Indians Transforming Alzheimer's Care Training (INTACT)

Study Protocol and Statistical Analysis Plan

Date: 10/05/2022
Unique Protocol ID: 19630

Indians Transforming Alzheimer's Care Training (INTACT)

Study Protocol

INTRODUCTION

Grant information

Title: Natives Engaged in Alzheimer's Research (NEAR)
Funder: National Institute on Aging (NIA)
Grant Number: 1P01AG066584-01A1

This research project is part of a large center grant composed of three research projects supported by four cores (administrative, biospecimen, scientific method and recruitment & engagement).

The objective of Natives Engaged in Alzheimer's Research (NEAR) is to understand, intervene on, and mitigate Alzheimer's disease and related dementia (ADRD)-related health disparities experienced by American Indians/Alaska Natives (AI/ANs) and Native Hawaiians and Pacific Islanders (NHPIs). This will be accomplished through the three main research projects:

1. Indians Transforming Alzheimer's Care Training (INTACT)
2. 'IKE Kupuna (Elder Wisdom) Project
3. Cognition After OSA Treatment Among Native American People (CATNAP)

Research Team

Patrik Johansson, MD, MPH (Cherokee) - PI, WSU
Dedra Buchwald, MD, Co-Leader and NEAR grant PI, WSU
Barak Gaster, MD, Co-Investigator (UW)
Clemma Muller, PhD, Co-Investigator (WSU)

IREACH WSU is the coordinating center for this project and will host all collected data

Abstract

The American Indian and Alaska Native (AI/AN) population is growing 3 times faster than the US all-races population. The number of AI/ANs aged 65+ is expected to triple to 1,624,000 by 2050, while the number of those aged 85+ will increase 7-fold to 300,000. These trends raise concerns about proportionate increases in Alzheimer's disease and related dementias (ADRD) among AI/AN elders, and concurrent demands for ADRD healthcare and services. Many AI/ANs obtain healthcare through a fragmented system that offers minimal geriatric or specialty care and creates barriers to obtaining high-quality care, resulting in late or under-diagnosis and inadequate care for ADRD. AI/AN elders typically receive their healthcare from primary care physicians (PCPs), who often lack the training and resources needed to diagnose and manage ADRD. The focus of the 2016 Alzheimer's Disease-Related Dementias Summit was on improving specialty skills in the community by training health professionals in dementia diagnosis, care, and research. PCPs are especially well-placed to detect mild cognitive impairment, which is often undiagnosed. While studies suggest that clinic-level interventions can improve ADRD diagnosis and care,

no pragmatic trial has focused on facilities or PCPs that serve AI/ANs. In partnership with an urban clinic serving AI/ANs, we therefore designed "INdians Transforming Alzheimer's Care Training" (INTACT), a clinic-level intervention to improve ADRD diagnosis and quality of care for AI/ANs. The active principal component of INTACT is PCP training in screening, diagnosis, and care for ADRD. Other elements include patient and family education, culturally informed videos, and brochures to create a "dementia-friendly clinic". **First**, we will conduct key informant interviews with PCPs in rural clinics to adapt the existing version of INTACT for delivery in rural settings. **Second**, we will test INTACT with a group-randomized trial at 28 urban or rural clinics that provide primary care to AI/ANs using a wait-control design. Data collection will rely on electronic medical records for clinic- and patient-level outcomes, and on self-report questionnaires at baseline and follow-up for PCP outcomes. Patient outcomes will additionally be assessed by manual chart review to document adherence to quality of care metrics for AI/ANs with diagnosed ADRD.

Specific Aims

1. Adapt INTACT for use in clinics serving AI/ANs.

2. Conduct a group-randomized trial to test INTACT's effects on PCP knowledge of ADRD, care confidence, and practice behavior.

3. Evaluate INTACT's effect on clinic-level outcomes (new diagnoses) and patient-level quality of care outcomes (e.g., treatments commonly used for ADRD).

