

MASSACHUSETTS
Alzheimer's Disease
Research Center

KEEP IN MIND

Annual Newsletter of the Massachusetts
Alzheimer's Disease Research Center

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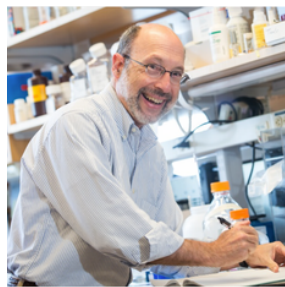
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A Message From our Chief

Updates from Brad Hyman, MD, PhD.



Dear MADRC Community,

Happy Spring! It is my absolute pleasure to write and express my deep gratitude for your continued dedication and commitment to the Massachusetts Alzheimer's Disease Research Center (MADRC). You – our patients, participants, families, care partners and community – are the reason and motivation for the work we do. We have a lot of exciting things happening at the Center, some of which I will

highlight here.

On the national front, there has been the **most exciting news in many years**. Three companies have announced results with new drugs that seem very promising at slowing the progression of Alzheimer's. They need to be approved by the FDA, decisions about insurance coverage need to be made, and mechanisms developed for how to get them (if approved) to all who might benefit from them need to happen. Right now, they are all given by vein, but who knows what the future holds? Each of them seems to clear the amyloid plaques from the brain- something that seemed impossible a decade ago. While there are side effects that might keep these drugs from working for everyone, the idea that we can actually change the course of the disease is amazing and fills me with hope. If you would like to learn more about these experimental advancements, please see our official comment, written by the head of the Memory Disorders Unit at MGH, our very own Dr Teresa Gomez-Isla. It is on the www.madrc.org/website "Announcements," which we will update as the path to bringing these drugs to patients becomes clearer. I invite you to turn to page 2 to hear more from Dr. Gad Marshall.

Locally, over the last six months, we have resumed pre-COVID operations. We are seeing participants in-person and heading back into the community to hold events. I think it is fair to say that everyone has really enjoyed re-connecting with one another in-person and with that it brings a feeling of hope to have returned to this normalcy.

Let me introduce our new Outreach, Recruitment and Education (ORE) Core leaders Drs. Christine Ritchie and Ana-Maria Vranceanu, who join Dr Dorene Rentz in reaching out to the community. We have been finding ways to bring research to the community- if you have an idea, let us know! It is a Center wide priority to make research more accessible, and we are committed to increasing diversity and representation within our research studies. To make this happen, we have partnered with Boston-area senior housing complexes. We have held several events at these facilities, both to provide education about Alzheimer's Disease and Related Disorders as well as offer the opportunity to learn about, and even participate in, research. We have also had a bit of fun – (Continued page 2)

Chief

(continued from p.1)

eating, playing bingo, and naming that tune! Please read more about these events on page 4.

We are also engaging our community via the MADRC Community Advisory Board (MCAB). The purpose of this board is to guide and inform our Center about how to optimize equity in research participation so that everyone can experience the benefits of research innovations and receive equitable high-quality care. We are grateful to our community members who participate on this board and take the time to make our Center better. To read more about our Community Advisory Board, please go to: page 6.

This year we created the 'Talk with the Doc (tor) Series' which is held monthly and discusses topics for patients, families, and care partners that are either living with or caring for, a loved one with a neurodegenerative disease. For example, the topic for April was 'Navigating the Caregiver Journey.' One of our speakers was our very own Judy Johanson, Program Coordinator for the Memory Study, who cared for her husband during his journey through early onset Alzheimer's disease. We have received feedback that these educational events are well received and attended. You can learn about this series on page 6.

I hope many of you have been able to follow us on social media. We find this is the best way to connect with you all and share what we are doing at our Center. You can find us on Twitter, Facebook, Instagram, LinkedIn and Youtube. See the last page for details.

