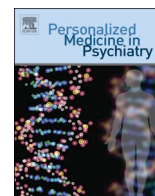




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## Expert opinion in Alzheimer disease: The silent scream of patients and their family during coronavirus disease 2019 (COVID-19) pandemic

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### ABSTRACT

COVID-19 pandemic is expected to be the greatest challenge for mental health since World War II in general, but the toll exacted on patients with Alzheimer's disease (AD) and their family is the greatest in several respects. AD patients are at the highest risk for contagion and death from the disease, but also at the very bottom in the list of priorities to access critical care services at times of medical resource scarcity. In this communication we examine the impact of the pandemic on AD patients and their family from the general medical, neurological, and mental health perspectives. We propose that instances of undue restriction of access to care based upon age and diagnosis show that society, governments, and health professionals need to exert maximum care, human compassion, and adherence to original Hippocratic values when addressing the needs of persons with AD and other major neurocognitive disorders during the COVID-19 pandemic, and that psychiatry is called to contribute to societal measures oriented to diminish human burden in this population.

### 1. Introduction

COVID-19 is expected to have a catastrophic impact on mental health globally. Apart from vivid, anecdotal illustrations of what the pandemic means to the mental health of patients suffering from COVID-19, health workers caring for them, and families deprived of the opportunity to help in care or assisting to humane deaths (e.g. [1]), quantitative estimations are being made on the potential scale of this human tragedy. A recent forecast of COVID-19 impact on mental health needs in England, for example, estimates that 20% of the entire population will need new or additional mental health interventions as a direct consequence of the pandemic, including a substantial proportion of children and adolescents [2]. Whereas immediate service demand has decreased as a consequence of lockdowns and physical distancing, following COVID-19 a significant proportion of the population is expected to require psychiatric interventions for heightened rates of depression, anxiety, substance use disorders, and post-traumatic stress disorder, at rates far beyond what could be expected from previous experiences with economic crises [2–4]. Worsening income and unemployment rates are but one of several additional problems caused by COVID-19, including social isolation, fear of dying, or restricted access to services, to name a few. The mental health impact of COVID-19 in patients with late-onset Alzheimer's Disease (LOAD), their families, and social services addressing

their needs is expected to be remarkably higher than that for other psychiatric disorders [5], in terms of risk of infection, risk of severe variants, death of COVID-19, and human suffering [5,6]. Older age emerged as the main risk factor from COVID-19 since the earliest available reports [6,7]. More recently, suffering from LOAD, other dementias, or other neurocognitive disorder are considered even stronger predictors of death, even after controlling for age [8,9]. However, the impact of COVID-19 on LOAD and other neurocognitive disorders far exceeds death. Patients and their families are affected by COVID-19 in many other ways.

### 2. Patients with LOAD have a higher risk of infection, hospitalization, and death

Heightened health risks related to COVID-19 among persons with LOAD begin with increased proneness to get the infection. Patients with cognitive compromise can have difficulties understanding and executing public health measures designed to minimize risks of infection, including forms of contagion, hand washing, physical distancing, and appropriate wearing of masks. Behavioral agitation characteristic of advanced LOAD worsens these difficulties and can even result in rapid spreading of the virus to other patients or their caregivers. Whereas virus shedding starts before the onset of characteristic symptoms, older people

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with dementia tend to show atypical presentations, like increased agitation and delirium, instead of shortness of breath, cough, or fever, which delays COVID-19 detection and prevents effective containment measures in nursing homes.

Once infected, older individuals with LOAD and less frequent dementias have the highest rates of adverse outcomes including hospitalization and death. For example, in the first wave of the pandemic in Europe, persons older than 65 years accounted for most COVID-19 deaths (e.g. [10,11]). Dementia, preexisting stroke, and a homozygous ApoE4 genotype are major risk factors for COVID-19 death independent of age [12]. Delays in seeking care for prevalent medical problems due to fears of contagion can also result in worse outcomes for general medical conditions such as cardiovascular disorders or infections.