The rapid growth of the elderly AI/AN population forecasts a ballooning number of Native elders at risk of ADRD. This study will be one of the few trials of a clinic-level intervention that foregrounds PCP education and training to improve ADRD care, and the only one designed for AI/AN communities.

Study Design

In this study, the research team will use **key informant interviews** to adapt the existing intervention to optimize its benefits for clinics serving AI/ANs. Next, the team will conduct a Group-Randomized Trial (GRT) with 28 urban or rural clinics that serve AI/ANs across the US. INTACT will be randomized at the clinic level (immediate intervention or waitlist control arm) and delivered to PCPs in clinics, with most outcome data derived from Electronic Health Records (EHRs.) Outcomes will be evaluated at the levels of clinic (new ADRD diagnoses), PCP (knowledge and self-efficacy for diagnosing and caring for AI/AN patients with ADRD), and patient (quality of care metrics for patients with diagnosed ADRD).

AIM 1: ADAPTING INTACT

INTACT adaptation will be done in 3 steps:

1) Adapt educational materials for AI/AN elder patients and caregivers
2) Adapt the UW Medicine Cognition in Primary Care Program for clinic serving AI/AN populations
3) Develop material to be used in the INTACT GROUP-RANDOMIZED TRIAL

Drs. Johansson (WSU) and Gaster (UW) will lead the adaptation of INTACT. They will oversee the key informant semi-structured interviews and work with the Recruitment and Engagement Core to adapt the Washington State Dementia Action Collaborative: Dementia Road Map brochure to be distributed to patients and caregivers, as well as the training material for primary care providers and guidelines for clinic on how to implement the INTACT program.

AIM 2: GROUP RANDOMIZED TRIAL

Study Design overview

The INTACT team will conduct a **group-randomized trial** (GRT) to test the effectiveness of the INTACT program, a culturally informed primary care provider training and clinic level workflow intervention for detection and appropriate management of AI/AN patients with Mild Cognitive Impairment (MCI) and ADRD in 28 urban and rural clinics serving AI/ANs. The clinics are the primary unit of randomization. Within each participating clinic, PCPs who are routinely seeing AI/AN patients ages 55 years and older will be recruited for data collection at baseline and 1-year follow-up. Each clinic will be randomized either to the immediate intervention or to a wait-list control arm. Data will be collected from PCP questionnaires, EHR data extraction and manual medical chart reviews. At the clinic level, we will rely on EHRs to document INTACT's effect on new ADRD diagnoses. At the PCP level, we will test whether INTACT increases knowledge and confidence in dementia assessment, ADRD care, and caregiver support. Patient-level data will be collected from the EHR and by manual chart review.

Once enrolled, clinics will complete a clinic profile interview and clinic and patient population information form, PCPs will be consented and complete a baseline survey. Next the clinics will be randomized into the immediate intervention or the wait-list control arms. Data collection will be conducted at baseline and 1-year follow-up. After completing the 1-year study period, clinics in the wait-list arm will have the opportunity to receive the INTACT intervention.

