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Authors

Dublin, Sascha
Greenwood-Hickman, Mikael
Karliner, Leah
et al.

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The electronic health record Risk of Alzheimer's and Dementia Assessment Rule (eRADAR) Brain Health Trial: Protocol for an embedded, pragmatic clinical trial of a low-cost dementia detection algorithm

Sascha Dublin, MD, PhD[a,b,c], **Mikael Anne Greenwood-Hickman, MPH**[a], **Leah Karliner, MD, MAS**[d], **Clarissa Hsu, PhD**[a], **R. Yates Coley, PhD**[a,e], **Leonardo Colemon, MA**[a], **Anna Carrasco, MPH**[d,*], **Deborah King, MSW**[a], **Andrea Grace, MD**[f], **Sei J. Lee, MD, MAS**[d], **Judith M.E. Walsh, MD, MPH**[d], **Tyler Barrett, MA, MPS**[a], **Jia Broussard, MSW**[d], **Umesh Singh, MPH, MSIS, PhD**[a], **Abisola Idu, MPH, MS**[a], **Kristine Yaffe, MD**[d], **Malaz Boustani, MD, MPH**[g], **Deborah E. Barnes, PhD, MPH**[d]

[a.]Kaiser Permanente Washington Health Research Institute, Seattle, Washington

[b.]Department of Epidemiology, University of Washington, Seattle, Washington

[c.]Kaiser Permanente Bernard Tyson School of Medicine, Pasadena, California

[d.]University of California, San Francisco, San Francisco, California

[e.]Department of Biostatistics, University of Washington, Seattle, Washington

[f.]Kaiser Permanente Washington, Seattle, Washington

[g.]Indiana University School of Medicine, Indianapolis, Indiana

Abstract

Background: About half of people living with dementia have not received a diagnosis, delaying access to treatment, education, and support. We previously developed a tool, eRADAR, which uses information in the electronic health record (EHR) to identify patients who may have undiagnosed

Corresponding author: Dr. Sascha Dublin, Sascha.Dublin@kp.org. Mailing address: 1730 Minor Avenue, Suite 1600, Seattle, WA 98101.

*Present address for Ms. Carrasco: New York University Langone Health, New York, New York

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Declaration of interests

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dementia. This paper provides the protocol for an embedded, pragmatic clinical trial (ePCT) implementing eRADAR in two healthcare systems to determine whether an intervention using eRADAR increases dementia diagnosis rates and to examine the benefits and harms experienced by patients and other stakeholders.

Methods: We will conduct an ePCT within an integrated healthcare system and replicate it in an urban academic medical center. At primary care clinics serving about 27,000 patients age 65 and above, we will randomize primary care providers (PCPs) to have their patients with high eRADAR scores receive targeted outreach (intervention) or usual care. Intervention patients will be offered a "brain health" assessment visit with a clinical research interventionist mirroring existing roles within the healthcare systems. The interventionist will make follow-up recommendations to PCPs and offer support to newly-diagnosed patients. Patients with high eRADAR scores in both study arms will be followed to identify new diagnoses of dementia in the EHR (primary outcome). Secondary outcomes include healthcare utilization from the EHR and patient, family member and clinician satisfaction assessed through surveys and interviews.

Conclusion: If this pragmatic trial is successful, the eRADAR tool and intervention could be adopted by other healthcare systems, potentially improving dementia detection, patient care and quality of life.

Keywords

dementia; Alzheimer's disease; screening; early detection; pragmatic trial; electronic health records

Background

More than 6 million people in the US are living with Alzheimer's disease and related dementias (ADRD).[1, 2] Studies estimate that only about half have received a formal diagnosis. [1, 3-10] Currently, the US Preventive Services Task Force (USPSTF) does not recommend for or against routine dementia screening in primary care because of insufficient evidence about the benefits and risks.[11] However, other organizations advocate for early detection so that patients and families can receive support and education.[12, 13] Furthermore, the US government requires "detection of cognitive impairment" as part of the Medicare Annual Wellness Visit.[14] It also provides higher reimbursement to Medicare Advantage insurance plans for patients with diagnosed dementia, providing a financial incentive to increase detection.

Earlier recognition of dementia has many potential benefits.[13, 15-18] Clinicians can treat potentially reversible causes and optimize care plans. Patients and families can plan for the future. On the other hand, patients may experience anxiety or depression, stigma, and loss of independence.[15, 16, 18] The diagnostic process may generate additional work for clinicians at a time when the primary care system is under strain.

Our team previously developed and validated the Electronic Health Records (EHR) Risk of Alzheimer's and Dementia Assessment Rule (eRADAR), a risk prediction tool using easily accessible data from the EHR (e.g., age, sex, chronic conditions, and healthcare utilization) to identify people with an elevated risk of undiagnosed dementia.[19, 20] We

also sought input from patients and caregivers,[18] clinicians, and healthcare system leaders about how to best implement eRADAR. Their input guided development of this protocol for a multisite embedded, pragmatic clinical trial (ePCT) to test whether using eRADAR to identify high-risk patients for targeted assessment increases dementia diagnosis rates and to examine the benefits and harms experienced by patients, families and clinicians. In this paper we also discuss challenges encountered during the design process and how they were addressed.

Methods

Study Aims

This ePCT seeks to assess the impact of implementing eRADAR [19] as part of a targeted screening and assessment process (referred to as the "eRADAR intervention") in primary care. The primary aim is to determine the impact of the intervention on dementia detection. We hypothesize that the eRADAR intervention will increase rates of dementia diagnosis compared to usual care. The secondary aim is to explore the impact on healthcare utilization and patient, family, and clinician experience, including potential adverse outcomes. We hypothesize that utilization of procedures that are often part of dementia evaluation (e.g., brain imaging, certain laboratory tests, neuropsychological testing) will be higher with the intervention than usual care, while healthcare utilization potentially affected by improved family support (e.g., Emergency Department visits) will be lower.