As the Center Director, I am very proud to highlight one of my colleagues' recent accomplishments. Dr. Liliana Ramirez-Gomez is a Neurologist in the Clinical Core of the Alzheimer's Disease Research Center and is an Assistant Professor of Neurology and the Clinical Director of the Memory Division in MGH Neurology. Dr. Ramirez-Gomez was recently awarded the Norman Geschwind Prize in Behavioral Neurology for her diligent work on aging and dementia, including providing clinical care and coordinating research activities for underserved and diverse populations and particularly marginalized Latinos. She has been instrumental in outreach efforts within our Latino communities and a valued member of our Spanish Memory Disorders Unit clinic.

Thank you again for your dedication and commitment to MADRC. I sincerely hope the future is brighter and that together, as a team, we can find even better treatments for these devastating diseases.

Warmly,
Brad

Alzheimer's Disease Treatment Updates

By Gad Marshall, MD

Over the past year, there have been a lot of new and exciting developments in the arena of Alzheimer's disease therapeutics. Several large clinical trials of experimental treatments for Alzheimer's disease were completed and their results have been shared with the public. These have been primarily of anti-amyloid monoclonal antibodies, a form of passive immunization against the protein amyloid that is abnormally deposited in the brains of patients with Alzheimer's disease. These drugs are administered intravenously every 2 to 4 weeks depending on the drug.

A phase 3 clinical trial (at the last stage of testing) employing one drug in particular, lecanemab (the Clarity-AD study), has shown both a robust biological benefit (clearance of amyloid plaque from the brain) and corresponding modest clinical benefit (slowing of decline in cognitive function and activities of daily living) when compared to placebo (no treatment) over 18 months in individuals with mild symptoms of Alzheimer's disease (either mild cognitive impairment or mild dementia). This drug also led to side effects, including infusion reactions (ex: nausea or rash), and swelling in the brain and tiny areas of bleeding in the brain that mostly did not cause symptoms but require repeat MRI scans to monitor the safety of individuals being treated. Lecanemab has received accelerated (conditional) approval from the FDA

for clinical use and is pending a decision for full/traditional approval in July 2023, which will then lead to corresponding decisions around coverage by Medicare and the potential ability to prescribe it in clinic (outside of a research setting). Recently, the preliminary results of the Trailblazer-ALZ 2 phase 3 trial employing donanemab, another anti-amyloid monoclonal antibody, were reported with similar encouraging results. An application for FDA full approval will likely be submitted in the coming months. Consequently, many hospitals and specialty clinics have been hard at work planning how to safely implement these new treatments for the many patients who may meet the criteria to benefit based on the study findings.

Research Phases Explained

When hearing about research studies in the news, the terms "phase 1, phase 2 and phase 3" are often mentioned, but what exactly does that mean?

Clinical trials (or studies) are the primary way that researchers find out if a new treatment is safe and effective in people. After initial research in the lab, the most promising new drugs move through a series of clinical trial phases. These phases are designed to ensure that the medication is safe and to determine the best method and dosage for administering the treatment.

Check out our graphics (next page) to learn about the specific purpose of each phase.

CLINICAL TRIAL RESEARCH PHASES

PHASE 1

Phase 1 of an experimental drug study involves evaluating the drug's safety before it advances to further clinical studies. A new drug candidate is typically tested on a small group of healthy research participant volunteers. Information about side effects is recorded to determine if the drug should move to Phase 2.

Phase 1 usually takes several months and involves 20-80 people.



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CLINICAL TRIAL RESEARCH PHASES

PHASE 2

In Phase 2, researchers administer the experimental drug to a group of patients who have the disease or condition for which the drug is being developed. Several doses of the drug may be tested to determine which dose is the safest. Phase 2 usually does not involve testing whether the drug is effective in treating the disease, but sometimes tests are administered to see if the drug might be effective in the future.

Phase 2 typically lasts up to two years and involves several hundred people.

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CLINICAL TRIAL RESEARCH PHASES

PHASE 3

In Phase 3, researchers compare the safety and effectiveness of the experimental drug to the current standard treatment. Study participants are usually randomized, meaning some participants get the new drug and others get a placebo, or a sugar pill.

This phase typically involves 1,000 – 3,000 participants and lasts from 1 – 4 years.

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CLINICAL TRIAL RESEARCH PHASES

PHASE 4

Following Phase 3, the new drug moves to the Federal Drug Administration (FDA) for approval. Once approved it advances to Phase 4 Clinical Trial/Post-Market Surveillance.