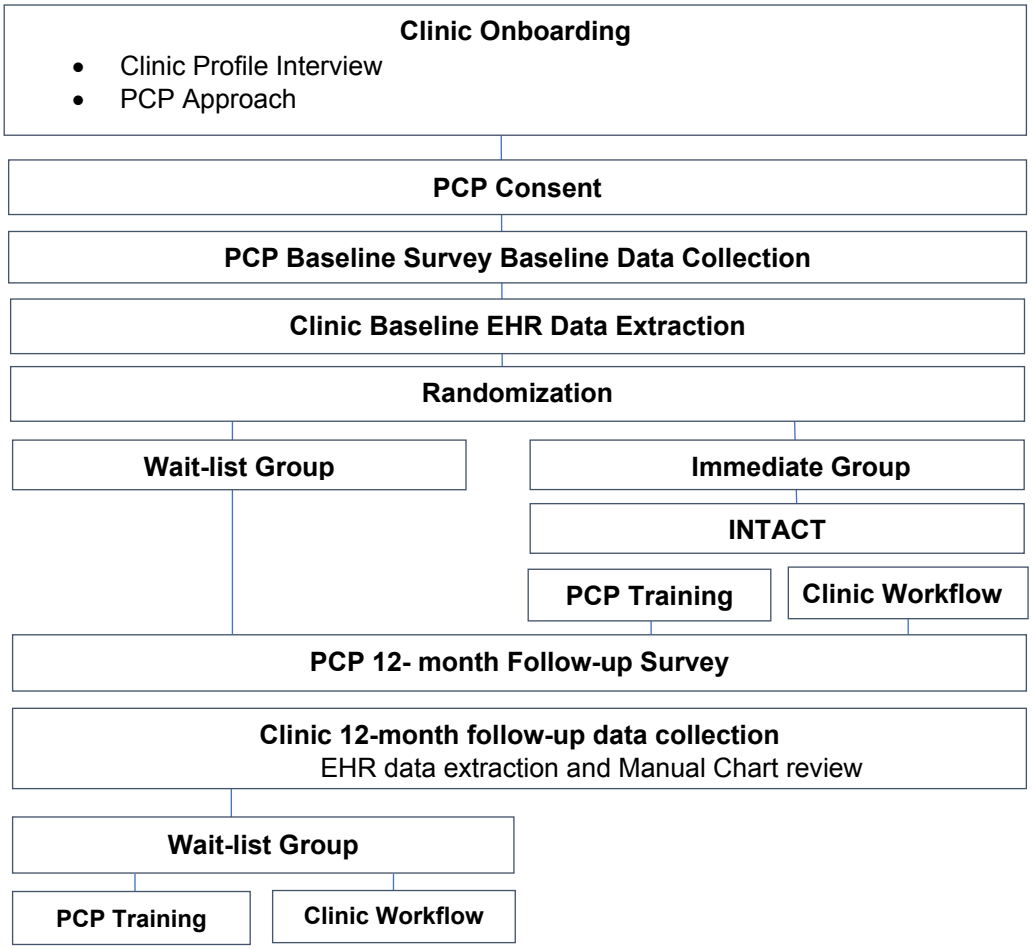

Figure 1: INTACT study flow chart

Recruitment

We will start our recruitment effort first with the clinics who have expressed an interest and provided a letter of support at the time of the grant proposal development. We will continue to reach out to new clinics, via NW HERON, a Washington based PBRN, and IREACH networking or are being recommended by a partner clinic or collaborator.

The study participation will last one year and it will be implemented in a staggered fashion creating at least three cohorts. Each cohort will be comprised of at least two clinics.

Clinic eligibility criteria

To be eligible to participate in INTACT a clinic must be:

1. A primary care clinic
2. Have at least 20 AI/AN active patients 55 years or older
3. Have an EHR system
4. Not intending to change EHR systems in the next year
5. Willing to conduct a total of 40 limited patient chart reviews to assess quality of care metrics for AI/AN patients with MCI and ADRD, staff permitting

IMPORTANT NOTE: power calculations assumed an average of 5 PCPs and 50 patients per clinic at each data collection; the actual numbers could be higher or lower in any given clinic. Therefore, the minimum criteria of 20 AI/AN patients 55 years or older and may be decreased or increased depending on average reached and success of recruitment efforts. We will check the average and the potential need to adjust this criterion approximately every 6 clinics.

PCP approach and eligibility

To be eligible to participate in the baseline and follow-up surveys a primary care provider must be 1) currently employed at a participating clinic, 2) have a title of MD, DO, Nurse Practitioner, or PA, and 3) regularly provides care to AI/ANs aged 65 and older.

Clinic's enrollment implies the involvement of all their PCP's in the study. Clinic leadership will announce their participation in INTACT and will encourage all PCPs to participate. Our team will send an invitation email using to the PCPs that will describe the study, what they will be asked to do and that their participation is voluntary. The email will also contain a link to the REDCap e-Consent form and survey. We will send one follow-up email to PCPs who have not consented two weeks after the initial email. No response to our invitation email will imply a refusal to participate. To protect PCP confidentiality and to protect them from coercion from the clinic leadership, or potential perception of, we will not share with the clinic's leadership the name of the participating PCPs.