### 3. COVID-19 displays neurotropic effects and worsens cognitive status of individuals with LOAD

The interaction of LOAD and COVID-19 can be considered a two-way street. Severe COVID-19 induces impaired consciousness, agitation, and delirium. And older age, dementia, and an ApoE4 genotype predispose to severe COVID-19 once infection ensues [13]. A discussion of the mechanisms explaining this two-way relationship exceed the objectives of this article, but such mechanisms are probably multifactorial and include hypoxia, stroke, postictal state, central and systemic inflammation, an ApoE4 genotype favoring blood–brain barrier disruption, and less frequently, viral presence in the central nervous system [14,15]. Therefore, patients with LOAD are at risk for neurotropic effects of COVID-19 apart from their heightened death risk.

### 4. Family members of patients with LOAD have a higher risk of mental health problems during the COVID-19 pandemic

Caring for patients with LOAD dementia can be extremely emotionally grievous to family members, and in order to relieve caregiver stress, strategies involving social activity, family and patient group support sessions can be very beneficial [16]. This is especially true in developing countries, which rely mostly on family support networks to care for members affected with dementia [17]. Strict governmental confinement measures have resulted in several adverse impacts on both patients and their families. The cessation of rehabilitation services and restricted help from family members other than the primary caregiver, results in worsening cognitive outcomes in patients and an increase in work burden stress, anxiety, and depression in family members [17]. This vicious cycle of worsened psychological status in patients and their caregivers resulting in cognitive deterioration in the former, can significantly affect overall health status and quality of life [5]. This helpless situation can be considered a silent cry of patients and families that health care workers and governments need to be attentive to hearing. But there is probably another silent cry being overlooked in relation to end-of-life decisions in the course of this pandemic.

### 5. Caring for severe COVID-19: are we trying hard enough to hear any silent scream of Alzheimer's disease patients dying of COVID-19?

As stated, age and suffering from a dementia (usually LOAD) are the strongest risk factors for being hospitalized and dying from COVID-19 [8,9]. The very same factors that put individuals at risk for these ominous outcomes, also put them at the bottom of priorities for getting access to life support in the form of a ventilator or other necessary measures when treatment is scarce [18]. The utilitarian ethical principle of “maximization of benefits” has the purpose of saving the most individual lives, but can also be interpreted as *saving the most life-years by giving priority to patients likely to survive the longest after treatment* [18,19]. Some authors have referred to this approach as “ageism” and proposed careful triage that is age-blind be considered instead [20]. Taken to an

extreme, the “maximization of benefits” principle leads to concluding that an older person with dementia should be actively removed from a ventilator (meaning a certain and almost immediate death) if room needs to be made for an incoming younger patient with more potential years of life [18]. This opinion has been scrutinized and sometimes vehemently questioned [21–24], but in theory remains an option in decision-making process in the pandemic. Some contrary arguments appeal to virtue ethics, for example invoking their potential for harming staff morale and public trust [23], and some are made from the deontological and judicial perspectives of protected legal rights and worth of all human beings, including those who are weak, old, and disabled [22], as is clearly the case of patients with LOAD and other dementias. Most important, a substantial number of individuals with LOAD enjoy meaningful personal and family lives until late in the disease, and therefore there is agreement in the medical community that older age or dementia should not be an umbrella concept automatically excluding patients from critical care at times of scarce resources. Such an exclusionary criterion would be based on unsubstantiated assumptions about quality of life [5].

The pandemic has hit at a time when ethical values informing these decisions are being explicitly or implicitly pondered not only by the medical community, but also by the general public. For example, in 2019 population surveys showed that a stunning 40% of adult Belgians were in favor of “not administering costly treatments to prolong life in anyone older than 85 years of age.” Only 28% of responders favored spending 50,000 euros or more in a vital treatment for persons who are 85 years of age and older [25]. It is intriguing that Belgium, an advanced country with top-notch medical care, and the seat of several European Union governing bodies, has the highest per capita COVID19-related mortality rate in the world along with San Marino, at 168.30 per 100,000 at the time of writing this article [26]. Claims that such a mortality rate is an overestimation, because untested patients dying in the pandemic were counted as COVID19, have been largely refuted [27]. Further, this mortality rate is disproportionately high when the nursing home population is considered [27], where older individuals with LOAD and other dementias are clearly overrepresented. At the first wave of the pandemic, 63% of COVID19 deaths had affected home care residents, a far greater proportion than that of other countries with aged populations [27]. Along with Luxembourg and the Netherlands, Belgium tops the countries with most residents over-65-year-old per capita in long-term care homes, at 71 per 1000 population as of 2012 [28]. At the individual-decision level, cultural and societal views on the value of life at different ages may arguably play a role on how assertive a treatment should be when the person at risk of dying is older and has an incurable disease like LOAD or another dementia.

