Programs facilitating integration of disease-modifying therapies (DMTs) and diagnostic testing into clinical practice: Mass General Brigham's experience

Seth Gale, M.D.
Assistant Professor of Neurology, Harvard Medical School
Director, Brain Health Program, Brigham and Women's Hospital

Kirk Daffner, M.D.
J. David and Virginia Wimberly Professor of Neurology, Harvard Medical School
S. Muss Clinical Director, Alzheimer Center, Brigham and Women's Hospital

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Disclosures

- Dr. Gale serves as site PI and Co-I at Mass General Brigham for Alzheimer disease clinical trials funded by the NIA/NIH, Eisai Inc., Eli Lilly, Biogen, and Cognition Therapeutics
- Dr. Daffner serves as a co-investigator of ALZ-NET, a multi-site network for collection of real-world data from patients receiving novel FDA-approved AD therapies; member of the Medical/Scientific Advisory Committee of the Alzheimer's Association, MA/NH

Presentation Outline

I. Introduction to the Mass General Brigham (MGB) healthcare system

II. Summary of existing Dementia Care Programs and current Alzheimer Clinical Research Programs

III. Bottlenecks, Challenges, and Opportunities -- how each stakeholder can contribute to solutions

- A. **Building a new infrastructure** to deliver DMTs *within* current Dementia Care Programs
  - Review MGB's emerging plans to identify patients eligible for DMTs and safely deliver medications
- B. **Coverage of the cost of DMTs and all components necessary** for determining eligibility, risk assessment, and monitoring safety
- **C. Capacity limits of dementia experts with requisite knowledge to confirm AD diagnoses/disease stages, guide patients through DMT treatment decisions, and monitor for safety**
- **D. Constraints on the time and capacity of primary care and community health providers to: identify and diagnose patients at the appropriate disease stage; refer to specialized programs; and care for potentially overwhelming numbers of newly diagnosed dementia patients**
- **E. Opportunity to work across government agencies, industry, and health systems/providers to bring novel diagnostics and DMTs to dementia care, and achieve equitable access for all patients, with attention to underserved and minoritized communities**

Mass General Brigham

(MGB)

- **Boston-based, non-profit hospital and physician network that includes**
  - **Brigham and Women's Hospital (BWH)**
  - **Massachusetts General Hospital (MGH)**
  - **Two of the major teaching hospitals of Harvard Medical School**
- **Founded in 1994**
- **Biggest healthcare provider and largest private employer in MA**
- **Cares for 1.5 million patients annually**
- **Staff of ~ 80,000**
- **$2 billion in research activities**

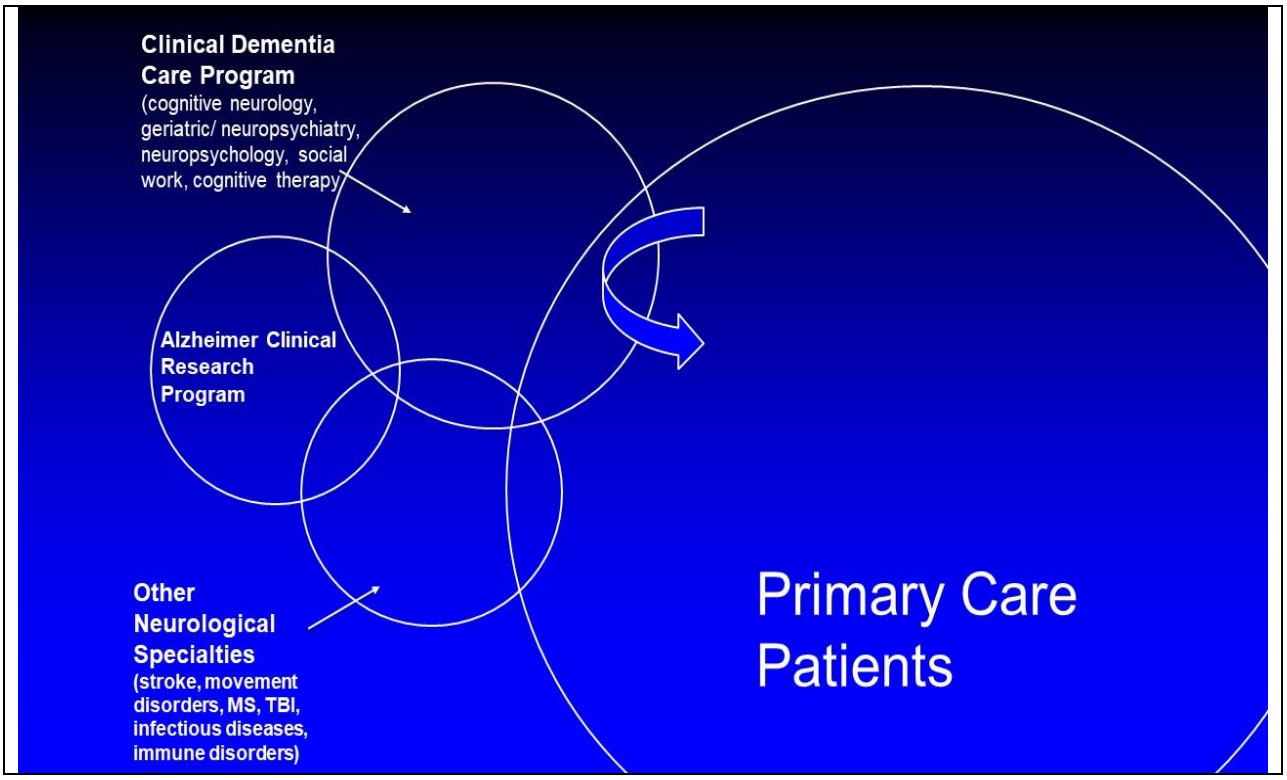
- **The plans and challenges associated with integrating novel diagnostics, disease identification strategies, and DMTs in to care are similar to ones facing academic medical systems around the U.S.**
  - **Challenges facing less-resourced health systems are likely much larger**