Study Design

This ePCT is set within primary care clinics at Kaiser Permanente Washington (KPWA) and the University of California, San Francisco (UCSF). The two healthcare systems serve as separate study sites to provide independent replication and represent different clinical settings with diverse patient populations. Figure 1 illustrates the study design. Within each clinic, primary care providers (PCPs) will be randomly assigned to have their patients with high eRADAR scores receive outreach and assessment or to usual care. The eRADAR algorithm has been previously described.[19] It is derived from a logistic regression model including 31 EHR-based predictors from five domains (demographic characteristics, diagnoses, vital signs, medications, and healthcare utilization) and generates a score estimating the risk of undiagnosed dementia.[19] eRADAR scores will be calculated for all eligible patients in both arms.

Settings

KPWA is an integrated healthcare delivery system serving patients in Washington State and Idaho. We aim to implement the trial in three primary care clinics in or near Seattle, Washington, that together have about 75 PCPs and serve about 18,000 people aged 65 or older. The first group of KPWA PCPs were randomized in May 2022. KPWA does not conduct routine screening for dementia, in line with current USPSTF guidelines.[21] Patients with cognitive concerns may be evaluated in primary care or referred to Neurology, Speech, Language and Learning, or Neuropsychology. Within the KPWA EHR, Epic, a SmartSet provides decision support to PCPs for evaluation of cognitive concerns.

UCSF is an urban academic health system serving patients in San Francisco, California and the surrounding Bay Area. At UCSF we plan to implement the trial at 5 primary care clinics that together have about 175 PCPs and serve about 9,000 patients aged 65 or older. The first group of UCSF PCPs were randomized in October 2022. UCSF does not conduct routine screening for dementia. Patients presenting with cognitive concerns are evaluated in primary care or can be referred to dementia specialists in the Neurology Department's Memory and Aging Center. PCPs can also utilize an electronic consult to get quick answers from dementia specialists about individual patients. Similar to KPWA, a SmartSet is available within the EHR providing decision support. UCSF also has a clinical note template available to support appropriate work-up and billing for a dementia evaluation visit.

Stakeholder Engagement

To ensure that study processes are patient-centered and address potential harms and stigma, the research team recruited patient advisors at each healthcare system who are paid for their time. We also identified clinician stakeholders from participating clinics and regularly seek input from clinic directors. Patient advisors reviewed study materials and processes and provided feedback. They shaped patient-facing materials, for instance recommending that outreach materials use positive language such as "brain health" rather than dementia. They participated in extensive piloting of the assessment visit as part of the research interventionists' training. Patient and clinician advisors provided input about the choice of a cut-off for the eRADAR score. Patient advisors recommended choosing a cut-off that would result in a larger number of patients being referred for a study visit, because they placed a high value on earlier detection.

Regulatory Review

Study procedures were approved by Advarra, our single Institutional Review Board (sIRB). The study is registered on ClinicalTrials.gov (NCT05356702 and NCT05905796).

Inclusion and Exclusion Criteria

Primary Care Providers (PCPs)—PCPs will be eligible if they provide care at a participating clinic, have a panel that includes older adults, are not working in the clinic on a temporary basis, and are not a medical resident. Clinic directors will have discretion to exclude other providers based on specific circumstances, such as a planned sabbatical. PCPs will be given the opportunity to opt out before randomization.

Patient Participants—Patients will be eligible if they are age 65 or older, have no prior diagnosis of dementia or use of dementia medications in the past 2 years, are paneled to a participating PCP, have adequate engagement with the healthcare system to ensure sufficient data to calculate the eRADAR score, and are not receiving hospice care. At KPWA, adequate engagement will be defined as ≥12 months of prior enrollment in the health plan. At UCSF, adequate engagement will be defined as being active in the practice (i.e., had ≥1 clinic visit or initiated a patient portal message to the practice in the past 24 months) and having had two or more visits in the past 36 months.

Care Partners—Patient participants will be encouraged (but not required) to bring a care partner (family member or trusted friend) to their brain health assessment visit to improve the accuracy of the information obtained about symptoms and functioning. Care partners must be at least 18 years old.

Randomization and Blinding

The KPWA biostatistician will create a computer-generated sequence to randomize eligible PCPs to the intervention vs. usual care groups. A detailed description is provided in the Appendix. In brief, we will stratify randomization by clinic and block by the number of eligible patients on each PCP's panel (broadly grouped). We block by number of patients to balance the number of patients in each arm and because panel size may correlate with physicians' engagement with and learning from the intervention. We will not be able to blind PCPs or patients to their treatment assignment, nor will research interventionists be blinded. Study outcomes derived from EHR data will be extracted in a blinded manner.

Participant Recruitment and Enrollment

Participant Identification and Outreach—Within each healthcare system, a programmer will extract EHR data to identify the eligible patient sample, calculate eRADAR scores, and identify people whose scores are above the chosen threshold. Based on stakeholder input and preliminary data demonstrating similar performance across most patient subgroups,[20] we selected a cutoff of 15% (that is, scores in the top 15% are considered high risk) for KPWA patients and most patient subgroups at UCSF. At UCSF, our analyses found that eRADAR's sensitivity was lower in Black patients (32%) than other groups (non-Hispanic white: 51%, Asian: 59%, Hispanic/Latino: 72%).[20] This difference was seen only at UCSF and not KPWA. Thus, for Black patients at UCSF we chose a different cutoff, 20%, to maintain equitable capture of true dementia cases across all groups.

