะสมองเสื่อม ซึ่งมีความบกพร่องของความจำและความเข้าใจ มีการพึ่งพิงด้านการดูแลตนเอง

ความใกล้ชิดของผู้ดูแลมีความเสี่ยงต่อทุกคนรวมทั้งต่อผู้ป่วยสมองเสื่อม

ผู้ป่วยสมองเสื่อม เมื่อเกิดอาการติดไวรัส อาจทำให้เกิดอาการเพ้อและทำให้อาการสมองเสื่อมรุนแรงขึ้น

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Pathophysiology of SARS-Cov2 & the brain

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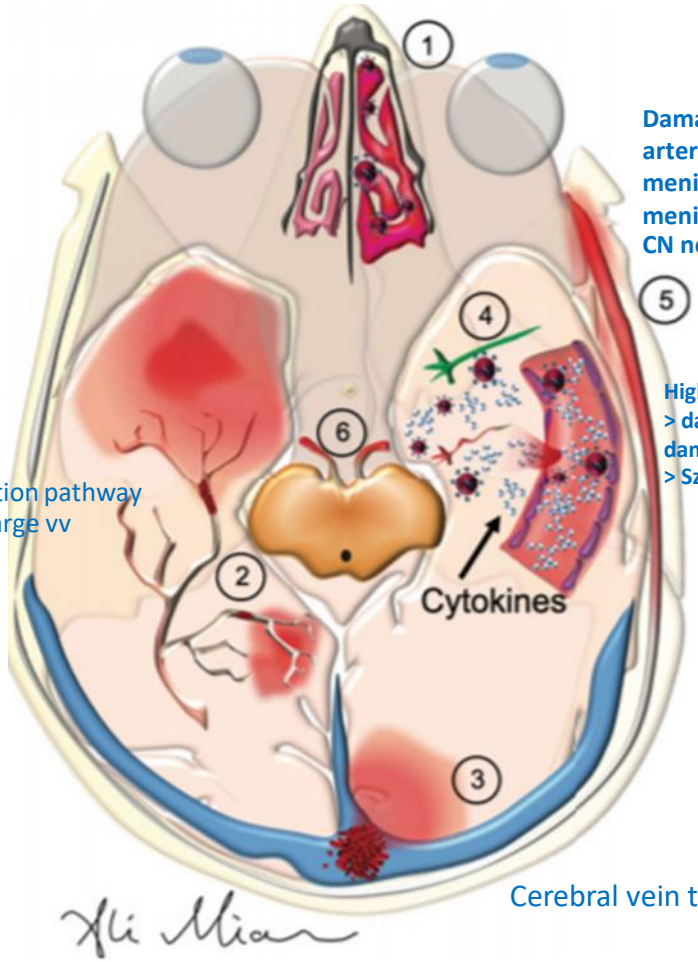
Fig. 2. SARS-Cov2: Pathophysiology of action in the nose, cranial nerves and the brain. SARS-Cov2 can cause a variety of neurological symptoms in patients with COVID-19 such as anosmia, strokes, encephalopathy, meningitis, and cranial nerve injury. 1) By binding and inhibiting nasal (and gustatory - not shown) epithelial cells, it reduces the sense of smell and taste. 2) By activating the cytokines and hypercoagulation pathways in the blood, it results in the formation of small and large vessel occlusion in cerebral arteries. 3) Formation of blood clots in the cerebral veins can results in cerebral venous thrombosis. 4) High levels of cytokines in the cerebral vessels can damage the blood-brain barrier, and once infiltrate the brain, damage neurons and glia which results in seizures and/or encephalopathy. 5) Damage to arteries in meninges can result in meningitis. 6) Formation of auto-antibodies, known as molecular mimicry, may lead to damage to cranial nerves (see Fig. 3).