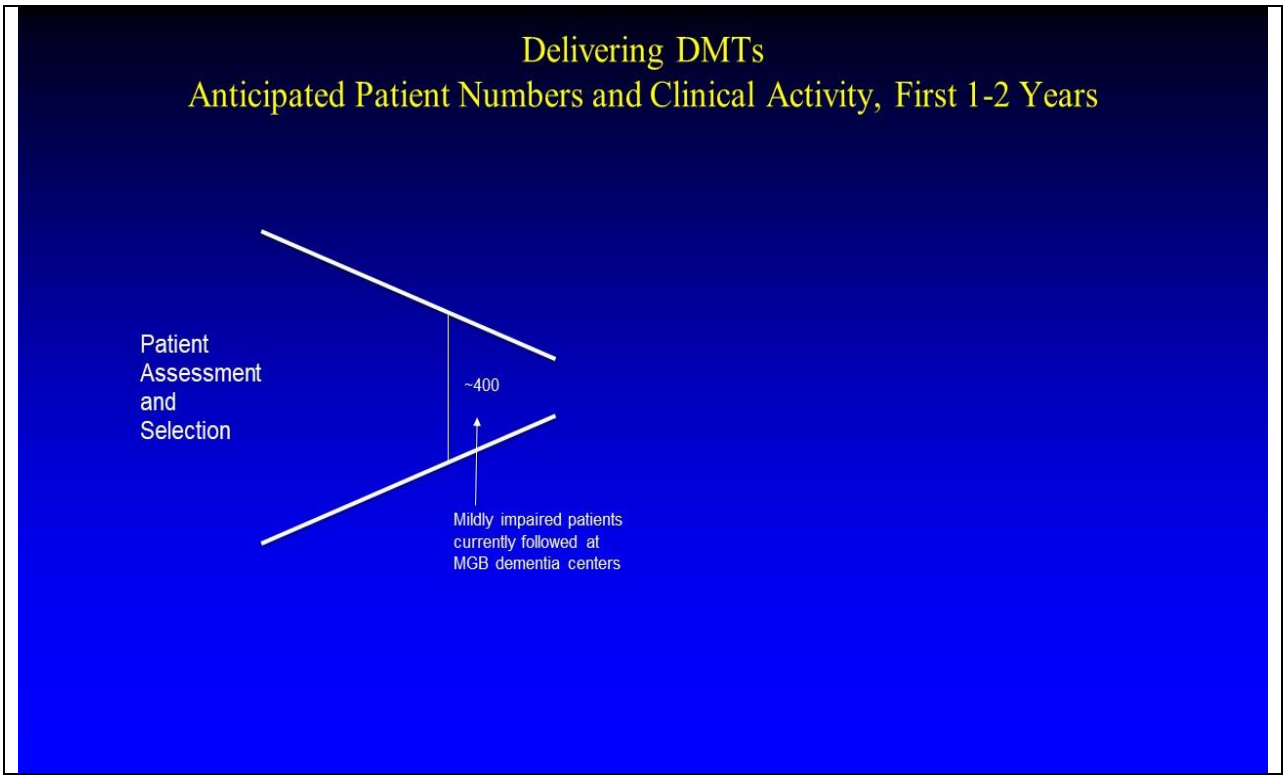
Current Dementia Care Programs – MGB

- **Interdisciplinary Dementia Care Centers**
  - Cognitive neurology
  - Geriatric Psychiatry/Neuropsychiatry
  - Neuropsychology
  - Social Work
  - Cognitive Therapy
  - Trainees (fellows in each of these subspecialties)
- **Patient referrals made to our center by PCPs, medical specialists (e.g., geriatrics, cardiology), general neurologists, general psychiatrists within our hospitals or broader healthcare system; some self-referrals**
  - **Concerns raised about changes in a patient's cognitive, neuropsychiatric, and functional status**
- **Interdisciplinary clinical assessment and evaluation (MRI, routine bloodwork) +/- AD biomarkers (e.g., CSF amyloid, tau) and other specialized testing (e.g., FDG-PET; neuropsychological evaluations) for some patients**
- **Patients and care partners are provided likely diagnosis**
- **Treatment plan created and implemented — by the dementia care team or via recommendations to referring clinician**
- **Symptomatic medical treatments are offered aimed at cognitive impairment (e.g., cholinesterase inhibitors, memantine); neuropsychiatric symptoms (e.g., escitalopram, sertraline), sleep disorders (e.g., CPAP), and medical conditions (e.g., antihypertensive meds, statins, oral hypoglycemic agents)**
- **Cognitive therapy, cognitive skills training groups, counseling/psychotherapy, clinical trial opportunities**
- **Social Work referrals; patient and care partner support provided by Alz. Association; additional resources**

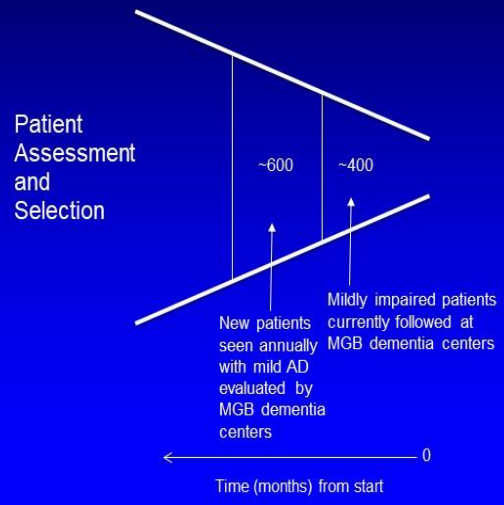
Current Alzheimer Clinical Research Programs - MGB

- **Subset of our dementia care providers actively involved as PIs, site PIs, Co-PIs**
- **Subset of patients participate in clinical research, some of which is supported by an NIA-funded Alzheimer Disease Research Center (ADRC)**
- **Well established infrastructure for delivering novel therapeutic agents**
  - **Observational studies**
  - **Intervention studies**
  - **Limited number of participants in any given study**
- **Systems have been developed for the following:**
  - **Selecting appropriate patients based on inclusion/exclusion criteria**
  - **Delivering DMTs (e.g., via infusion)**
  - **Carefully measuring, recording, monitoring and managing side-effects of drugs**
  - **Measuring and recording impact on cognitive, neuropsychiatric, functional status**
  - **Collecting data on impact on AD biomarkers, MRIs**
- **Large cadre of study coordinators and research assistants to ensure patients follow study protocols (e.g., infusions, scheduled study visits, safety surveillance tests (e.g., MRIs, blood work))**
- **Current Dementia Clinical Care Programs**
  - **Do not have the infrastructure or staffing levels found in the Alzheimer Clinical Research Programs**
  - **These systems and infrastructure need to be built within the Clinical Dementia Care Programs**


Clinical Dementia Care Program
(cognitive neurology, geriatric/ neuropsychiatry, neuropsychology, social work, cognitive therapy)
Alzheimer Clinical Research Program
Other Neurological Specialties
(stroke, movement disorders, MS, TBI, infectious diseases, immune disorders)
Primary Care Patients


Delivering DMTs
Anticipated Patient Numbers and Clinical Activity, First 1-2 Years
Patient Assessment and Selection
~400
Mildly impaired patients currently followed at MGB dementia centers

Delivering DMTs
Anticipated Patient Numbers and Clinical Activity, First 1-2 Years



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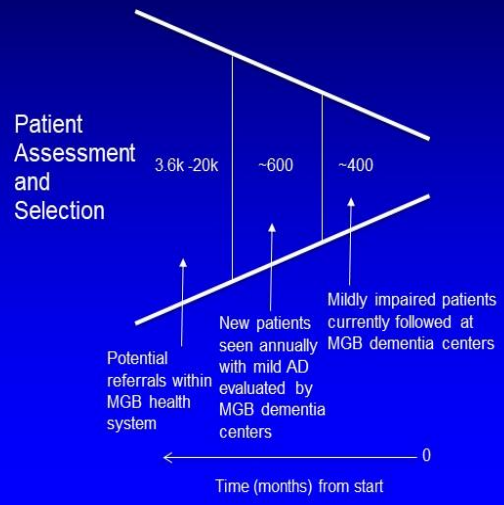

