Alzheimer’s Disease Research Enterprise in the Era of COVID-19/SARS-CoV-2

The emergence and increasing incidence of the severe acute respiratory syndrome-associated coronavirus 2019 (SARS-CoV-2, or COVID-19), a respiratory illness caused by a novel zoonotic form of the betacoronavirus, presents unprecedented new challenges to global biomedical research, public health research, and medical care delivery communities. This current outbreak has important implications for research in Alzheimer’s disease and related disorders (ADRD).

The current COVID-19 contagion represents a completely novel phenomenon in terms of the geographical and temporal spread. In response, many countries have implemented social distancing measures such as quarantines within urban areas, prohibition of travel to and from certain countries, and suspension of activities entailing large numbers of people, all as means to control the pace of viral transmission. Not unexpectedly, the population segment with the highest mortality from COVID-19 are older adults and individuals with weakened immune systems. This is particularly true for those with co-morbid medical conditions that include all those affected by primary neurodegenerative disorders and most of their caregivers.

The editors of Alzheimer’s & Dementia: The Journal of the Alzheimer’s Association identify the following topics, focused specifically on research, on which readers and researchers should focus immediate attention during this global outbreak.

1. Sponsors of clinical studies, and investigators leading or participating in ADRD studies should:
   a. Be resolutely committed to the safety of study participants and research staff. In keeping with this commitment, we call on clinical research sites to initiate proactive communication through diverse channels with study participants to ascertain their wellness, to provide information about mitigating risk, and to provide information about the status of a given study. As such, the studies themselves can be leveraged for structured, efficient health education and promotion.
   b. Have contingency plans in place to deal with site closures (clinics, hospital, research sites), and travel restrictions (quarantines, curfews, lack of private or public transportation) in order to preserve study integrity to the maximal extent possible. Potential solutions such as remote visits, remote monitoring (e.g., telemedicine), or even direct-to-patient delivery of investigational products need to be rapidly explored and vetted in coordination with relevant review boards.
   c. Work together to ensure staff retention and maintenance of staff certification to administer protocols. This will allow for data collection to be initiated as soon as it is deemed safe to do so. As many research activities will cease for an undetermined period of time, many staff will not be used at full capacity. Ensuring that staff can be paid or used in other capacity during down time is imperative to ensure research continuity.
2. Given that many AD clinical research centers conduct trials for multiple sponsors, trial sponsors should plan to collaborate and share their contingency plans with each other in order to ensure a coordinated response across the board.
3. There is a high likelihood that the COVID-19 outbreak will result in research participants being unable to keep their appointments (e.g., clinics, labs, MRI, PET) within protocol-specified windows, potentially generating a higher-than-expected rate of protocol deviations. Health regulatory agencies and other health research sponsors/funders of ADRD research are encouraged to initiate an immediate dialogue on how protocol deviations resulting from the outbreak should be handled. Data Safety and Monitoring Boards as well as Observational Study Monitoring Boards should seek guidance on the handling of these inevitable protocol deviations. The editors of A&D welcome the opportunity to support any agency’s communication activities though the dissemination and publication of draft proposals, white papers, or policy guidance.
4. Institutional Review Boards should strive to swiftly review and approve any necessary protocol changes or proposed communications with research participants.
5. We can expect novel and unprecedented occurrences of data missingness. Clinical research in AD, whether observational or interventional, includes some of the longest and most complex studies ever designed and deployed. Many of these studies cannot be feasibly re-funded or re-started. Therefore, given the enormous investment made by research participants, family members, investigative teams, and research sponsors, every effort should be made to preserve the integrity and value of this critical ongoing research while balancing the dynamic risks associated with study participation during an outbreak. Methodologists in statistics, epidemiology, and clinical trials should publish appropriate methods for handling these data anomalies. In fact, this may be an opportunity to develop new tools and conventions for assessing missingness. Regulatory agencies and study sponsors, whether academic, governmental or industrial, should review such potential methodological approaches to explore the consequences of subject discontinuations and missing data.
Recent experience with other zoonotic viruses e.g., Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS), Ebola Virus Disease (EVD), and Zika Virus (ZIKV) suggests that these types of outbreaks are likely to be recurrent and potentially more frequent. A very large proportion of current and future AD patients live in medically underserved communities and countries whose public health infrastructure is under-resourced and therefore most unlikely to cope with any major future outbreak. In such communities, research participation may be the only source of health care. The AD research and global public health research communities should identify critical gaps in care for dementia in the face of an outbreak and propose potential solutions for the current COVID-19 outbreak that can serve as a blueprint for those to come.

The Alzheimer’s Association Research Roundtable, the Alzheimer’s Association International Society to Advance Alzheimer’s Research and Treatment Professional Interest Areas, and other Alzheimer’s and dementia related professional societies are encouraged to submit open-peer commentaries, letters to the editor, or perspective articles that describe established, developing, or recommended procedures for rectifying the issues outlined here. Alzheimer’s & Dementia remains committed to publishing novel public health initiatives from countries with large or growing AD populations in order to protect these vulnerable patients and their caregivers.

Ensuring the safety and well-being of patients, research participants, caregivers, and staff involved in the care of their patients, as well as those involved in conducting clinical research, is a core obligation for everyone involved in clinical research. We are also tasked to make every effort to preserve the integrity of the clinical data collected from our participants. Through proactive risk mitigation strategies and streamlined collaboration throughout the Alzheimer’s disease research enterprise – participants, caregivers, research staff, regulatory bodies, sponsors and funders alike – we can uphold our commitments to patients and their families in the face of COVID-19 and future, inconceivable global catastrophes.

-Alzheimer’s & Dementia