Because it will not be possible to reach out to all high-risk patients in a clinic simultaneously, we will identify eligible participants in blocks; the size of the blocks will vary over time depending on the study's capacity for conducting outreach and study visits. All high-risk patients will be assigned an "index date" for follow-up purposes, defined as the date on which eligibility criteria were applied and eRADAR scores calculated for their PCP's panel. Specific eRADAR scores will not be shared with PCPs in either group. At UCSF, intervention PCPs will be given their list of high-risk patients and asked to identify anyone who should not be contacted (e.g., due to serious physical or mental illness). At KPWA, intervention PCPs will be offered the option of reviewing their lists. PCPs in the usual care group will not receive any information about their patients' eRADAR scores or high-risk status. All high-risk patients will be included in intention-to-treat analyses, since PCPs in the usual care group will not have the opportunity to exclude individuals.

Prior to trial initiation at a clinic, short educational sessions will be offered to all PCPs regardless of randomization assignment. The goal is to introduce the study and review basic principles of evaluation and diagnosis of dementia to ensure all providers have a similar understanding of best practices and available tools.

Study staff will mail materials to intervention patients inviting them for a brain health assessment visit. Patients will have the option to opt out of further contact or express interest by phone or secure online portal. If no response is received after one week, study staff will follow up via phone.

Consent—Verbal consent will be obtained during the initial recruitment call. In addition, we received waivers of consent and HIPAA authorization for identification of potential participants from EHR data and safety monitoring and outcome ascertainment for all patients in both arms.

Capacity assessment and role of the legally authorized representative (LAR).: Because some potential participants might have severe cognitive impairment, the consent process includes assessing patient capacity to give consent following procedures we have previously described.[22] During the recruitment call, study staff will ask questions to gauge the person's understanding of key elements including 1) that this is a research study; 2) that they can choose whether to participate; 3) what the study involves; and 4) that they can stop participating at any time. If someone answers incorrectly, they will be provided with the correct information and given another chance. After 3 unsuccessful attempts, we will seek to identify a LAR who can consent on their behalf. Participants who lack capacity will still be asked for assent.

Intervention Design

Figure 2 depicts the flow of the intervention. Briefly, people with high-risk eRADAR scores will be invited to meet with a clinical research interventionist for a brain health assessment visit. The interventionist role was designed to reflect current healthcare system roles (e.g., nurses or clinical social workers); these study staff will be embedded in the clinics and will communicate with the intervention PCPs. The 30-to-60-minute visit will include asking about relevant symptoms and selected instrumental activities of daily living (IADLs) and screening for depression and cognitive impairment using validated instruments (Table 1). At the end of the visit, the interventionist will inform the participant of their results and recommend next steps. They will give each participant a handout on maintaining brain health adapted from the Alzheimer's Association website.[23] The research interventionist will use an EHR note template developed for the study to summarize the visit. For participants with normal results, the note will simply be sent to the PCP. For results suggesting mild cognitive impairment (MCI), the interventionist will inform the PCP via a routing comment attached to the note (UCSF) or a separate staff message (KPWA) recommending future follow-up. For results suggesting dementia, interventionists will contact the PCP via similar channels highlighting results and recommending rapid in-person follow-up. These approaches were tailored for each site based on input from clinician leaders. PCPs will be responsible for ordering follow-up tests and making final diagnoses. Both KPWA and UCSF provide support for PCPs via site-specific EHR tools (SmartSets with decision support, including a note template, recommended orders, and patient-facing content for the after-visit summary). If a participant is subsequently diagnosed with dementia, the interventionist will offer a follow-up phone visit to provide support and

connect them with resources such the Alzheimer's Association, relevant books or websites, or home care agencies.

Electronic Health Record Outcomes (Table 2)

All eligible patients with a high-risk eRADAR score, regardless of treatment assignment or participation in the brain health visit, will be followed for study outcomes. The primary outcome will be the rate of new dementia diagnosis over 12 months, assessed from the EHR at each study site based on standard ICD-10 codes (Appendix Table 1a) [35]. Secondary analyses will examine dementia and MCI diagnoses (Appendix Table 1b), and sensitivity analyses will examine outcomes at 6 and 18 months.

Secondarily, we will explore the intervention's impact on healthcare utilization (Table 2), including utilization likely to increase as a direct result of the intervention (e.g., laboratory test orders and neuroimaging) and utilization that could decline if people with dementia were to receive better support (e.g., Emergency Department visits and appointment no-shows).

Formative & Summative Evaluations

We will perform a formative evaluation early in the study, using feedback from patients and care partners to refine and improve intervention implementation, as is allowable in a pragmatic framework.[38] In addition, we will perform a summative evaluation at the end of the study to understand the intervention's impact on patient, care partner and clinician experience and satisfaction. Modes of data collection include 1) a post-visit survey sent to all participants who attend a brain health assessment visit; 2) direct observation of a subset of brain health assessment visits by trained study staff; and 3) semi-structured interviews with a subset of participants, care partners, and PCPs. See Table 3 for more information.

Post-Visit Survey—Within one week after the brain health assessment visit, each patient participant will receive a brief survey that can be completed by mail or online (Appendix 2). The survey will ask about their perceptions of and satisfaction with the outreach and assessment process. Surveys from the first approximately 40 patients at each site will be used for the formative evaluation. Participants who complete the survey will receive a $5 incentive.

Brain Health Assessment Visit Observation—After the study has been underway in a clinic for about 2 months, study staff will observe a subgroup of visits, either in person or via a recording. The goals are to 1) identify any patient distress, so we can improve study processes; and 2) monitor fidelity to study procedures. In each healthcare system, trained qualitative team members will conduct about 30 observations. They will fill out a brief structured notes template focused on the outcomes of the visit, key questions raised, signs of emotional distress, and feedback from patients and care partners.