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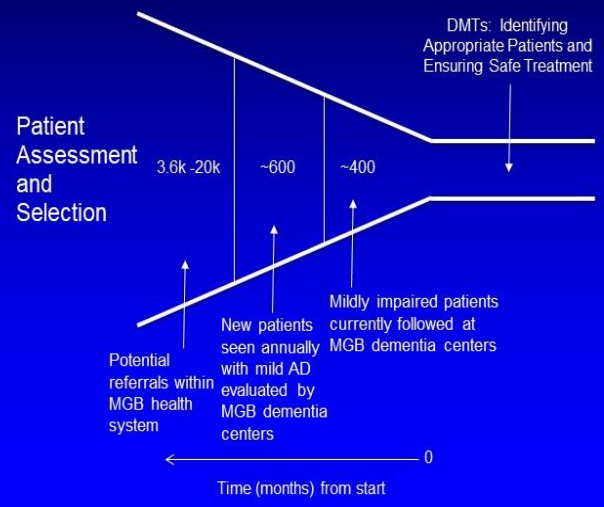

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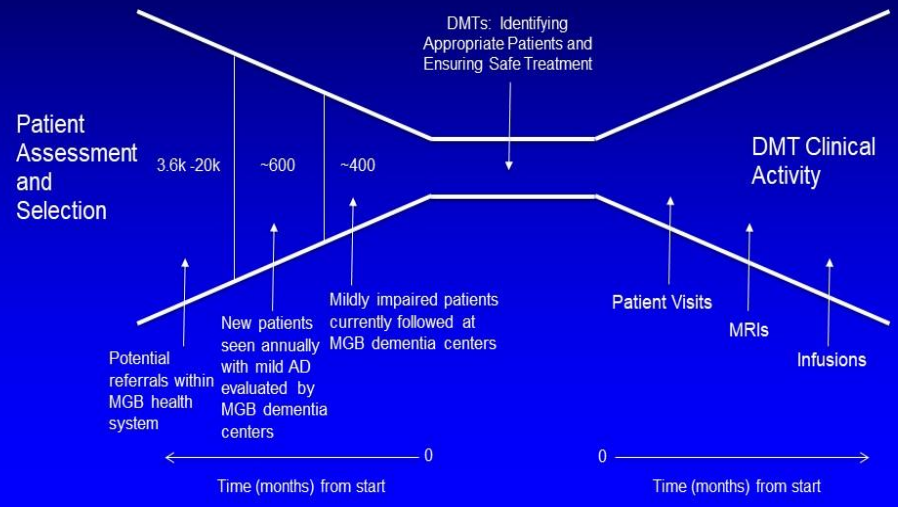
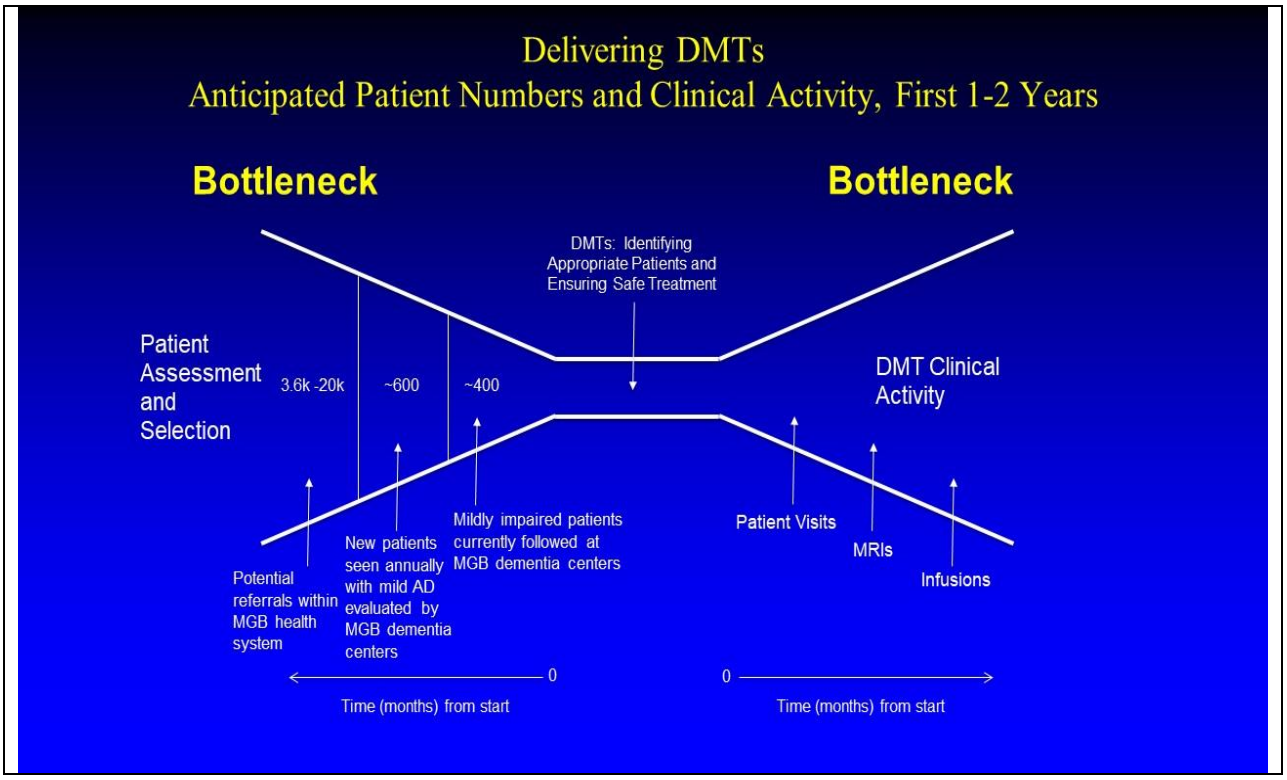
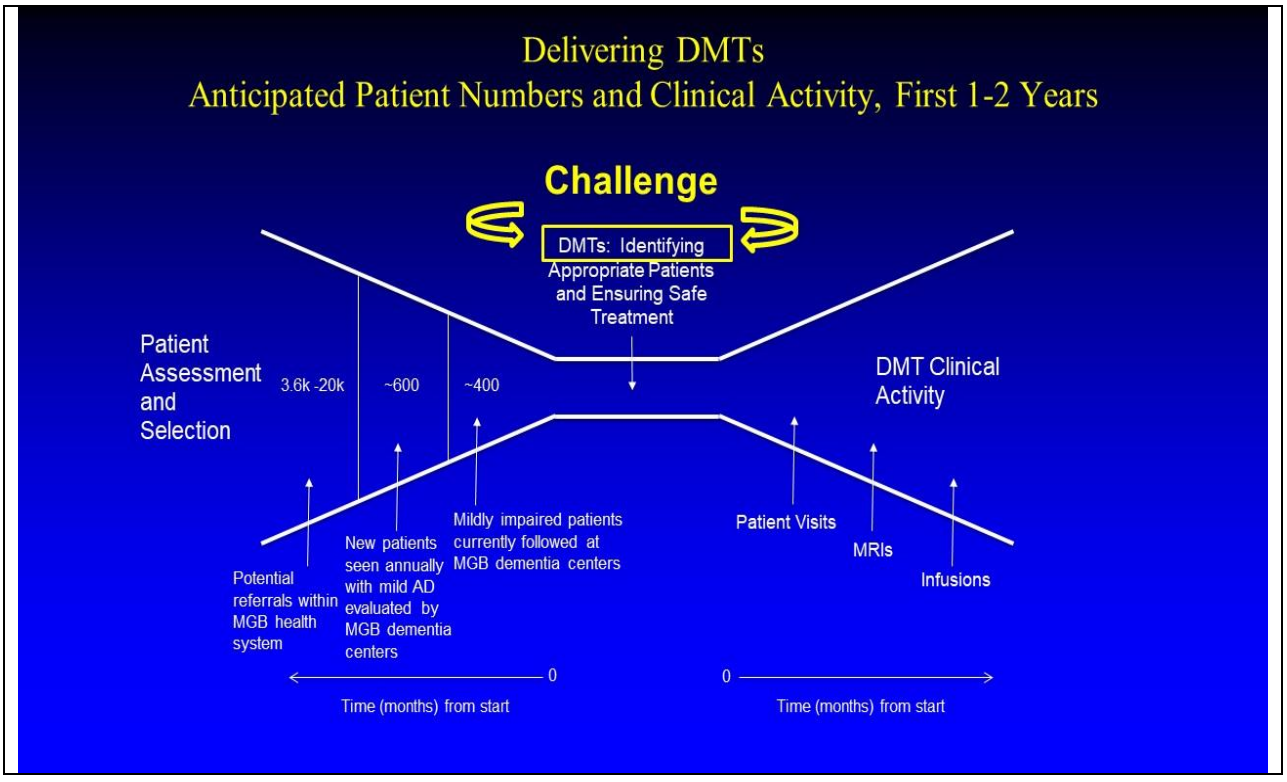