The FDA monitors the drug for safety and potential adverse effects.

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The Positives From a Negative Study Outcome

Recent results from an international clinical trial to prevent Alzheimer's disease symptoms, the Anti-Amyloid Treatment in Asymptomatic Alzheimer's study ("A4 Study"), showed that the investigational drug, Solanezumab, when compared to placebo, did not slow memory loss. For a detailed report of results see the press release here:

<https://bit.ly/A4Release>

While these results are disappointing, every study conducted helps scientists learn and make new advancements. Here are some of the positives that participants in the A4 Study contributed to:

- This was the first of its kind secondary prevention trial in cognitively asymptomatic older adults with biomarker risk for AD (elevated amyloid noted on PET scan) using a disease-modifying drug (in this case, an anti-amyloid drug). As such, there were many unknowns going into this trial that had to be figured out before and during the trial. It was, therefore a great opportunity to change how we think about Alzheimer's disease and its treatment.
- This trial showed us that we can design and execute a clinical trial in preclinical AD (individuals with biological evidence of AD but no significant symptoms). Again, this is something that has never been done before so it was no small feat. In order to be successful in future prevention trials, we needed this first one under our belts to pave the way.
- We were able to define an at-risk population (based on a biomarker)—we were able to identify the individuals who were likely going to develop symptoms of AD over time in order to include them in such a prevention trial.
- We developed new outcome measures (clinical assessments and biomarker tests) that were appropriate for this stage of disease (most of the tests we had before were aimed at dementia or mild cognitive impairment and were not sensitive enough).
- We learned a lot about how to recruit participants for such a prevention trial (community advocacy, registries, existing cohorts, etc.).
- We learned how to disclose biomarker results to participants (these types of results were previously only disclosed to individuals who already had symptoms of AD). We learned how to address the participants' psychological well-being, concerns, and stigma in this context.
- All the work that went into the A4 study has already informed the design of other prevention trials, such as AHEAD. Therefore, we were able to learn from A4 and design better trials, which will hopefully result in effective treatments.
- The A4 large and rich dataset will be available to answer many questions about early-stage AD over the coming years. Research projects that will be done using this data will surely better inform early diagnosis and treatment of AD and spawn new ideas and directions.

What are Biomarkers and why are They Important in Research?

Biomarkers are characteristics of the body found in fluids such as blood, cerebrospinal fluid (fluid that surrounds the brain and spinal cord) or tissue that you can measure. They may serve as a sign of an abnormal or normal process in the body. Examples of this include a blood test, or fluid obtained from a lumbar puncture or spinal tap that measures a kind of protein in the body that may suggest certain kinds of dementia.

Since biomarkers are measurable, they can be used to predict the risk of developing a disease or condition, as well as determine how well the body responds to a treatment for a disease or condition. Many of them are not yet ready for “prime-time” as part of routine clinical practice but are very important in research studies.

Biomarkers are critical to research studies because they help measure the risk for disease and the effects of investigational treatments in clinical trials.

Hope & Empowerment Through Research

No one can describe what it's like to participate in a research study more accurately than the actual study participants. That's why we sat down with several of them and asked the group to talk about why they chose to get involved and what the experience has been like. The result is an inspirational video titled, Hope & Empowerment Through Research, featuring the personal stories of five study participants.

If you have ever thought about taking part in a study but were on “the fence,” we urge you to watch this video at: <https://bit.ly/ResearchHope>



Bringing Research to the Community

The team at MADRC wants to make it as easy as possible for people interested in research to learn about dementia research and get involved in a study. We know that some of the reasons people do not participate are due to time commitments and/or transportation issues. To help with this, MADRC has been hitting the road and bringing its research out into the community.

This year the MADRC research staff has already gone mobile to several locations in the Greater Boston area, including Blue Ledge Co-Op Apartments in Roslindale, Central Boston Elder Services, New Academy Estates in Roxbury, and St. Patrick's Manor in Framingham. During these sessions, attendees learn about the importance of brain health and how they can reduce their risk of developing dementia. They also learn about and can participate in, some unique research studies that can be done on cell phones and/or tablets.