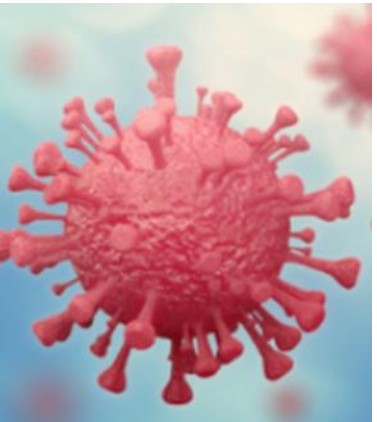
Binding & inhibiting nasal epithelial cells



Damage arteries in meninges> meningitis, CN neuropathy

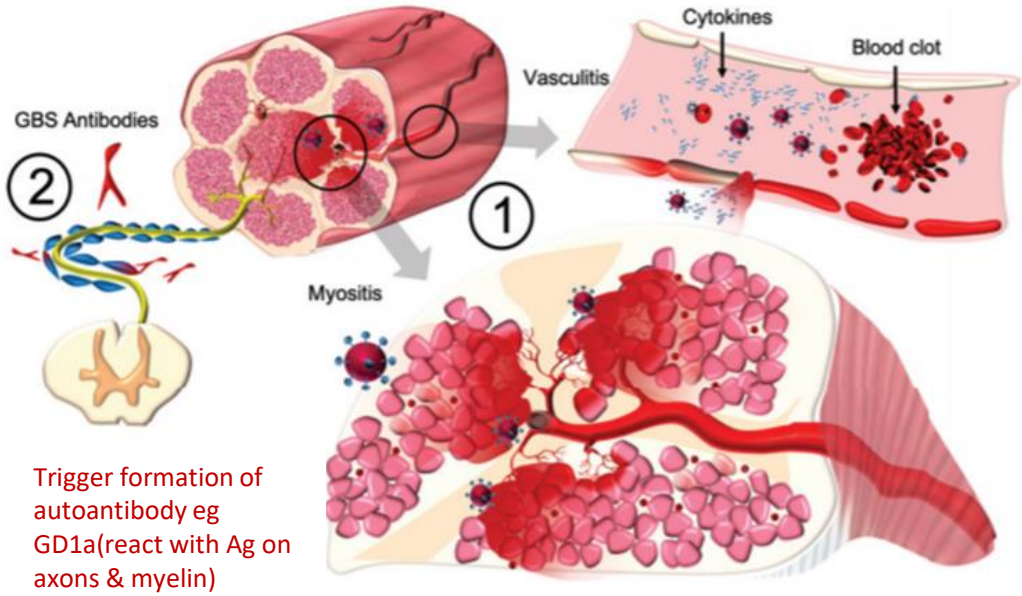
High levels of cytokines > damage BBB > damage neurons & glia > Sz, encephalopathy

Activating cytokines & hypercoagulation pathway in the blood > occlusion of sm vv & large vv



Cerebral vein thrombosis

Activation of cytokines>injury to bl vv>vasculitis, myositis



Trigger formation of autoantibody eg GD1a(react with Ag on axons & myelin) causing GBS

Fig. 3. SARS-Cov2: Pathophysiology of action in peripheral nerves and muscle. 1) SARS-Cov2 activation of cytokines causes inflammatory injury to epithelial cells in the blood vessels (vasculitis) and muscles cells (myositis). In cardiac arteries and muscles (not shown), cytokine storm, triggered by SARS-Cov2, can result in hypercoagulopathy and formation of blood clots (myocardial infarction) or endocarditis. 2) SARS-Cov2 can trigger the formation of autoantibodies (such as GD1a) which react with antigens on axons and myelin cells to cause Guillain-Barre syndrome (GBS).

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NeuroCovid staging

NeuroCovid Stage III

- Cytokine storm in the blood vessels is severe and causes an explosive inflammatory response that damages the blood brain barrier; entry of cytokines, blood components, and viral particles into the brain parenchyma causes neuronal cell death and encephalitis.
- Symptoms may include seizures, confusion, delirium, coma, loss of consciousness, or death.

NeuroCovid Stage II

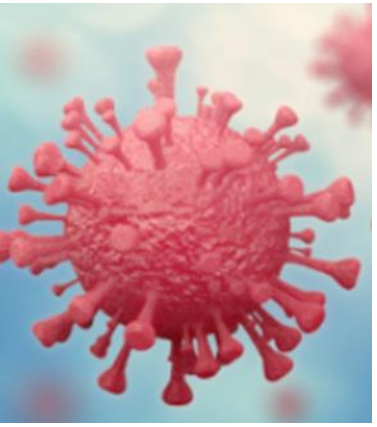
- Cytokine storm causes inflammation in the blood vessels and increases levels of hypercoagulability factors; blood clots are formed in both cerebral arteries and veins to cause small or large strokes.
- Neurological symptoms may include fatigue, hemiplegia, sensory loss, aphasia, or ataxia.
- Molecular mimicry can damage cranial nerves or peripheral nerves; symptoms may range from double vision to tetraplegia.