Semi-Structured Patient and Care Partner Interviews—From among those whose visit was observed, we will recruit approximately 24 patients and 24 care partners (~12 from each healthcare system) for in-depth telephone interviews at 1 and 4 months after their brain

health visit. People whose results suggest dementia will be oversampled. We will aim for a sample with racial and ethnic diversity. The interviews will ask about experiences with the intervention including the initial outreach, the assessment visit, the process of clinical evaluation leading to a final diagnosis (if relevant), and any emotional and/or practical impacts of the intervention. The 4-month follow-up interview will explore longer-term impacts including on planning and decision making. Participants and care partners will be paid $50 for each interview. Interviews will be performed by trained qualitative team members and will be audio-recorded and transcribed.

Semi-Structured PCP Interviews—We will interview 10 PCPs at each healthcare system whose patients have received the intervention. PCPs will be invited for interview after all their patients have completed the intervention process. These 30-minute interviews will explore their awareness of the eRADAR process, impact on their workflow, communication between the eRADAR team and primary care team, and interactions with patients about the intervention. PCPs will be offered $75 for their time.

Analysis

Analyses will include all individuals with a high-risk eRADAR score in either the intervention or usual care arm. For our primary aim, we will compare the rate of new dementia diagnosis by treatment arm. We will conduct an intention-to-treat analysis fitting a modified Poisson regression model[39] via generalized estimating equations (GEE) regression with log link to estimate the relative rate of dementia diagnosis following study initiation (the “index date” described above) comparing high-risk patients of PCPs randomized to the intervention versus usual care. We will use robust variance estimates (also known as empirical sandwich variance estimates) to account for clustering of patients on the provider level.[40, 41] Sensitivity analyses will explore the impact of different specifications of the outcome (described above). We will also explore whether the effects of the intervention differ across subgroups by age, gender, race, or ethnicity by performing stratified analyses and formally testing for interaction between treatment effect and each grouping variable. The goal of these analyses is to assess whether the eRADAR intervention might be more or less beneficial or causing unintended harms for certain subgroups, particularly marginalized groups.

To test secondary hypotheses related to utilization, we will compare rates of healthcare utilization and diagnoses of other conditions that could be identified by the intervention visit (e.g., depression) between the intervention and usual care arms. We will use GEE regression with the appropriate distribution and link function (e.g., log link for binary and count outcomes, identity link for continuous outcomes) and robust sandwich variance estimates.[40, 41] Again, we will perform subgroup analyses by stratifying and testing for interactions.

Secondary outcomes related to patient, care partner and provider experience and satisfaction will be analyzed both quantitatively and qualitatively. Quantitative data (e.g., satisfaction ratings from surveys) will be analyzed using means, standard deviations, and proportions. For formative purposes, study team members will debrief after completed observations

and interviews and provide feedback to study leadership when emerging themes require possible study modification. For summative purposes, qualitative data from interviews (e.g., perceptions and impact of process) will be analyzed using a template analysis approach, a common thematic analysis method.[42, 43] A code list with detailed definitions will be developed to identify key themes in the data both a priori and inductively through data review. The code list will be used to conduct detailed coding of transcripts. Once coded, data will be extracted by code and further reviewed. This process identifies key insights and relationships between themes.[44, 45] Atlas.ti will be used to manage the coded data.

Power and Sample Size

We will conduct analyses separately for the two healthcare systems. We calculated power to detect an increase in the rate of new diagnoses of dementia, assuming a baseline rate of 3% per year. Based on our prior work, we estimate that the positive predictive value (PPV) of having an eRADAR risk score above the 85th percentile of the risk score distribution will be 0.10 [19]. At KPWA we assume a sample size of 18,000 patients (2,700 high-risk) and 75 PCPs, while at UCSF we assume a sample size of 9,000 patients (1,350 high-risk) and 175 PCPs. We varied the assumptions about the proportion of intervention patients accepting the assessment visit (50 or 75%), and the intraclass correlation coefficient (0.01 or 0.05). We used the R package “clusterPower” to account for clustering.[46, 47] We will have power ≥ 90% at both KPWA and UCSF under scenarios with a range of assumptions, including the most pessimistic scenario (50% participation, ICC 0.05).

Safety Monitoring

The National Institute on Aging has convened an external Data and Safety Monitoring Board (DSMB) for this study. Because the intervention involves very few contacts with participants, we have limited ability to conduct individual-level safety monitoring. At brain health assessment visits, we will assess for depression and suicidal ideation. Detailed protocols have been developed to address concerns about self-harm or potential elder abuse that surface during the study. If we become aware of deaths in the intervention group, we will review and report these outcomes. The primary approach to safety monitoring will be extraction of group-level data from the EHR for each treatment arm for the following outcomes: new diagnoses of depression, suicide attempts or self-harm, hospitalizations, and deaths. DSMB reports will include rates of these events by study arm and compare events for people in the intervention group who underwent a brain health visit vs. those who declined, accounting for baseline characteristics.

Design Challenges

In designing this study, one major challenge was determining whether and how to obtain consent from participants. Pragmatic trials often seek a waiver of consent for study activities, which can reduce barriers to participation. Although we are using an sIRB, one local IRB required that we obtain individual consent because the brain health assessment is part of research and results will be entered in the medical record. Therefore, we developed a process for obtaining verbal consent, which includes assessing capacity to consent. Individuals who lack capacity (e.g., due to possible dementia) can participate only if they have a LAR consent on their behalf. This requirement could exclude people with

cognitive impairment who lack close family members or friends. To address this gap, we will communicate with the individual's PCP about their lack of capacity and encourage the PCP to follow up.