These informative sessions are also fun as they include games such as Brain Bingo and Name That Tune! So far, these events are receiving thumbs up from attendees!

If you are interested in scheduling a session in your community, call the MADRC Outreach team at (617) 278-0600 or via email to BWHMADRCeducation@partners.org.



Teamwork Makes the Dream Work at MADRC

Collaboration is the key to success at the Massachusetts Alzheimer's Disease Research Center (MADRC). While all our affiliated research teams are working on the same overall problem – ending brain disease – each brings their own expertise to the table. Our research team members may have diverse backgrounds, but they have common goals and objectives and benefit immensely from the data and resource sharing that takes place within MADRC. From Primary Investigators mentoring graduate students, to Clinical Research Coordinators sharing best practices for study participant recruitment, we truly work stronger together.

The commitment to collaboration spans our research labs situated across multiple locations on the campuses of Brigham and Women's Hospital (BWH) and Massachusetts General Hospital (MGH). Regardless of where each lab is located, the teams work together to lead cutting-edge research in the form of about 40 clinical trials and observational studies. Read on to learn about some of the different MADRC research study teams!

The MADRC Longitudinal Cohort Memory Study Team

The MADRC Clinical Core runs a critically important longitudinal study (the Memory Study) that follows participants on a yearly basis with imaging, cognitive testing and questionnaires to better understand the course of AD and related dementias. The Memory Study 'LC' study is an ongoing observational study of individuals with or without memory problems that is part of a large national study to inform our understanding of what happens to the brain as we age.

For more information call: 617-726-5571 or email: JJOHANSON1@mgh.harvard.edu

The Alzheimer's Clinical & Translational Research Unit (ACTRU) Team

ACTRU takes a multidisciplinary, basic science to clinic translational approach to designing patient-oriented experimental and clinical trials for aging, dementia, and other neurodegenerative disorders. These involve advanced digital health assessments, neuroimaging, and ultra-sensitive molecular biomarker detection technologies in blood, cerebrospinal fluid and brain tissue.

For more information call: 617-643-2351 or email: actrustudies@mgh.harvard.edu

Center for Alzheimer Research and Treatment (CART) Team

CART, in collaboration with Brigham and Women's Hospital and Harvard Medical School, offers numerous innovative prevention and treatment trials. Their mission is two-fold:

1) to improve the early diagnosis of Alzheimer's disease (AD) employing more sensitive clinical evaluations, biological markers, and neuroimaging; and 2) to assess promising new treatments for AD.

For more information call: 617- 732-8085 or email: CART@partners.org

Frontotemporal Disorders Unit Team

The FTD Unit provides diagnosis and treatment for frontotemporal dementia and related disorders, including Primary Progressive Aphasia, Semantic Dementia, Corticobasal Degeneration Syndrome, and Progressive Supranuclear Palsy. They work with patients and families with young-onset and atypical forms of Alzheimer's disease, as well as



Frontotemporal Disorders Unit Team



Longitudinal Cohort Memory Study Team



Alzheimer's Clinical & Translational Research Unit

collaborate with the Frontal Temporal Lobe Society to offer unique services for caregivers. The FTD Unit closely collaborates with other centers including Brigham & Women's Hospital, Beth Israel Hospital, Jamaica Plain VA Aphasia Research Center, the Association for FTD and the Alzheimer's Association. For more information call: 617-726-8689 or email: MGHFTDUnit@partners.org

Lewy Body Dementia Unit Team

The Lewy Body Dementia Unit provides diagnosis and treatment for patients with the Lewy body dementias – dementia with Lewy bodies and Parkinson's disease associated dementia, as well as patients with mild cognitive impairment arising in these diseases. Management of cognitive, motor, sleep, psychiatric, and other nonmotor manifestations of these diseases is provided. Ancillary services provide disease-focused physical therapy, occupational therapy, and speech therapy. Our social work staff provide opportunities for caregiver support. The LBDU is a Lewy Body Dementia Association Research Center of Excellence. For more information call: 617-726-1728 or email: mquan4@mgh.harvard.edu