In the realm of end-of-life medicine, it might be important to consider that, along with the Netherlands, Belgium has the most lenient legal access to euthanasia and assisted suicide (EAS). Also, recent data show that, in the Netherlands, “suffering” as a reason for increasing numbers of EAS in the geriatric population occurs in diverse forms, not strictly end-of-life, medically incurable situations [29]. Understandably, this has raised concerns of a “slippery slope” of evolving EAS beyond initially conceived eligibility criteria. There appears to be an implicit societal agreement that some lives are no longer worth the investment required to preserve them or, in other words, that both the individual, family, or the society would be better off if the patient were dead [30]. The concoction of COVID19, an ageing population, and high prevalence of LOAD has probably put the medical community and the society at large, at a deeply troubling crossroads where decisions on who lives and who dies from a disease are truly compelling. This “perfect storm” brings to the forefront the values and beliefs guiding actual health behaviors. In particular the (deontological) value of human life in and of itself, is contrasted with (utilitarian) values such as society's presumable “best interest,” especially in financial terms. The author believes older, disabled persons like those with Alzheimer's Disease can be very easily turned into silent, defenseless casualties when those societal values are

shaky, and in the case of the medical profession, when core Hippocratic concepts emphasizing human life as an immanent value, no longer play a necessary role guiding all patient care. There are reasonable concerns this has played a part already in the current pandemic, when nursing home patients older than 65 years were denied critical care, even at times when availability of critical care resources was not an issue [31,32]. Psychiatry, often invoked to opine on issues like capacity, quality of life, and emotional suffering, should encourage explicit conversation about these societal dilemmas.

## 6. Conclusions

Whereas the COVID-19 is expected to be the greatest challenge for mental health since World War II [2], the toll exacted on patients with Alzheimer's disease and their families is the greatest in most respects. They are at the highest risk for contagion and death from the disease, but also maximally affected by the restriction in the access to health care services due to the pandemic. Due to considerations of number and quality of life years lived if recovered, older individuals with dementia are at the very bottom in the list of priorities to access critical care services at times of medical resource scarcity. This situation requires that society, governments, and health professionals exert maximum care, human compassion, and adherence to original Hippocratic values when addressing the needs of this population during the COVID-19 pandemic.

## Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## References

- Arango C. Lessons learned from the coronavirus health crisis in Madrid, Spain: how COVID-19 has changed our lives in the last 2 weeks. *Biol Psychiatry*. 2020;88(7):e33–4.
- O'Shea N, Covid-19 and the nation's mental health. Forecasting needs and risks in the UK: October 2020. Centre for Mental Health; 2020. [https://www.centreformentalhealth.org.uk/sites/default/files/publication/download/CentreforMentalHealth\\_COVID\\_MH\\_Forecasting3\\_Oct20\\_0.pdf](https://www.centreformentalhealth.org.uk/sites/default/files/publication/download/CentreforMentalHealth_COVID_MH_Forecasting3_Oct20_0.pdf).
- Economou M, Madianos M, Peppou LE, Patelakis A, Stefanis CN. Major depression in the era of economic crisis: a replication of a cross-sectional study across Greece. *J Affect Disord* 2013;145(3):308–14.
- Fancourt D, Steptoe A, Bu F, Trajectories of depression and anxiety during enforced isolation due to COVID-19: longitudinal analyses of 59,318 adults in the UK with and without diagnosed medical illness; 2020. <https://www.medrxiv.org/content/10.1101/2020.06.03.20120923v3.full.pdf+html>.
- Mok VCT, Pendlebury S, Wong A, Alladi S, Au L, Bath PM, et al. Tackling challenges in care of Alzheimer's disease and other dementias amid the COVID-19 pandemic, now and in the future. *Alzheimer's Dement* 2020;16(11):1571–81.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395(10229):1054–62.
- Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020;20(6):669–77.
- Atkins JL, Masoli JAH, Delgado J, et al. Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort. *J Gerontol A Biol Sci Med Sci*, 2020;75(11):2224–30.
- Zhou J, Liu C, Sun Y, Huang W, Ye K. Cognitive disorders associated with hospitalization of COVID-19: Results from an observational cohort study. *Brain Behav Immun* 2021;91:383–92.
- Ferrari R, Maggioni AP, Tavazzi L, Rapezzi C. The battle against COVID-19: mortality in Italy. *Eur Heart J* 2020;41:2050–2.
- Kluge H. Statement – Older people are at highest risk from Covid-19, but all must act to prevent community spread. Copenhagen, Denmark: World Health Organization; 2020.
- Williamson E, Walker AJ, Bhaskaran KJ, et al. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. medRxiv; 2020. 2020.05.06.20092999.
- Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. *N Eng J Med* 2020;382(23):2268–70.
- Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuroepidemiology and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: a review. *JAMA Neurol* 2020;77:1018–27.
- Montagne A, Nation DA, Sagare AP, Barisano G, Sweeney MD, Chakhoyan A, et al. APOE4 leads to blood-brain barrier dysfunction predicting cognitive decline. *Nature* 2020;581(7806):71–6.
- Hughes TB, Black BS, Albert M, Gitlin LN, Johnson DM, Lyketsos CG, et al. Correlates of objective and subjective measures of caregiver burden among dementia caregivers: influence of unmet patient and caregiver dementia-related care needs. *Int Psychogeriatr* 2014;26(11):1875–83.
- Cohen G, Russo MJ, Campos JA, Allegri RF. Living with dementia: increased level of caregiver stress in times of COVID-19. *Int Psychogeriatr* 2020;32(11):1377–81.
- Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair allocation of scarce medical resources in the time of Covid-19. *NEJM* 2020;382(21):2049–55.
- Persad G, Wertheimer A, Emanuel EJ. Principles for allocation of scarce medical interventions. *Lancet* 2009;373(9661):423–31.
- Cesari M, Proietti M. COVID-19 in Italy: Ageism and decision making in a pandemic. *J Am Med Dir Assoc* 2020;21(5):576–7.
- Brown MJ, Goodwing J. Allocating medical resources in the time of Covid-19 (comment). *NEJM* 2020;382(1):e79.
- Liddell K, Martin S, Palmer S. Allocating medical resources in the time of Covid-19 (comment). *NEJM* 2020;382(1):e79.
- Firth P, Eyal N. Allocating medical resources in the time of Covid-19 (comment). *NEJM* 2020;382(2):e79.
- Hyder AA. Allocating medical resources in the time of Covid-19 (comment). *NEJM* 2020;382(2):e79.
- <https://www.lesoir.be/213111/article/2019-03-19/sante-40-des-belges-sont-pour-larret-des-soins-pour-les-plus-de-85-ans>.
- <https://coronavirus.jhu.edu/data/mortality> [accessed 12/28/2020].
- Molenberghs G, Faes C, Verbeeck J, et al. Belgian COVID-19 Mortality, Excess Deaths, Number of Deaths per Million, and Infection Fatality Rates (9 March — 28 June 2020). Rxiv 2020. <https://doi.org/10.1101/2020.06.20.20136234>.
- <https://stats.oecd.org/Index.aspx?QueryId=30142> [accessed 12/30/2020].
- van den Berg V, van Thiel G, Zomers M, Hartog I, Leget C, Sachs A, Uiterwaal C, van Wijngaarden E. Euthanasia and physician-assisted suicide in patients with multiple geriatric syndromes. *JAMA Internal Medicine*; 2020, in press.
- Meier DE. The treatment of patients with unbearable suffering -the slippery slope is real. *JAMA Internal Medicine*; 2020, in press.
- <https://www.nytimes.com/2020/08/08/world/europe/coronavirus-nursing-home-s-elderly.html> [accessed 12/31/2020].
- Medecins sans frontiers. Left behind in the times of COVID-19. Medecins sans Frontieres/Doctors without borders (MSF) sharing experiences from its intervention in care homes in Belgium. July 2020. <https://www.msf.org/sites/msf.org/files/2020-07/Left%20behind%20-%20MSF%20care%20homes%20in%20Belgium%20report.pdf>, [accessed 12/31/2020].