NeuroCovid Stage I

- Virus binds to cells in the nasal passage and tongue (no entry in the brain).
- Cytokine storm is contained and does not affect the brain.
- Main symptoms may include loss of smell and taste.

Increasing Severity of SARS-Cov2 Infection and Cytokine Storm

Fig. 4. NeuroCovid Stage I, II, and III. SARS-Cov2's neurological manifestation can be grouped into three stages. In NeuroCovid Stage I, the virus damage is limited to epithelial cells of nose and mouth. In NeuroCovid Stage II, patients may experience blood clots in their brain or have auto-antibodies that damage their peripheral nerves and muscles. In NeuroCovid Stage III, the cytokine storm damages the blood-brain barrier and patients may develop seizures, coma, or encephalopathy.



JAD 2020;76: 3–19

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อาการทางคลินิกของการติดเชื้อ COVID19 ในผู้ป่วยสมองเสื่อม ผู้ป่วย627คน ประเทศอิตาลี

Characteristics of 627 patients consecutively hospitalized for COVID19 pneumonia in two Italian hospitals according to the diagnosis of dementia

Characteristics	Sample	Dementia	no Dementia	p
No, (%)	627 (100)	82 (13.1)	545 (86.9)	
Sex, No (%)				
men	292(46.6)	35(42.7)	257(47.2)	NS*
women	335 (53.4)	47(57.3)	288(52.8)	
Age, mean (SD), y	70,7 (12.9)	82.6 (5.3)	68.9 (12.7)	<0.001**
Mortality, no (%)	194 (30.9)	51 (62.2)	143 (26.2)	<0.001*

* Pearson's chi-squared test; ** Student's t-test

Symptoms at ER admission among 82 dementia patients consecutively hospitalized for COVID19 pneumonia in two Italian hospitals

Symptoms, No (%)	
Delirium	55 (67.1)
Hypoactive	41 (50.0)
Hyperactive	17 (20.7)
Functional status worsening	46 (56.1)
Behavioral symptoms	9 (11.0)
Fever	39 (47.6)
Cough	11 (13.4)
Dyspnea	36 (43.9)

Characteristics of 627 patients consecutively hospitalized for COVID19 pneumonia in two Italian hospitals according to CDR classification

Characteristics	CDR0	CDR1	CDR2	CDR3	p
No, (%)	545 (86.9)	36 (5.8)	15. (2.4)	31 (5.0)	
Sex, No (%)					
men	257(47.2)	20 (55.6)	5 (33.3)	10 (32.3)	NS*
women	288(52.8)	16 (44.4)	10 (66.7)	21 (67.7)	
Age, mean (SD), y	68.9 (12.7)	82.0 (5.1)	83.0 (7.4)	83.1 (4.2)	<0.001*
Mortality, no (%)	143 (26.2)	15 (41.7)	10 (66.7)	26 (83.9)	<0.001*

* one-way ANOVA

A. BIANCHETTI et al. J Nutr Health Aging. 2020

alzheimers.org.uk/news/2020-06-23/ons-figures-show-almost-13000-people-who-died-covid-19-had-dementia

ONS figures show almost 13,000 people who died from Covid-19 had dementia

Tuesday 23 June 2020

Alzheimer's Society comments on the latest ONS figures showing almost 13,000 people who died from Covid-19 had dementia.

Updated figures from the Office for National Statistics (ONS) today show the number of deaths involving COVID-19 in England and Wales from 1 March to 30 May.

- There were 46, 687 deaths involving Covid-19 in England & Wales across March to May.
- Of the 46,687 people who died of Covid-19, 27.5% had dementia (12,856). This is an increase from 25.3% from the previous data for March and April.