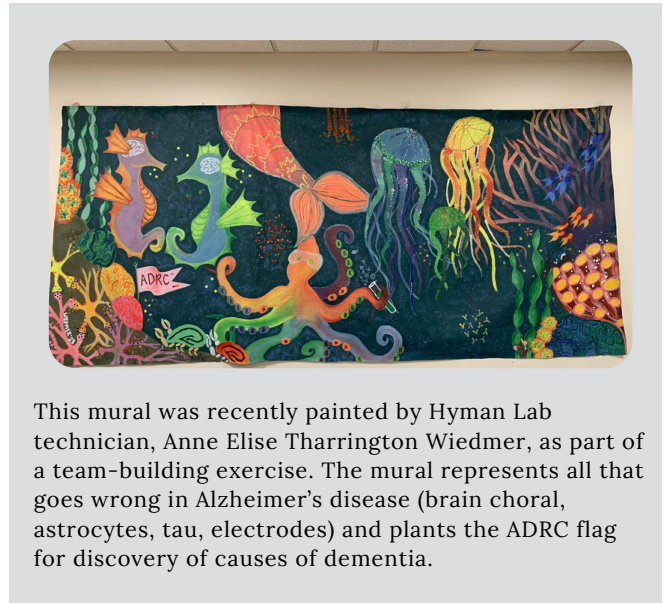
While each of the aforementioned centers are under different roofs, we are all on the same team working together to advance science in dementia research. To learn about the many different research studies we offer, visit: www.madrc.org/join-a-study/

Community Advisory Board Provides Guidance

The Outreach, Recruitment & Engagement (ORE) Core at MADRC meets quarterly with the members of our Community Advisory Board (CAB). This group was formed to guide our work and provide suggestions on how to optimize equity in research participation. Our goal is to ensure that everyone is able to experience the benefits of research innovations and receive equitable high-quality care.

The CAB assists ORE in forming partnerships with community groups located in Boston neighborhoods. Members also provide community feedback on questions and opinions related to research. Additionally, the CAB offers recommendations on our program offerings and the content of our community resources.

We appreciate this valuable feedback from the community representatives who serve on our CAB.



This mural was recently painted by Hyman Lab technician, Anne Elise Tharrington Wiedmer, as part of a team-building exercise. The mural represents all that goes wrong in Alzheimer's disease (brain coral, astrocytes, tau, electrodes) and plants the ADRC flag for discovery of causes of dementia.

New Educational Program Launched

MADRC kicked off its new Talk with the Doc(tor) series in January. This program features a different MADRC-affiliated researcher each month who presents about their area of expertise. Each doctor is joined by a current research participant who shares their experience of what it's like to take part in a study.

These monthly presentations alternate between being conducted in English and Spanish. Thus far, topics have included How Can Research Improve Lives? Making a Difference Through Research, Developments in Dementia Research, Navigating the Caregiver Journey and How is Alzheimer's Disease Diagnosed?

If you missed hearing them live, you can watch the presentations on the MADRC YouTube page @ADRCMASS. Keep an eye on our Events page for future sessions: madrc.org/events/



Road Map Series Expands

MADRC's popular Aging & Memory Loss Road Map Education Series has expanded to cover even more topics! In the past year, we added the following two programs in response to requests for information in these specific areas:

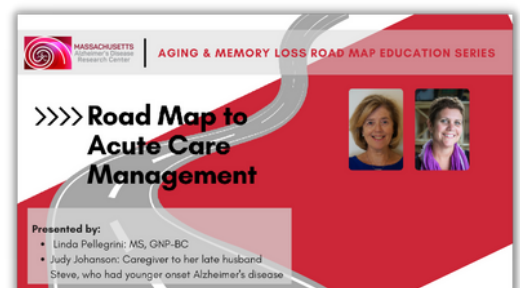
Road Map to Acute Care Management

This guidebook provides documents and information to help caregivers navigate an unexpected trip to the emergency room (ER). Unanticipated events such as this can be particularly difficult for a person living with dementia. This publication includes tips on how to speak with medical personnel, advice on reducing stress during long waits in the ER and information on important forms such as the Medical Orders for Life-Sustaining Treatment (MOLST).