Delivering DMTs
Anticipated Patient Numbers and Clinical Activity, First 1-2 Years
Bottleneck
Bottleneck
DMTs: Identifying Appropriate Patients and Ensuring Safe Treatment
Patient Assessment and Selection
3.6k -20k
~600
~400
DMT Clinical Activity
Potential referrals within MGB health system
New patients seen annually with mild AD evaluated by MGB dementia centers
Mildly impaired patients currently followed at MGB dementia centers
Patient Visits
MRIs
Infusions
0
0
Time (months) from start
Time (months) from start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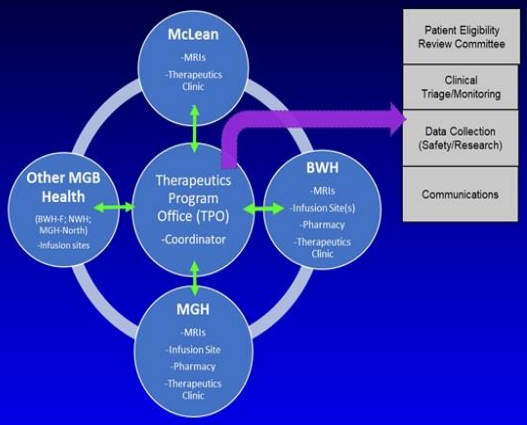
MGB Alzheimer Therapeutics Program (ATP)