Epidemiology

- Increased deaths in later stages of dementia may change prevalence figures
- Role of dementia as a specific factor in deaths from infections need clarification

153 UK corona nerve study:2020

Broad clinical syndromes associated with COVID-19 were classified as

1. cerebrovascular event (defined as an acute ischaemic, haemorrhagic, or thrombotic vascular event involving the brain parenchyma or subarachnoid space),
2. altered mental status (defined as an acute alteration in personality, behaviour, cognition, or consciousness),
3. peripheral neurology (defined as involving nerve roots, peripheral nerves, neuromuscular junction, or muscle),
4. other

Methods During the exponential phase of the pandemic, we developed an online network of secure rapid-response case report notification portals across the spectrum of major UK neuroscience bodies, comprising the Association of British Neurologists (ABN), the British Association of Stroke Physicians (BASP), and the Royal College of Psychiatrists (RCPsych), and representing neurology, stroke, psychiatry, and intensive care. Broad clinical syndromes associated with COVID-19 were classified as a cerebrovascular event (defined as an acute ischaemic, haemorrhagic, or thrombotic vascular event involving the brain parenchyma or subarachnoid space), altered mental status (defined as an acute alteration in personality, behaviour, cognition, or consciousness), peripheral neurology (defined as involving nerve roots, peripheral nerves, neuromuscular junction, or muscle), or other (with free text boxes for those not meeting these syndromic presentations). Physicians were encouraged to report cases prospectively and we permitted recent cases to be notified retrospectively when assigned a confirmed date of admission or initial clinical assessment, allowing identification of cases that occurred before notification portals were available. Data collected were compared with the geographical, demographic, and temporal presentation of overall cases of COVID-19 as reported by UK Government public health bodies.

Findings The ABN portal was launched on April 2, 2020, the BASP portal on April 3, 2020, and the RCPsych portal on April 21, 2020. Data lock for this report was on April 26, 2020. During this period, the platforms received notification of 153 unique cases that met the clinical case definitions by clinicians in the UK, with an exponential growth in reported cases that was similar to overall COVID-19 data from UK Government public health bodies. Median patient age was 71 years (range 23–94; IQR 58–79). Complete clinical datasets were available for 125 (82%) of 153 patients. 77 (62%) of 125 patients presented with a cerebrovascular event, of whom 57 (74%) had an ischaemic stroke, nine (12%) an intracerebral haemorrhage, and one (1%) CNS vasculitis. 39 (31%) of 125 patients presented with altered mental status, comprising nine (23%) patients with unspecified encephalopathy and seven (18%) patients with encephalitis. The remaining 23 (59%) patients with altered mental status fulfilled the clinical case definitions for psychiatric diagnoses as classified by the notifying psychiatrist or neuropsychiatrist, and 21 (92%) of these were new diagnoses. Ten (43%) of 23 patients with neuropsychiatric disorders had new-onset psychosis, six (26%) had a neurocognitive (dementia-like) syndrome, and four (17%) had an affective disorder. 18 (49%) of 37 patients with altered mental status were younger than 60 years and 19 (51%) were older than 60 years, whereas 13 (18%) of 74 patients with cerebrovascular events were younger than 60 years versus 61 (82%) patients older than 60 years.

Interpretation To our knowledge, this is the first nationwide, cross-specialty surveillance study of acute neurological and psychiatric complications of COVID-19. Altered mental status was the second most common presentation, comprising encephalopathy or encephalitis and primary psychiatric diagnoses, often occurring in younger patients. This study provides valuable and timely data that are urgently needed by clinicians, researchers, and funders to inform immediate steps in COVID-19 neuroscience research and health policy.

Lancet Psychiatry 2020. https://doi.org/10.1016/S2215-0366(20)30287-X

153 UK corona nerve study: 2020

Complete clinical datasets were available for 125 (82%) of 153 patients.