Road Map to Grief and Loss

The newest booklet in the series, this guide discusses the many types of grief that a loved one of a person with dementia may experience. This includes ambiguous loss, anticipatory grief, disenfranchised grief, and complicated grief. Advice on how to manage grief and as well as suggestions for support and recovery are included.

The Road Map series booklets can be accessed on the "[Community](https://www.madrc.org/Community)" page of our website at [www.MADRC.org](https://www.madrc.org).



Focus on Caregivers

The majority of MADRC research studies have centered around people living with various types of dementia. However, we also have important studies available for the people who care for them. Our researchers know they can learn valuable information from care providers, which will better guide treatments. For more information about study opportunities for caregivers, visit www.madrc.org/join-a-study/ and select “Caregiver” under “Additional Studies.”

To further support care providers, the MADRC team collaborates with groups that offer critical resources for caregivers and we list the information on our website. This includes support group contacts, tips on how to best communicate with a person living with dementia, advice on how to navigate vacations and holidays, and much more. These resources can be located on the MADRC website on the “[Patients and Caregivers](#)” page.



Ramirez-Gomez Receives Accolades for Diversity Work

MADRC’s own, Liliana Ramirez-Gomez, MD was awarded the 2023 Norman Geschwind Prize in Behavioral Neurology, by the American Academy of Neurology. Dr. Ramirez-Gomez was recognized for her work with providing clinical care and coordinating research activities for underserved and diverse populations, – in particular, marginalized Latinos.

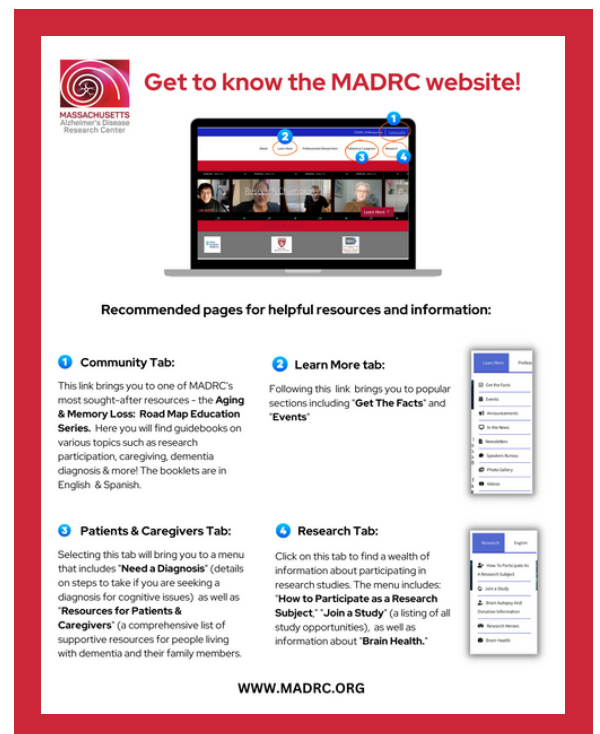
Ramirez-Gomez says her research goals are to improve methods for providing culturally competent clinical care to patients from minoritized communities with dementia, and their caregivers, and to increase the representation of Latinos in research.



Get Acquainted With the MADRC Website

Did you know the MADRC website (www.MADRC.org) is not only an excellent source of information for research studies, but also for topics like brain health tips, and caregiver resources? There are lots and lots of useful resources and other information on the site, including Fact Sheets explaining the different types of dementia, upcoming events, and instructions on how to get a diagnosis.

Check out our flyer below which helps visitors navigate to the most popular sections on the site.



5 Reasons to Get Involved with Research:

- Opportunity to access treatments not yet available to the public
- Take an active role in advancing science
- Receive care from expert medical staff who closely monitor your health
- Get compensated for your study participation
- Be a part of history!

Vist: www.MADRC.org to learn more about research opportunities.

Follow Us!

To stay on top of all the MADRC-related news throughout the year, be sure to follow along on all of our social media platforms!



To