Main Goal:
Ensure expedited and safe implementation of novel DMTs for AD patients, leveraging expertise and resources across the MGB system

- A system-wide collaboration led by the Departments of Neurology at MGH and BWH
- Partnerships with Geriatric Psychiatry, Pharmacy, Radiology, Nursing (Infusion), allied clinicians across MGB



Alzheimer Therapeutics Program (ATP)

ATP Clinic Model

- Specialized therapeutic MGB clinic (MGH and BWH will serve as primary locations)
  - Created specifically to identify/evaluate, treat, and monitor patients receiving advanced AD therapeutics
  - Analogous to an "Anticoagulation Management Service" (AMS) and its approach to warfarin therapy
  - Oversight of clinics at BWH and MGH will be managed by ATP providers (dementia experts) on weekly rotations
  - Patient care will be the shared responsibility of the ATP clinic, not individual clinicians
  - Consensus conference for adjudication of therapy for complex cases (similar to a tumor board)
- Providers not affiliated with the MGB specialty clinic (e.g., PCPs) would not Rx meds or monitor
- AD patients would maintain relationships with a specialist (neurologist/geriatric psychiatrist) outside this ATP clinic for ongoing care
- Treatment and monitoring linked to DMTs take place within the clinic (at least until there is broader experience with prescribing and monitoring).
- Participation in ALZ-NET, a multi-site network for collection of real-world data from patients receiving novel FDA-approved AD therapies in the US (Alzheimer Association)
  - Collect baseline and longitudinal patient data (cognition, neuropsychiatric status, function, safety)
  - Collect and archive imaging, genetic data, and fluid biomarkers, track health outcomes.
  - Share de-identified data and samples with the research community

Alzheimer Therapeutics Program (ATP)

Comprehensive Framework for Implementation

- **Development**
  - Evidence-based diagnostic/selection criteria for system-wide use.
  - Evidence-based therapy monitoring protocol.
  - Epic EMR order sets.
- **Logistical Planning**
  - Management of referrals from MGB dementia centers, Department of Neurology, the larger healthcare system.
  - Determination of amyloid status (currently CSF, amyloid PET; future blood biomarkers).
  - Implementation of Infusion center treatments - Distribution of patients across MGB infusion centers, ideally close to patient's home.
- **Communication/Education/Training**
  - Patients and caregivers.
  - Clinicians (especially neurologists, psychiatrists, PCPs, geriatricians, radiologists, infusion center staff, emergency department providers).
- **Start-up and Future Expansion**
  - Program roll-out within a specialized MGB clinic, staffed by dementia experts.
  - Critical need for increasing capacity/access to evaluate and treat appropriate AD patients within the MGB system.

Opportunities:
Build programs for accessible, safe delivery of DMTs

Stakeholder	Near term	Long term
Health systems (academic medical centers)		
Federal Agencies (CMS, FDA)		
Pharmaceutical, biotech/device industry		

Opportunities:
Build programs for accessible, safe delivery of DMTs

Stakeholder	Near term	Long term
Health systems (academic medical centers)	• Develop/implement programs that can deliver DMTs and carefully monitor patient safely • Identify and train APPs and other personnel regarding DMTs (help fill gaps due to limited number of MD dementia experts)	• Develop more efficient, patient-friendly programs • Train a wider range of providers (primary, specialty) on how to deliver high quality, safe care.
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Federal Agencies (CMS, FDA)	• Approve and reimburse for appropriate use of DMTs and for all relevant services (e.g., infusions, MRIs, clinical visits) needed for patient safety • Ensure access not limited to only those who can afford to self-pay	• Support reimbursement for AD evaluation time and DMT safety/monitoring activities (non F2F patient care) • Set guidelines and review medical diagnostics/devices (e.g., digital phenotyping; data mining)
Pharmaceutical, biotech/device industry		

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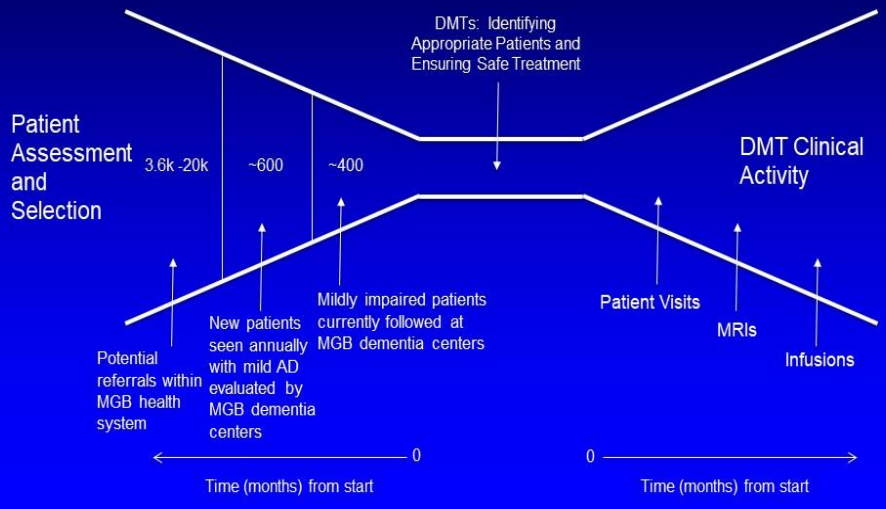
Pharmaceutical, biotech/device industry	• **Help defray cost of training existing, pertinent specialists (dementia, neuroradiology) for specific DMT care**	• **Support educational programs for patients, caregivers, and clinicians;** • **Collaborate with health systems and federal agencies to sponsor "real-world" pragmatic research to study DMT implementation science using EHRs, databases**