	All cases (n=153)	Cerebrovascular (n=77)	Altered mental status (n=39)	Peripheral (n=6)	Other (n=3)
Sex at birth					
Male	73 (48%)	44 (57%)	23 (59%)	5 (83%)	1 (33%)
Female	44 (29%)	30 (39%)	14 (36%)	0	0
Not reported	36 (24%)	3 (4%)	2 (5%)	1 (17%)	2 (67%)
Age, years					
≤20	0	0	0	0	0
21–30	4 (3%)	1 (1%)	3 (8%)	0	0
31–40	4 (3%)	1 (1%)	3 (8%)	0	0
41–50	10 (7%)	5 (6%)	4 (10%)	1 (17%)	0
51–60	17 (11%)	6 (8%)	8 (21%)	2 (33%)	1 (33%)
61–70	23 (15%)	16 (21%)	5 (13%)	2 (33%)	0
71–80	31 (20%)	23 (30%)	8 (21%)	0	0
81–90	23 (15%)	18 (23%)	5 (13%)	0	0
≥91	5 (3%)	4 (5%)	1 (3%)	0	0
Missing	36 (24%)	3 (4%)	2 (5%)	1 (17%)	2 (67%)
Median (range; IQR)	71 (23–94; 58–79)	73·5 (25–94; 64–83)	71 (23–91; 48–75)	59 (44–63; 50–62)	54 (54–54)

Data are n (%), unless otherwise indicated.

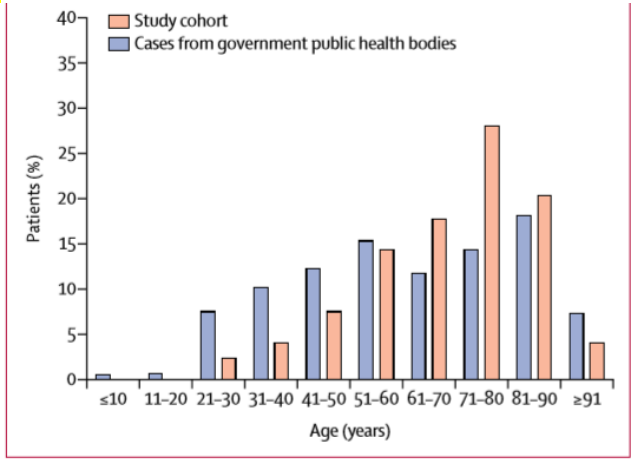


Figure 2: Age distribution of all cases notified to the CoroNerve Study Group and national data collected by UK Government public health bodies within the first 3 weeks of CoroNerve accepting notifications

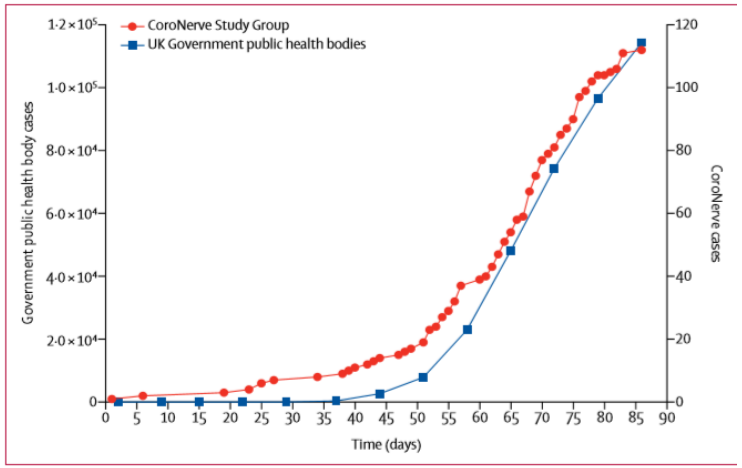


Figure 1: Temporal distribution of the date of admission or first assessment for cases notified to the CoroNerve Study Group and those identified by UK Government public health bodies

- 77 (62%) of 125 patients presented with a CVD ((74%) had an ischaemic stroke, 9(12%) ICH, 1(1%) CNS vasculitis)

- 39 (31%) of 125 patients presented with altered mental status, comprising 9 (23%) patients with unspecified encephalopathy and7(18%) encephalitis.