The COVID-19 pandemic impacted our study design. During the pandemic, both healthcare systems shifted a large proportion of visits to the remote setting, and for a period of time, KPWA did not allow in-person research visits other than for vaccine clinical trials. Thus we developed an option for remote brain health visits (by phone or video). We have also worked closely with clinical leaders to ensure study protocols follow current healthcare system "best practices" for reducing the risk of COVID-19 transmission.

Finally, there is potential for low participation in the brain health visit. In some prior RCTs, a low proportion of participants agreed to cognitive evaluation; for instance, in the CHOICE trial, only about 1/3 of patients screening positive for possible dementia accepted follow-up testing.[48] Several aspects of our protocol were designed to reduce stigma and improve acceptability. We offer the option of remote study visits, which helps overcome barriers such as impaired mobility or difficulty with transportation. In-person visits take place within the participant's primary care clinic. Outreach materials were co-designed with patient advisors and emphasize "brain health" rather than pathology.

Discussion

This paper provides the protocol for an ePCT of a novel approach to improving dementia detection in primary care. This study is innovative because it will test a validated, EHR-based algorithm developed using machine learning that has been assessed for potential impact on health equity.[20] The intervention design was shaped by input from patients, family members, clinicians, and delivery system leaders, aiming to make it patient-centered, feasible and scalable. The study is set within 8 clinics at 2 healthcare systems and will draw on a large population, about 27,000 individuals, with diverse racial and ethnic backgrounds. While we will assess most outcomes pragmatically using longitudinal EHR data, we will also collect qualitative data to gain richer insight about the intervention's benefits and harms.

Given that about half of people living with dementia have not received a diagnosis [1, 3-10], this trial addresses a timely and important gap in care. Results will provide valuable information about many aspects of dementia detection, including 1) the accuracy of this EHR-based algorithm in two real-world settings; 2) people's willingness to undergo a brain health assessment as part of a research study embedded in their primary care clinic; 3) the potential impact and burden on the healthcare system of implementing such a program; and 4) the net balance of benefits and harms experienced by patients, families, and other stakeholders. If successful, the eRADAR intervention has potential to improve care, support, and quality of life for the millions of older adults currently living with undiagnosed dementia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Bradford A, et al., Missed and delayed diagnosis of dementia in primary care: prevalence and contributing factors. Alzheimer Dis Assoc Disord, 2009. 23(4): p. 306–14.
2. Alzheimer's Association. 2022 Alzheimer's Disease Facts and Figures. 2022 [cited 2023 02/25/2023]; Available from: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf.
3. Lang L, et al. , Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. BMJ Open, 2017. 7(2): p. e011146.
4. Boise L, Neal MB, and Kaye J, Dementia assessment in primary care: results from a study in three managed care systems. J Gerontol A Biol Sci Med Sci, 2004. 59(6): p. M621–6. [PubMed: 15215282]
5. Boustani M, et al. , Implementing a screening and diagnosis program for dementia in primary care. J Gen Intern Med, 2005. 20(7): p. 572–7. [PubMed: 16050849]
6. Chodosh J, et al. , Physician recognition of cognitive impairment: evaluating the need for improvement. J Am Geriatr Soc, 2004. 52(7): p. 1051–9. [PubMed: 15209641]
7. Connolly A, et al. , Underdiagnosis of dementia in primary care: variations in the observed prevalence and comparisons to the expected prevalence. Aging Ment Health, 2011. 15(8): p. 978–84. [PubMed: 21777080]
8. Ganguli M, et al. , Detection and management of cognitive impairment in primary care: The Steel Valley Seniors Survey. J Am Geriatr Soc, 2004. 52(10): p. 1668–75. [PubMed: 15450043]
9. McCarten JR, et al. , Finding dementia in primary care: the results of a clinical demonstration project. J Am Geriatr Soc, 2012. 60(2): p. 210–7. [PubMed: 22332672]
10. Wilkins CH, et al. , Dementia undiagnosed in poor older adults with functional impairment. J Am Geriatr Soc, 2007. 55(11): p. 1771–6. [PubMed: 17916120]
11. Lin JS, et al., U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews, in Screening for Cognitive Impairment in Older Adults: An Evidence Update for the U.S. Preventive Services Task Force. 2013, Agency for Healthcare Research and Quality (US): Rockville (MD).
12. Cordell CB, et al. , Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. Alzheimers Dement, 2013. 9(2): p. 141–50. [PubMed: 23265826]
13. Gerontological Society of America, The Gerontological Society of America Workgroup on Cognitive Impaitment Detection and Earlier Diagnosis: Report and Recommendations, G.S.o. America, Editor. 2015.
14. Network ML Medicare Wellness Visits. 2022 [cited 2022 July 11]; Available from: https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/preventive-services/medicare-wellness-visits.html.
15. Borson S, et al. , Improving dementia care: the role of screening and detection of cognitive impairment. Alzheimers Dement, 2013. 9(2): p. 151–9. [PubMed: 23375564]
16. Dubois B, et al. , Timely Diagnosis for Alzheimer's Disease: A Literature Review on Benefits and Challenges. J Alzheimers Dis, 2016. 49(3): p. 617–31. [PubMed: 26484931]
17. Dreier-Wolfgramm A, et al. , Dementia care management in primary care : Current collaborative care models and the case for interprofessional education. Z Gerontol Geriatr, 2017. 50(Suppl 2): p. 68–77. [PubMed: 28364258]
18. Palazzo L, et al. , Patient and caregiver perspectives on a tool to increase recognition of undiagnosed dementia: a qualitative study. BMC Geriatr, 2021. 21(1): p. 604. [PubMed: 34702167]