IMPORTANT NOTE: This study is conducted at the clinic level, any PCPs employed at the clinic can join the study at any time. All eligible PCPs will be able to participate in the study at any point. Those joining after randomization will not be asked to complete the baseline survey.

Clinic Onboarding

The clinic onboarding process involves conducting a clinic profile interview and recruiting PCPs. Once a clinic has agreed to participate, Drs. Johansson and Gaster will conduct an in-depth clinic profile interview and Drs. Muller and Blaz will work with clinic staff to clearly communicate required elements of data collection.

Clinic Profile Interview

Prior to starting data collection and delivering the INTACT intervention program, Drs. Gaster and Johansson will conduct a Clinic Profile Interview to learn about the clinic's set up, unique organizational and clinical workflow features, current protocol, and practices with ADRD, the clinic and local resources,

and their AI/AN patient population, The information will be used to tailor the implementation of the INTACT intervention at the PCP and clinic level, and EHR data extraction procedures.

Randomization

Randomization will occur at the clinic level after completion of the PCP baseline data collection. Clinic- and patient-level data collection rely on EHR queries and manual chart review, and it is not logistically feasible to complete these before randomization. Clinics will be randomized in batches with at least 2 clinics per batch, to ensure simultaneous launch with at least one clinic in each study arm.

Note on immediate intervention arm engagement

For the 14 clinics randomized to the immediate intervention arm, clinic leadership will announce their participation in INTACT and will encourage all PCPs to participate in the programmatic elements for professional development and ADRD-related capacity-building. All PCPs employed at the clinic at any time during the 1-year study period are invited to engage with all aspects of the intervention, including those who are newly hired during the study period. For clinics in the immediate intervention arm, PCP participation in the study-specific data collection is not contingent on active engagement with the intervention; any PCP who meets eligibility criteria can complete the self-report questionnaires at baseline and follow-up.

Data collection

Data will be collected in three ways: self-report (PCP surveys and clinic profile data), EHR query (clinic and patient data), and manual chart review (patient data).

PCP Survey

Within each clinic, each participating PCP will complete a baseline and a 12-month follow-up survey. Outcomes will include basic demographics (sex, age, race), care confidence in providing dementia care to patients and their families and other PCP-level variables such as medical specialty, years of practice, tenure at the clinic.

EHR data Extraction

With the Research Methods Core, Drs. Muller and Blaz will standardize data between clinics to the extent possible and determine the best approach to create a pooled dataset. Baseline EHR data collection will commence immediately after randomization. Follow-up data collection will be conducted after the 1-year study period is complete.

Clinic level - patient volume (number of active adult patients aged 18+ years during the 12-month study period, total number of primary care clinic visits), number of PCPs, and number of patients at risk of ADRD (active patients aged 55+ with no prior ADRD diagnosis), total number of visits, visits by PCP and provider type, and aggregate counts of new diagnoses (MCI, ADRD, other dementia) based on the ICD-10 codes for these diagnoses. Total patient volumes for patients aged 55-64 and 65+ will be used for clinic-based calculations of the cumulative incidence and prevalence of MCI, ADRD, and dementia.

Patient Level - The goal of this analysis is to determine whether patients with diagnosed ADRD received healthcare consistent with current quality of care standards. Eligible clinic patients are active clinic patient with prevalent ADRD as of the first day of the 12-month baseline [or follow-up] surveillance interval, age 55 or older at the start of the surveillance interval, at least one primary care clinic visit during the 12-month baseline [or follow-up] surveillance interval.