Delivering DMTs
Anticipated Patient Numbers and Clinical Activity, First 1-2 Years

Bottleneck



Current Dementia Care – Challenges with Diagnosis

Some studies in the U.S. suggest that up to 80% of patients with dementia are not diagnosed, and perhaps up to ~90-95% with MCI (some of which are *not* due to AD) are not diagnosed

For every 1 patient currently identified as being cognitively impaired/demented, there are likely 5-6 times as many who have not yet been diagnosed

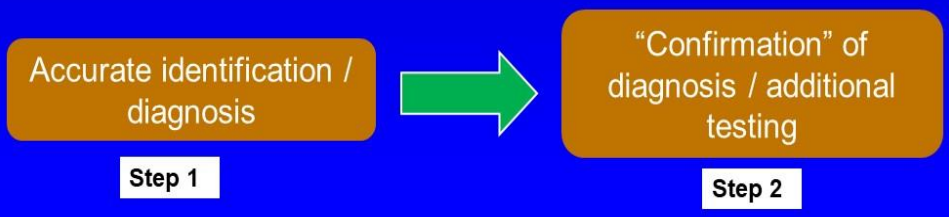
When AD and related dementias *are* diagnosed during "first line'" evaluations (primary care; community health center), patients are often in the mild-to-moderate stage when DMTs are ineffective, *or* their stage or cause of dementia (AD vs. Not AD) is not characterized well enough to determine eligibility

Challenges: Disease Identification/Confirming Diagnoses

Step 1:
Patients *potentially* eligible for DMTs must be first identified by diagnosis / code

-Direct referral by providers of potentially eligible individuals for treatment
-Searching EHRs for relevant diagnostic codes within primary care/specialty clinics (codes are inconsistently used, often without stage);

Step 2:
AD diagnoses and stage must be "confirmed" (biomarker; PET, CSF); genetic status determined (blood test) to fully inform about risks; and additional criteria evaluated (exclusions due to medications, imaging); **all require AD expertise**



Opportunity: Disease Identification/Confirming Diagnoses

Stakeholder	Near term	Long term
Health systems (academic medical centers)		
Federal Agencies (CMS, FDA)		

Opportunity: Disease Identification/Confirming Diagnoses

Stakeholder	Near term	Long term
Health systems (academic medical centers)	• Additional disease training about dementia for primary care/general neurologists (e.g., CME requirement in MA)	• New systems to educate personnel; care algorithms for primary care to manage newly identified patients
Federal Agencies (CMS, FDA)		

Opportunity: Disease Identification/Confirming Diagnoses

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Federal Agencies (CMS, FDA)	• Support cost coverage (CMS) and scientific evaluation (FDA) of tools to confirm early diagnosis and assess DMT risk (APOE; biomarkers; diagnostic screening tools)	• Reimburse dementia experts consulting to PCPs who are evaluating patients • Set guidelines and review diagnostics/devices (e.g., digital phenotype, data mining)

Opportunity: Disease Identification/Confirming Diagnoses

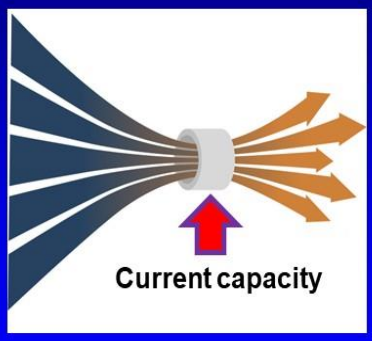
Stakeholder	Near term	Long term
Pharmaceutical, biotech/device industry	• Work directly with health systems on DMT "readiness" by funding current, validated models of AD screening in primary care/community health centers	• Develop digital screening techniques and strategies for efficient, accurate identification/diagnosis (e.g., big data/machine learning for identification of disease; digital diagnostics [e.g., digital Clock Drawing Test; analysis of brief recorded language samples, computerized cognitive screening on smartphones]

Challenge: Care for Newly Identified Patients (Primary Care and Specialties)

Increasing awareness of DMTs and improved disease identification tools/systems → a substantial number of new patients will receive dementia diagnoses (a majority likely *ineligible* for near-term DMTs)