Lancet Psychiatry 2020. https://doi.org/10.1016/S2215-0366(20)30287-X

153 UK corona nerve study:2020

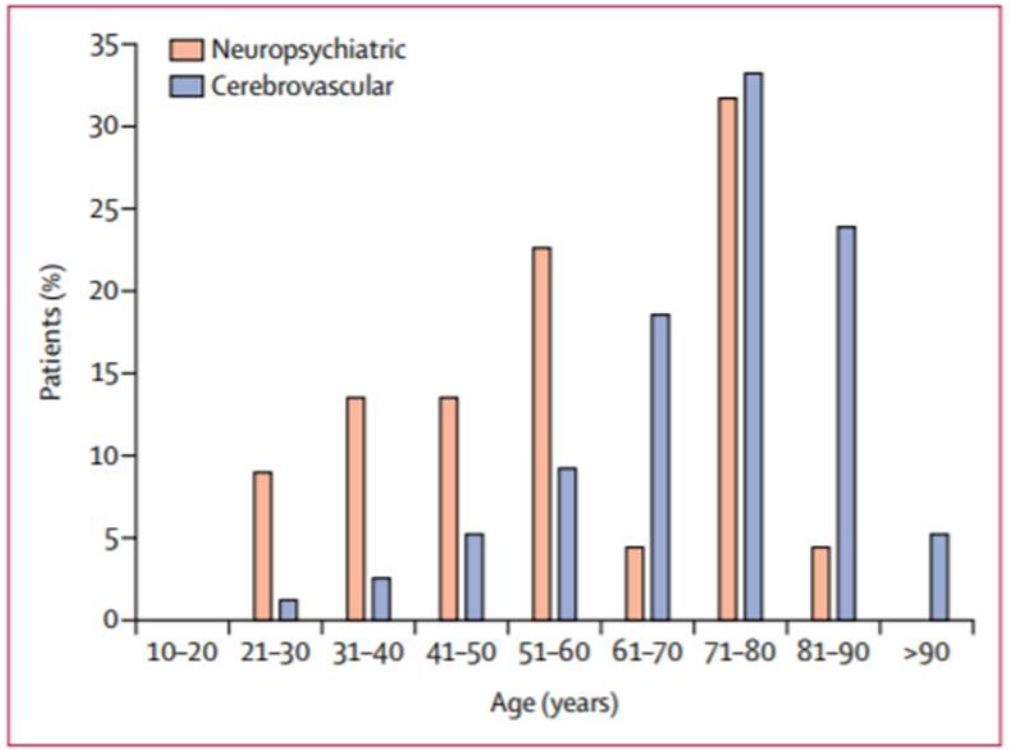


Figure 4: **Age distribution of patients identified through the CoroNerve surveillance study meeting the clinical case definitions for cerebrovascular and neuropsychiatric events**

Lancet Psychiatry 2020. https://doi.org/10.1016/S2215-0366(20)30287-X

- 23 (59%) patients with altered mental status fulfilled the for psychiatric diagnoses as classified by the notifying psychiatrist or neuropsychiatrist, and 21 (92%) of these were new diagnoses

10 (43%) of 23 patients with neuropsychiatric disorders had **new-onset psychosis**, 6 (26%) had a neurocognitive (dementia-like) syndrome, and 4 (17%) had an **affective disorder**

18 (49%) of 37 patients with altered mental status were < 60 years and 19 (51%) were > 60 years, whereas 13 (18%) of 74 patients with CVD were < 60 years versus 61 (82%) patients > 60 years

UK Biobank is a community cohort currently aged 48 to 86

ApoE4 gene

Table 1. Risk of Severe COVID-19, Comparing Participants With *ApoE* e3e4 or e4e4 to e3e3 Genotypes in UK Biobank

	n	Negative or not Tested	Positive	Positivity Rate per 100,000	OR (95% CI)[a]	*p*-value
All						
e3e3	223,457	223,056	401	179	-	-
e3e4	90,469	90,285	184	203	1.14 (0.95, 1.35)	.15
e4e4	9,022	8,985	37	410	2.31 (1.65, 3.24)	1.19E-06
Excluding dementia						
e3e3	222,968	222,574	394	177	-	-
e3e4	90,013	89,840	173	192	1.09 (0.91, 1.31)	.338
e4e4	8,877	8,840	37	417	2.39 (1.71, 3.35)	4.26E-07
Excluding hypertension						
e3e3	151,018	150,792	226	150	-	-
e3e4	61,249	61,157	92	150	1.00 (0.79, 1.28)	.981
e4e4	6,120	6,098	22	359	2.41 (1.56, 3.74)	8.21E-05
Excluding coronary artery disease						
e3e3	204,017	203,684	333	163	-	-
e3e4	82,099	81,948	151	184	1.13 (0.93, 1.37)	0.207
e4e4	8,164	8,132	32	392	2.43 (1.69, 3.50)	1.65E-06
Excluding type 2 diabetes						
e3e3	211,482	211,136	346	164	-	-
e3e4	85,983	85,827	156	181	1.11 (0.92, 1.34)	.275
e4e4	8,616	8,581	35	406	2.51 (1.77, 3.55)	2.42E-07