Data extraction domains

1. Demographics - age, sex, marital and employment status/income, education, language(s) spoken, health insurance
2. Comorbidities - hypertension, type 2 diabetes, hyperlipidemia, obesity, heart disease, stroke, sleep apnea, and smoking
3. Neuroimaging orders

4. New prescriptions for potentially beneficial drugs for ADRD symptoms (e.g., cholinesterase inhibitors, N-methyl-D-aspartate antagonists, antidepressants, and antipsychotics) in clinics that track such information in their EHR.
5. ADRD quality of care measures, as reported during the Clinic Profile Interview with clinic directors or administrative leadership.
6. Quality of care outcomes will be based on existing quality indicators. These comprise 5 domains of care for patients diagnosed with dementia: annual cognitive assessments, annual evaluation of functional status, annual behavioral and psychiatric screening, advance care directives, pharmacological treatment changes.

Manual Medical Chart review

The manual chart review (MCR) will serve to capture details that cannot be extracted from the EHR, and to validate accuracy of patient-level EHR data. It will be conducted once at the 12 month follow-up and will cover both the baseline and 12-month follow-up timepoints for a random selection of at least 20 patients per clinic per time point to 1) document ADRD screening rates and 2) ascertain whether patients with diagnosed ADRD had the quality of care outcomes listed in data collection table above.

- 10 randomly selected patients eligible for cognitive screening will be reviewed to document ADRD screening rates within the EHRs at each site. Screening for MCI or dementia (e.g., Mini-Cog or AD8) may not be captured if the PCP does not use Annual Wellness Visit, Cognitive Assessment and Care Planning, Advanced Care Planning, or Neurobehavioral Status Exam CPT codes.
- 10 randomly selected patients with a previous dementia diagnosis will be examined to assess healthcare quality metrics such as completion of advanced directives, which are not always captured by the Advanced Care Planning CPT codes.

INTACT Intervention

The INTACT Intervention has two components: 1) provide a training for Primary Care Providers (PCPs) training in screening, diagnosis, and care for ADRD and 2) at the clinic level provide a workflow model for cognitive evaluation and setting a plan for the newly diagnosed patient. The INTACT intervention lasts 12 months and Continuing Medical Education credits will be available to PCPs who complete the INTACT training program.

Part 1 PCP training

The INTACT program is composed of 5 online sessions, 4 quarterly webinars and a resource packet. The intervention will be delivered over a period of 12 months, 5 PCP training sessions are designed to be delivered over four months.

Training Sessions

INTACT PCP online training program has 3 didactic sessions and 2 additional sessions focusing on the implementation of the training content in the clinic's unique operational and clinical workflow.

- Session 1: Make a diagnosis of cognitive impairment. An efficient framework for evaluating memory and other cognitive concerns in the primary care setting
- Session 2: Set a plan for the newly diagnosed patient. Structure a discussion about a new diagnosis of mild cognitive impairment including words to use, talking about prognosis, and how to provide high quality community resources to support patients and families.
- Session 3: Manage dementia as it progresses. Medications to treat cognitive impairment, managing agitation, advance care planning, and more.
- Session 4: Integrating the sessions' content into the clinical workflow
- Session 5: Follow-up on session 4 and check on integration of INTACT content into the clinical workflow

Webinars

Dr. Gaster will convene 4 quarterly webinars for PCPs during the 12-month intervention period. Topics will address 1) Driving and dementia; 2) Communication tips for someone with dementia; 3) Eating and drinking in advanced dementia; and 4) Advance care planning for dementia. Dr. Gaster will also work with the clinics to identify and incorporate additional topics of interest.

Part 2 In-clinic workflow to facilitate cognitive evaluations

INTACT has developed an in-clinic workflow to facilitate cognitive evaluations that is comprised of the following items. Clinics will be given access to them and receive support on how to implement them:

a) **Culturally informed educational material** (clinic and PCP levels) for the clinic to distribute to AI/AN patients and families to provide appropriate patient education on ADRD. Such materials include brochures and a short documentary to be played in waiting rooms
b) **Resource lists** tailored for each clinic location
c) **Dementia Advance Care Directive** (PCP level) is available for free. The directive describes the stages of dementia and offers choices regarding personal goals for medical care at each stage, making it easier for patients to share their views with loved ones who may need to make difficult decisions on their behalf.