19. Barnes DE, et al. , Development and Validation of eRADAR: A Tool Using EHR Data to Detect Unrecognized Dementia. J Am Geriatr Soc, 2020. 68(1): p. 103–111. [PubMed: 31612463]
20. Coley RY, et al. , External Validation of the eRADAR Risk Score for Detecting Undiagnosed Dementia in Two Real-World Healthcare Systems. J Gen Intern Med, 2022.
21. Force USPST, et al. , Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force Recommendation Statement. JAMA, 2020. 323(8): p. 757–763. [PubMed: 32096858]
22. Bames DE, et al. , Preventing loss of independence through exercise (PLIÉ): a pilot clinical trial in older adults with dementia. PLoS One, 2015. 10(2): p. e0113367. [PubMed: 25671576]
23. Association, A.s. 10 Ways to Love Your Brain. [cited 2022 July 14]; Available from: https://www.alz.org/help-support/brain_health/10_ways_to_love_your_brain.
24. Nasreddine ZS, et al. , The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc, 2005. 53(4): p. 695–9. [PubMed: 15817019]
25. Smith T, Gildeh N, and Holmes C, The Montreal Cognitive Assessment: validity and utility in a memory clinic setting. Can J Psychiatry, 2007. 52(5): p. 329–32. [PubMed: 17542384]
26. Lawton MP and Brody EM, Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist, 1969. 9(3): p. 179–86. [PubMed: 5349366]
27. Mao HF, et al. , Diagnostic accuracy of Instrumental Activities of Daily Living for dementia in community-dwelling older adults. Age Ageing, 2018. 47(4): p. 551–557. [PubMed: 29528375]
28. Koskas P, et al. , The Lawton Instrumental Activities Daily Living/Activities Daily Living Scales: A Sensitive Test to Alzheimer Disease in Community-Dwelling Elderly People? J Geriatr Psychiatry Neurol, 2014. 27(2): p. 85–93. [PubMed: 24578460]
29. Kroenke K, Spitzer RL, and Williams JB, The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med, 2001. 16(9): p. 606–13. [PubMed: 11556941]
30. Na PJ, et al. , The PHQ-9 Item 9 based screening for suicide risk: a validation study of the Patient Health Questionnaire (PHQ)-9 Item 9 with the Columbia Suicide Severity Rating Scale (C-SSRS). J Affect Disord, 2018. 232: p. 34–40. [PubMed: 29477096]
31. Posner K, et al. , The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry, 2011. 168(12): p. 1266–77. [PubMed: 22193671]
32. Galvin JE, et al. , The AD8: a brief informant interview to detect dementia. Neurology, 2005. 65(4): p. 559–64. [PubMed: 16116116]
33. Chen HH, et al. , The diagnostic accuracy of the Ascertain Dementia 8 questionnaire for detecting cognitive impairment in primary care in the community, clinics and hospitals: a systematic review and meta-analysis. Fam Pract, 2018. 35(3): p. 239–246. [PubMed: 29045636]
34. Galvin JE, et al. , Patient's rating of cognitive ability: using the AD8, a brief informant interview, as a self-rating tool to detect dementia. Arch Neurol, 2007. 64(5): p. 725–30. [PubMed: 17502472]
35. Veterans Health Administration Geriatrics and Extended Care Dementia Initiative, FY19 VHA Dementia ICD Code List.
36. Centers for Medicare and Medicaid Services. Medicare 2018 Part C & D Star Ratings Technical Notes. 2017 09/06/2017 [cited 2019 June 25]; Available from: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDragCovGenIn/Downloads/2018-Star-Ratings-Technical-Notes-2017_09_06.pdf.
37. Zullig LL, Mendys P, and Bosworth HB, Medication adherence: A practical measurement selection guide using case studies. Patient Educ Couns, 2017. 100(7): p. 1410–1414. [PubMed: 28214168]
38. Glasgow RE, What does it mean to be pragmatic? Pragmatic methods, measures, and models to facilitate research translation. Health Educ Behav, 2013. 40(3): p. 257–65. [PubMed: 23709579]
39. Yelland LN, Salter AB, and Ryan P, Performance of the modified Poisson regression approach for estimating relative risks from clustered prospective data. Am J Epidemiol, 2011. 174(8): p. 984–92. [PubMed: 21841157]
40. Liang KY and Zeger SL, Longitudinal data analysis using generalized linear models. Biometrika, 1986. 73(1): p. 13–22.
41. Zeger SL, Liang KY, and Albert PS, Models for longitudinal data: a generalized estimating equation approach. Biometrics, 1988. 44(4): p. 1049–60. [PubMed: 3233245]

42. King N, Qualitative Organizational Research, in Doing Template Analysis, Symon CGC, Editor. 2012, Sage. p. 426–450.

43. Brooks J, et al. , The Utility of Template Analysis in Qualitative Psychology Research. Qual Res Psychol, 2015. 12(2): p. 202–222. [PubMed: 27499705]

44. King N, Doing Template Analysis, in Qualitative Organizational Research: Core methods and current challenges. 2012, Sage Publications: London.

45. Crabtree BF and Miller WL, Using codes and code manuals: a template organizing style of interpretation, in Doing Qualitative Research: 2nd Edition. 1999, Sage Publications: Thousand Oaks, CA. p. 163–177.

46. Reich NG, et al. , Empirical power and sample size calculations for cluster-randomized and cluster-randomized crossover studies. PLoS One, 2012. 7(4): p. e35564. [PubMed: 22558168]

47. Kleinman K. Power Calculations for Cluster-Randomized and Cluster-Randomized Crossover Trials. 2021 [cited 2023 February 25]; Available from: https://cran.r-project.org/web/packages/clusterPower/clusterPower.pdf.

