

LETTER TO THE EDITOR

# Will “social distancing” lead to future “research distancing”: A reflection on COVID-19 impacts on Alzheimer’s disease research

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## Abstract

Coronavirus disease 19 (COVID-19) has dramatically altered everyday life, including the field of Alzheimer’s disease (AD) research. This perspective article explores some of the ways in which COVID-19 has already impacted the field, anticipates some of the long-lasting effects, and explores strategies for addressing current and future needs. Areas of impact include study integrity, regulatory and industry issues, and participant engagement. Proposed strategies for addressing these challenges include analytic methods to deal with large degrees of missing data and development of patient-centered, user-friendly, remote data collection tools and assessments. We also highlight the importance of maintaining participant well-being as a first and constant priority.

The coronavirus disease 19 (COVID-19) pandemic has disrupted everyday life around the globe.<sup>1</sup> For those of us working in the area of Alzheimer’s disease (AD) prevention and treatment, it is important to take stock of the immediate impact, anticipate some ongoing effects, respond to current needs, and anticipate future challenges. This letter is focused on the impact of COVID-19 on clinical research in populations of individuals at risk for or with dementia. Although several of these challenge areas were addressed briefly in a recent *Alzheimer’s & Dementia* editorial, we expand upon them here and offer thoughts for a path forward.<sup>2</sup>

## 1 | STUDY INTEGRITY

The immediate impact of COVID-19 includes analytic challenges with ongoing studies that, due to requirements for social distancing, will now have inconsistent adherence to protocols as designed with visit schedules and medication and intervention adherence all more fluid than in ideal circumstances.<sup>3</sup> Addressing this challenge will require skilled statisticians using available, and perhaps novel, analytic methods to ensure that we do not incorrectly conclude that a new treatment is ineffective due to midstream pauses and interruption of drug dosing.

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Although we are all still reeling from the rapid onset of this crisis, we also need to consider the possibility that higher than anticipated study attrition may lead to failed trials.

## 2 | REGULATORY AND INDUSTRY ISSUES

It remains unclear, but of critical importance, how will regulatory agencies consider the data stemming from AD trials interrupted by COVID-19. In the United States, the U.S. Food and Drug Administration (FDA) has issued statements of assurance that they understand the need for study interruptions and protocol deviations, but how they will resolve the impact of such study conduct on future regulatory decisions remains unknown. Given these considerations, industry sponsors are currently weighing the cost/risk/benefit ratios of continuing ongoing studies or simply halting trials altogether and beginning anew once the crisis has abated.

## 3 | IMPACT ON CURRENT PARTICIPANTS AND PROSPECTIVE RECRUITMENT

We have encountered mixed feelings among participants; some are voluntarily pulling back from their research engagement in the face of the immediate threat the COVID-19 crisis posits to their health and well-being and others wish to push on as they understand AD's profound and ongoing impact. Today's social distancing requirements may have long-lasting effects, including lingering apprehension about social contact and a shift from altruistic research motivations to choices to remain more isolated to protect one's own health. The limited pool of participants willing to engage in AD research may become even more limited in the future if heavy demands are placed on research activities within centers that may be perceived in the future as hotspots for contagion. Maximal impacts for such societal change would be seen in the area of invasive study procedures and biomarker collections, which are critical for the conduct of state-of-the-art clinical trial research in the area of preclinical, prodromal, and even fulminant AD. Furthermore, with morbidity, mortality, and economic hardship disproportionately affecting those who are already disadvantaged, we anticipate increased challenges engaging diverse and underrepresented individuals in research, raising concerns for generalizability.<sup>4</sup> These challenges and the need for innovation will coexist within an uncertain funding landscape as we deal with the global economic fallout from this pandemic.

## 4 | CHANGES WE HOPE TO SEE IN THE CLINICAL TRIAL LANDSCAPE

After we move past the most acute period of COVID-19, the effects on AD clinical research will persist. Because the need for remote

### RESEARCH IN CONTEXT

1. Systematic Review: Due to the recent and rapid emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 19 (COVID-19) and its impact, this perspective piece incorporates the expert opinions of the authors and their careful consideration of the areas of Alzheimer's disease (AD) research likely to be affected now and moving forward, as well as ways in which the field can adapt. A brief PubMed review for relevant articles paralleled this effort.
2. Interpretation: This perspective piece highlights important considerations and a path forward to help transform the challenges that COVID-19 brings to AD research into constructive change.
3. Future Directions: Moving forward it will be important to evaluate how proposed changes affect participant and research outcomes and whether they can make the field more resilient to future challenges.

data collection has been clearly demonstrated, we anticipate an increased investment in the development of remote tools and assessments that will enable gathering of clinical and neuropsychological data from the participant's home. This is a welcome move toward increased participant-centeredness. This transition, however, will be accompanied by additional challenges to ensure that we do not exacerbate existing health disparities by leaving those without access to technology, which may be required for remote monitoring activities, behind.

## 5 | CONCLUSION

We believe the field can rise to meet the current challenges, transforming the need for social distancing into an impetus for positive change. These potential beneficial changes in trial design, statistical methodologies to address even large swaths of missing data, changes in regulatory rules and oversight, and the development of new tools for remote assessment of cognition and decline are critical priorities for the field. These areas provide a real opportunity for constructive change in the face of what is otherwise a devastating crisis.

While responding to and anticipating these challenges, we need to keep our participants at the forefront of our thoughts. Demonstrating that protecting participants is a priority will go a long way to building and maintaining trust in research. In contrast, if we put research needs above participant health we will have significant distrust to overcome in the future. Our efforts today can dramatically improve the clinical trial landscape as we move forward.

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