There is a significant capacity limitation of dementia care experts/providers and infrastructure

Newly identified dementia patients



Need for comprehensive, longitudinal care

Notably, given patient numbers, **most dementia care in the U.S. will still need to be carried out in the primary care/community health center setting**, even with capacity/personnel expansion in specialties

Opportunity: Care for Newly Identified Patients (Primary Care and Specialties)

Stakeholder	Near term	Long term
Health systems (academic medical centers)		
Federal Agencies (CMS, FDA)		
Pharmaceutical, biotech/device industry		

Opportunity: Care for Newly Identified Patients (Primary Care and Specialties)

Stakeholder	Near term	Long term
Health systems (academic medical centers)	• Expand capacity by hiring and training new providers (APPs, care navigators) to support patients/families, reduce ER/hospital utilization	• Implement validated systems of longitudinal care, like the Care Ecosystem (UCSF) and Comprehensive Dementia Care Program (UCLA)
Federal Agencies (CMS, FDA)		
Pharmaceutical, biotech/device industry		

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Federal Agencies (CMS, FDA)	• Support reimbursement for direct consult of AD experts by PCP re: dementia care • Expand Medicare/Medicaid coverage of home health services, adult day centers • Work with payers to ensure DMT coverage for early onset AD patients (younger than 65 years old)	• Support the cost of training cognitive neurologists, neuropsychiatrists, AD specialists (CMS does not cover clinical fellowships in cognitive neurology/ neuropsychiatry) • Expand programs of quality, safety, and oversight, like the National Partnership (dementia care in nursing homes)
Pharmaceutical, biotech/device industry		

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Pharmaceutical, biotech/device industry	• **Consider pooling finances to provide transparent, charitable contributions to non-profits/health systems for AD training and care activities**	• **Support educational programs for patients, caregivers, and clinicians** • **Develop digital therapeutics, caregiver coordination IT**

Challenge: Equitable Access to Diagnostic Tools and DMT treatment

Black and Hispanic Americans are 1.5-2 times more likely to suffer from dementia, but are much less likely to be diagnosed and treated (>65% less than white counterparts)

Diagnosis for these populations usually occurs in later stages of disease than white counterparts, reducing potential access to DMTs

Research shows that compared to white counterparts, Black and Hispanic Americans have had lower use of AD medications, poorer treatment adherence, and higher discontinuation of AD medications

Between 85-90% of surveyed Black, Hispanic, Native and Asian Americans say it is important for Alzheimer/dementia providers to understand their racial or ethnic background and experiences, and between 25-40% felt they have not been listened to because of their race/ethnicity.

Opportunity:
Equitable Access to Diagnostic Tools and DMT treatment

Stakeholder	Near term	Long term
Health systems (academic medical centers)		
Federal Agencies (CMS, FDA, CDC)		

Opportunity:
Equitable Access to Diagnostic Tools and DMT treatment

Stakeholder	Near term	Long term
Health systems (academic medical centers)	• Ensure cognitive screening and DMT implementation and infrastructure (e.g., infusion chairs; CSF/lab testing) reaches centers serving racial/ethnic minority populations (clinics; community health centers)	• Expand community outreach, education programs and partnerships with Community Based Organizations and influencers • Adopt culturally competent care models for older adults of all races/ethnicities, like Stanford's Memory Support Program (MSP)
Federal Agencies (CMS, FDA, CDC)		

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Federal Agencies (CMS, FDA, CDC)	• Financially support essential community health workers who liaise with health care systems • Link and update current CDC funding efforts (like BOLD public health programs [Alzheimer's Act] and the Healthy Brain Initiative) to all new DMT initiatives	• Fund research on racial/ethnics differences in service-specific and out-of-pocket expenditures (home health, ER); correlate with access to care

Opportunities: Equitable Access to Diagnostic Tools and DMT treatment

Stakeholder	Near term	Long term
Pharmaceutical, biotech/device industry	• Develop programs for paying for DMTs and diagnostic tools for whom any out-of-pocket expenditures remain cost-prohibitive	• Require sponsored clinical trials for DMTs, devices and digital diagnostics/therapeutics to reflect representative samples of all racial/ethnic subpopulations who may be benefit from product (in line with NIH study trends) • Incorporate social determinants of health in analyses of all research

Conclusions

We have summarized the many challenges/opportunities facing health systems that try to integrate wide-scale, accurate disease identification and diagnostic testing with the safe and effective delivery of DMTs

The challenge of limited expertise in identification/staging of AD *and* inexperience with DMTs in clinical settings may be reduced with targeted public and private funding for the training of primary care and specialty providers

It is imperative to study DMT-delivery programs, like the ATP at Mass General Brigham, with a focus on implementation/health services delivery to ensure equitable and safe access for all

Both *near* and *long-term* solutions to the challenges and bottlenecks of DMT care will require close collaboration across all public and private stakeholders