Note: [a]Adjusted for sex, age at the COVID-19 test or age on April 26, 2020 (the last test date), assessment center in England, genotyping array type, and the

The Journals of Gerontology: Series A, glaa131;2020. https://doi.org/10.1093/gerona/glaa131

COVID19 general advice

- Stay at home

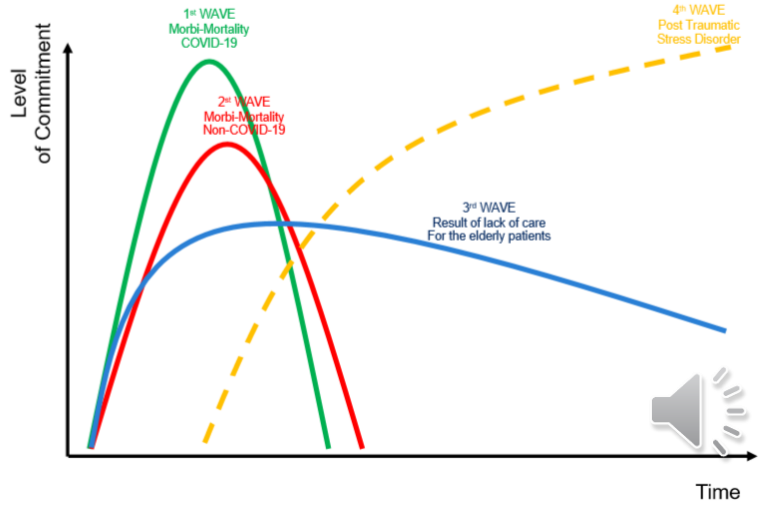
- Social distancing

DEMENTIA:

- Stay home> The strictest social isolation
- Social distancing> Discontinuation of family visit, assistance and rehabilitation.

Results:

1. Negative psychological impact: anxiety, irritability, etc
2. Deterioration of existing cognitive symptoms
3. Irrational management of the patients and caregivers



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Consequences for dementia patients in Thailand

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March2020-Almost complete shut down of outpatient visits; decrease in diagnostic activities eg MRI scanning, neuropsychological assessment, blood tests

- Some family can switch to telemedicine; positive feedback in >90%; patients afraid to come even if possible
- From June2020 gradual upscaling back to 25-50% of historical production

In Europe

- Closure of all daycare facilities
- Lockdown forces patients to stay in

} increase in caregiver burden/loss contact to medical care/service

- Nursing homes closed for visitors
- Increased death rates in nursing homes; staff under pressure

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Siriraj Hospital

Thailand

ADI Global approach

Courtesy Prof. Ricardo Allegri

Telemedicine: Telehealth follow-up rather than hospital visits after the initial diagnostic assessment
Increase in caregiver education on line:

Majority ขาดยา
Drug delivery by mailing

Frailty is a clinical state defined as an increase in an individual's vulnerability to developing adverse health-related outcomes

SAVE model for preventing frailty progression

SOCIALIZATION

Engage older adults using social media and telephone or video calls to overcome social isolation and provide cognitive stimulation.

ADEQUATE NUTRITION

Encourage adequate nutrition and provide recommendation to emphasize protein intake to preserve muscle mass and physical function.

VITAMIN D

Incorporate outdoor time with social distancing to stimulate Vitamin D synthesis and/or implement diet supplementation.

EXERCISE

Promote multi-component exercise using body weight. Encourage breaking up sedentary time and activity of any duration.

J Frailty Aging 2020;9(3)130-131

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