Lifestyle research studies to reduce risk of Alzheimer's respond to COVID-19 challenges

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The impact of the COVID-19 pandemic on public health is staggering; more than one hundred million cases and two million deaths worldwide. In response, most countries and local governments have taken substantial

measures—such as travel restrictions and physical distancing—to keep their citizens safe. Both the pandemic and related protective measures pose challenges for ongoing clinical research studies seeking to treat and prevent the world's greatest public health emergencies including COVID-19, but also Alzheimer's disease and other dementia.

In a new paper from the World-Wide FINGERS network in Alzheimer's & Dementia: Translational Research and Clinical Interventions, first author Susanne Röhr, Ph.D., clinical psychologist at the Institute of Social Medicine, Occupational Health and Public Health, University of Leipzig, Germany, and colleagues provide timely guidance on the design and management of clinical research during COVID-19—specifically on the conduct of lifestyle-based risk reduction studies in people at risk for cognitive decline and dementia.

The article describes the COVID-19-related experiences of three trials—each at a different stage of the study process—conducted in conjunction with the World-Wide FINGERS (WW-FINGERS), the first global network of lifestyle-based multidomain trials for dementia risk reduction and prevention, which includes over 30 countries.

J-MINT: Japan-multimodal intervention trial for prevention of dementia—mainly in the recruitment process (~December, 2020) and intervention delivery.

U.S. POINTER: U.S. study to protect brain health through a lifestyle intervention to reduce risk—recruitment process and intervention delivery.

German AgeWell.de study—intervention adherence and post-intervention follow-up.

"The COVID-19 pandemic has profoundly altered the landscape for the

design and conduct of clinical trials of multidomain lifestyle interventions. This is especially true in studies focused on cognition, Alzheimer's and other dementia, where the study population has some of the greatest health risks," said Röhr, who also is an Atlantic Fellow for Equity in Brain Health at the Global Brain Health Institute.

"With this collaborative publication, we bring together and discuss our experiences of the challenges we've faced, and continue to face, and how we've responded to them. By sharing our collective knowledge about the lessons learned so far, we can provide real-world, evidence-based recommendations to similar ongoing and prospective lifestyle intervention trials," Rohr added.

In response to COVID-19, the WW-FINGERS network created a shared space for its members to discuss the challenges of research during the pandemic. They gathered international teams with expertise to address, almost in real-time, the challenges that cut across the research. This allows studies at earlier stages to adjust to these potential challenges, while more advanced studies will still be able to access expertise to adapt to their specific circumstances.

"By working together, we can address and solve common problems and find effective strategies to prevent cognitive decline and Alzheimer's disease," said Mark Espeland, Ph.D., professor of Internal Medicine at Wake Forest School of Medicine and senior author on the newly published article.

"The WW-FINGERS collaborative efforts are needed more than ever in the current landscape. The network's joint knowledge and expertise is shaping lifestyle interventions both during and in the post-pandemic scenario," said Miia Kivipelto, M.D., Ph.D., professor of Clinical Geriatrics at Karolinska Institute, founder and scientific leader of the WW-FINGERS network and co-author of the article.

"Looking at the impact of COVID-19 across the WW-FINGERS network of clinical trials enables us to evaluate the effectiveness of our responses to the pandemic across different cultures, local environments, and phases of the pandemic," said Maria C. Carrillo, Ph.D., Alzheimer's Association chief science officer and a co-author of the article. "The lessons learned through WW-FINGERS might be helpful for other lifestyle intervention research as well."

"Conducting a clinical trial such as J-MINT is a huge challenge during the pandemic, but we have learned a lot about how to prevent the infection. Applying this knowledge to this and other clinical trials should be useful for improving future implementation of lifestyle-based dementia prevention measures," said Hidenori Arai, M.D., Ph.D., President, National Center for Geriatrics and Gerontology, and co-author of the newly published article.

Lifestyle intervention research may be particularly susceptible to disruption from the pandemic. Traditionally, lifestyle interventions focus on strong bonds through group and individual face-to-face sessions. Social isolation—which can result from physical distancing—can also challenge lifestyle interventions. Research studies focused on preventing cognitive decline often recruit individuals for whom COVID-19 poses greater risks due to their older age and greater burden of age-related noncommunicable diseases.

Each of the four WW-FINGERS studies adapted by altering designs and analysis plans—changing recruitment plans, timelines, and modes of delivery for interventions and assessments. For example:

Due to the COVID-19 pandemic, J-MINT was forced to halt recruitment and initial evaluation of participants from late February to mid-May 2020. Enrollment activities resumed in late May 2020 with appropriate measures to defend against infection. To help ensure safety of

participants and study staff, new rules and procedures for testing and intervention were implemented. This added extra time and cost. As a result, progress of the study was delayed more than half a year. Nonetheless, by December 2020, planned recruitment was completed. The potential statistical problem caused by the four-month gap on average from the initial evaluation to the intervention will be addressed through additional analysis to see if this is correlated with the magnitude of cognitive changes. If the time between the initial evaluation and the start of the intervention is longer than 6 months, the team will conduct a reevaluation and may conduct a sub-analysis that excludes the study participants who were reevaluated.

During a study-wide pause from March to July 2020, U.S. POINTER researchers maintained contact with study participants through phone calls that encouraged participants to continue to meet their study intervention goals. Intervention delivery shifted from in-person meetings to video conferencing. Some data were accumulated continuously during the pause, but others were postponed and rescheduled. Following the pause, intervention meetings were held remotely and full adherence monitoring was resumed.

In Germany, infection control measures, including the first nationwide lockdown, largely coincided with AgeWell.de's intervention period. As the quarantine measures put restrictions on lifestyles, concerns specifically arose regarding social and physical activity and mental wellbeing. In addition, face-to-face post-intervention assessments were at risk; and changing the assessment mode would violate the data integrity. Therefore, a safety and hygiene protocol was developed, including an option to be interviewed at the study site instead of at home. To better understand the pandemic impact, the researchers mailed a survey to participants during the first lockdown to measure changes to everyday life, social and mental health and resilience. The survey will be repeated to gain a longitudinal perspective of the pandemic impact.

More information: Susanne Röhr et al. Impact of the COVID-19 pandemic on statistical design and analysis plans for multidomain intervention clinical trials: Experience from World-Wide FINGERS, *Alzheimer's & Dementia: Translational Research & Clinical Interventions* (2021). DOI: 10.1002/trc2.12143

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