48. Fowler NR, et al. , Risks and Benefits of Screening for Dementia in Primary Care: The Indiana University Cognitive Health Outcomes Investigation of the Comparative Effectiveness of Dementia Screening (IU CHOICE) Trial. J Am Geriatr Soc, 2020. 68(3): p. 535–543. [PubMed: 31792940]

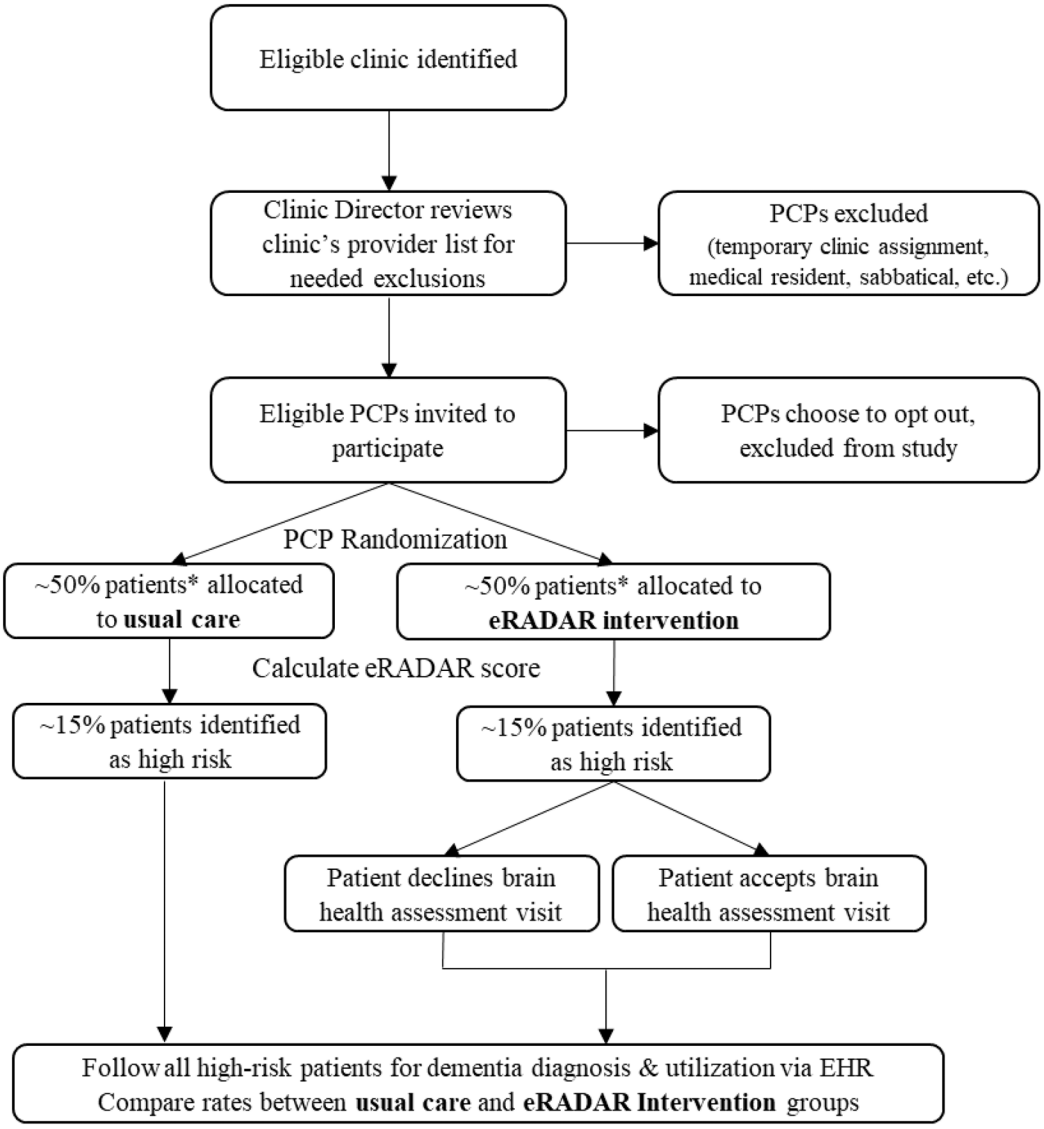

Figure 1.

Overview of embedded, pragmatic clinical trial (ePCT) design testing eRADAR intervention
*PCPs will be matched on approximate panel size during blocked randomized to ensure that about 50% of patients are included in each trial arm.

Figure 2.
Intervention patient flow

Table 1.