Continuing Medical Education (CME)

CME credit for the 4 educational sessions will be offered through the Washington State University Elson S. Floyd College of Medicine

AIM 3: EVALUATE INTACT

Analysis

Analyses will be conducted by using the Stata and R statistical software packages. Inferential results will be presented as point estimates with 95% confidence intervals.

PCP Outcomes (Aim 2)

PCP self-efficacy, care confidence, and knowledge scores derived from multiitem scales will be modeled as continuous data. PCP practice behavior will be analyzed as a dichotomous outcome.

We will use hierarchical regression models with a random intercept for clinic; model specification will reflect that all PCPs within a clinic share the same intervention status. Linear hierarchical models will be used for continuous outcomes and logistic hierarchical models for binary outcomes. The intervention effect will be interpreted as the fixed effect for the INTACT × time (baseline vs. follow up) interaction. We will analyze PCP-specific outcomes using 2 approaches: a within-PCP change analysis and a within-clinic change analysis. For the analysis of within-PCP change, we will restrict the dataset to PCPs who participate in both baseline and follow-up data collection. These models will specify longitudinal data with 2 time points per PCP. Here, the INTACT × time interaction term will be interpreted as the intervention's effect on individual PCPs over time. For the analysis of within-clinic change, the dataset will include all PCPs who participate in data collection at baseline or follow-up regardless of whether they participate in both. The INTACT × time interaction term will be interpreted as the intervention's effect on the clinic environment. Primary analysis will not adjust for covariates. Secondary analyses will adjust for the same set of clinic covariates selected a priori, as above, and for clinic- and PCP-level covariates observed to be unbalanced between groups by chance alone.

Clinic Outcomes (Aim 3)

Incidence rates of new MCI, ADRD, and other dementia diagnoses will be estimated at each clinic for the 12-month intervention period using HER data. All patients aged 55+ who are at risk of the outcome during the study will be included. Poisson regression models will be used to estimate the effect of the intervention on changes in diagnosis rates for MCI, ADRD, and other dementia between intervention and control arms. Poisson models will include number of person years as an offset term. We will be parsimonious in our choice of adjustment variables, but will consider patient volume, state, and type of

facility if an imbalance is apparent after randomization. If we find evidence of an imbalance in covariates between study arms, we will adjust for those variables in the regression analysis.

Patient Outcomes (Aim 3)

For symptom-specific ADRD treatment, the primary outcome is documented treatment with medications. For healthcare quality metrics in patients with newly diagnosed or pre-existing ADRD, healthcare quality indicators will be summed for each chart reviewed. The quality metric score will be the primary outcome for this analysis; secondary analyses will evaluate each metric separately. For symptom-specific treatment and healthcare quality, outcomes will be evaluated as described for PCP outcomes, above. Hierarchical models (linear for continuous measures and logistic for binary) will additionally reflect the potential clustering of multiple patients per PCP; but sensitivity analyses will adjust for covariates that appear unbalanced between groups at baseline, as described above.

Effect Modification by Sex

Exploratory analyses will evaluate effect modification by sex. We will first conduct stratified analyses at the PCP and patient levels; we will then estimate a post-test only model for the combined dataset that includes adjustment for the baseline value and a coefficient for the interaction between INTACT and sex (or location) to formally test for effect modification. This analysis will be considered exploratory and hypothesis-generating, because the study is not powered to detect interactions.

Power

We assumed an average of 5 PCPs per clinic at each data collection time point, an average of 50 patients with data extracted from the EHR for analysis, alpha = 0.05, and clinic-level intraclass correlation ranging from 0.01 to 0.05. We estimated 80% power to detect standardized effect sizes (Cohen's *d*) as low as 0.5 for PCP-level outcomes and 0.2 to 0.3 for patient-level outcomes. By convention, these effect sizes are considered indicative of moderate and excellent statistical power, respectively.