Instruments used for Brain Health Assessment Visits

Domain	Instrument	Description
General Health History & Functioning	None	Involves asking the patient and care partner (if available) about changes they have noticed in memory and thinking, as well as current or recent problems with vision, hearing, sleep, and falls.
Memory & Cognition	Montreal Cognitive Assessment (MoCA) [24, 25]	The MoCA is a cognitive assessment that screens for MCI and dementia. Scores of 26 and above are considered normal. We will refer patients with a score <18 for rapid follow-up assessment with their PCP for possible dementia. Participants with scores of 18-25 receive different recommendations based on their results for IADLs. Those with impairment in ≥1 IADL due to cognition or memory are referred for rapid follow-up assessment with their PCP for possible dementia. People with a score of 18-25 but no IADL impairment (or IADL impairment due exclusively to non-cognitive limitations) are referred back to their PCP for possible MCI; they are advised to have follow-up in about 1 year (or sooner at the PCP's discretion).
Instrumental Activities of Daily Living (IADLs)	None; influenced by Lawton IADLs [26-28]	Patient and care partner (if available) are asked about the patient's ability and level of independence for 5 activities: managing medications, tracking finances, driving and transportation, shopping, and preparing food. For patients with MoCA scores in the range from 18-25, impairment in 1 or more IADLs results due to memory and/or cognition is what determines which patients are referred back to their PCP rapidly for evaluation for a possible dementia diagnosis.
Depressive Symptoms	Patient Health Questionnaire (PHQ-2); if positive, progress to PHQ-9[29, 30]. If indicated, Columbia-Suicide Severity Risk Assessment[31] to assess for suicidal ideation.	The PHQ-2 is a brief screen to detect the presence of depression symptoms. Patients who score a 2 or higher on either of its two questions will be assessed further with the PHQ-9 to determine the severity of depression. Patients who score a 2 or 3 on question 9 (about suicidal ideation) of the PHQ-9 will be administered the Columbia-Suicide Severity Risk Assessment [31] to assess suicide risk and allow triage as appropriate.
Care Partner Perspective (if available)	AD8 [32-34]	The AD8 screening tool will be used to gather information on cognitive changes from a care partner if available. Scores of 2 or above in the 8-item questionnaire indicate likely impairment, and scores in this range combined with a MoCA score of 18-25 would provide support for a referral to the PCP for rapid follow-up evaluation.

Table 2.

Outcomes Measures Derived from the EHR

Description of Category	Measures
Dementia diagnosis rates	• Primary outcome: Rate of new dementia diagnoses in the 12 months following index date • Secondary outcome: Rate of new dementia or MCI diagnoses in the 12 months following index date
Healthcare utilization or burden potentially resulting from eRADAR intervention	• Number of PCP visits in the 6 months following the index date • Laboratory tests performed (e.g., Thyroid Stimulating Hormone, vitamin B12, syphilis) • Neuroimaging (e.g., brain Magnetic Resonance Imaging) • Specialty referrals (e.g., Neurology or Neuropsychology) • New prescriptions for dementia medications
Healthcare utilization measures that could improve with better detection and support of patients	• PCP visits in 1 year following the index date • Urgent care or Emergency Department visits in 1 year • Inpatient stays in 1 year, especially for Ambulatory-Care Sensitive conditions • “No shows” for clinic visits • Medication adherence (measured as Proportion of Days Covered)[36, 37]

Table 3.

Summary of Planned Formative and Summative Evaluation Activities and Measures.

Evaluation Activity	Formative*	Summative*
Post-Visit Survey	**Activity**: Survey findings from early patient participants reviewed to inform refinements and improvements to study implementation (outreach, visit, follow-up)	**Activity:** Survey findings collected from all patient participants over course of study analyzed to assess overall patient-reported satisfaction and acceptability of intervention.
	Participants:first ~40 patient participants in first clinic at each health system (N=80 total)	**Participants:** All patient participants (with care partner assistance as needed) at all clinics in each health system
	Analysis: Descriptive analysis of survey satisfaction scores & qualitative themes from comments	**Analysis:** Descriptive statistical analysis of survey satisfaction scores.
Brain Health Assessment Visit Observation	**Activity:** Brain health assessment visits observed by qualitative evaluator and structured field notes collected and analyzed to inform intervention implementation improvements. A subset of those observed also invited to interview.	N/A
	Participants: ~30 patient participants at first clinic in each health system after first 2 months in clinic	N/A
	Analysis: Team debrief after each observation. Feedback will be provided to study leadership about emerging themes requiring possible study modification.	N/A
Patient & Care Partner Semi-Structured Interviews	**Activity:** One-on-one interview with a subset of patients and care partners who completed the brain health assessment visit at 1 and 4 months post-visit to elucidate impacts and reflections to inform needed refinements to study implementation.	**Activity:** One-on-one interview with a subset of patients and care partners who completed the brain health assessment visit at 1 and 4 months post-visit to elucidate perceived impacts and reflections to inform patient-reported outcomes of perceived impact and acceptability.
	Participants: Purposive sample of ~12 observed patient participants and ~12 care partners from each health system (~40-48 patients & care partners total)	**Participants:** Purposive sample of ~12 observed patient participants and ~12 care partners from first clinic in each health system (~40-48 patients & care partners total; same as formative sample)
	Analysis: Team debrief after each interview, with feedback provided to study leadership about emerging themes requiring possible study modification.	**Analysis:** Formal thematic template analysis of interview transcripts to extract key themes related to implementation, impact, and acceptability.
PCP Semi-Structured Interviews	**Activity:** One-on-one interview with a subset of PCPs with patients completing a brain health assessment visit to gather perspectives and input on study activities and workflow impacts to inform implementation refinement.	**Activity:** One-on-one interview with a subset of PCPs with patients completing a brain health assessment visit to gather perspectives and input on study activities and workflow impacts to inform outcomes of provider perceived impact and acceptability.
	Participants: Purposive sample of ~10 PCPs per health system with patient(s) who completed a brain health assessment visit (~20 total)	**Participants:** Purposive sample of ~10 PCPs per health system with patient(s) who completed a brain health assessment visit (~20 total; same as formative sample)
	Analysis: Team debrief after each interview, with feedback provided to study leadership about emerging themes requiring possible study modification.	**Analysis:** Formal thematic template analysis of interview transcripts to extract key themes related to implementation, impact, and acceptability.

*Formative evaluation activities are those conducted during the implementation of the eRADAR intervention with the goal of program improvement. Summative evaluation activities are those conducted during and post-implementation with the goal of assessing the efficacy and acceptability of the eRADAR intervention.