Official Title:	COVID-19 Serologic Strategies for Skilled Nursing Facilities (CERO)
NCT Number:	NCT05270980
Study Number:	20-01281
Document Type:	Study Protocol and Statistical Analysis Plan
Date of the Document:	• August 16, 2021

COVID-19 Serology Strategies in Skilled Nursing Facilities (CERO)

Protocol

Version 3.1

Updated as of 8/11/21

x

A. SPECIFIC AIMS: COVID-19 SEROLOGIC STRATEGIES FOR SKILLED NURSING FACILITIES

The COVID-19 pandemic is a public health crisis that has been particularly devastating for older persons with Alzheimer's disease and related dementia (ADRD), especially those living in close congregant environments.[1,2,3] The largest proportion of COVID-19 deaths in many states has been in skilled nursing facilities (SNF),[5] in which over 60% of residents have ADRD.[2] These residents are particularly high risk for acquiring and spreading the infection due to their heavy reliance of staff for their personal care and their inability to comply with prevention behavior practices, such as social distancing, isolation and wearing masks.[4,5] Moreover, ADRD residents are especially vulnerable to the adverse social sequelae of COVID-19 outbreaks, such as cessation of routine activities, lack of visitation by their loved ones, and heightened confusion related to interacting with caregivers in protective gear. Taken together, compassionate and scientifically sound strategies to limit the spread of COVID-19 in SNFs are critical to mitigating the adverse effects of this devastating pandemic on the millions of residents with ADRD, their professional caregivers, and their family members.

A main strategy for monitoring COVID-19 in SNFs focuses on PCR testing. Asymptomatic infection challenges our ability to achieve isolation practices without complete isolation of all residents, yet the optimal protocol for such testing is unclear. Currently, PCR specimens are obtained through nasopharyngeal swabs; an uncomfortable procedure that is especially challenging to conduct in ADRD residents with a propensity for agitation. Additional problems with PCR testing include suboptimal sensitivity, making viral screening insufficient for infection control.[6] Furthermore, inadequate attention has been paid to front-line nursing home staff, who deliver the majority of personal care to ADRD residents.[5,7] Infection rates have been high among nursing staff resulting in fear in delivering care and reluctance to even come to work.[8]

In sum, as the COVID-19 pandemic continues to ravage US SNFs, novel strategies that maximize the safety and quality of life for SNF residents with ADRD and staff who care for them are urgently needed. To our knowledge, no SNFs have utilized a combined COVID-19 PCR/serology (antibody) testing-based strategy to dictate resident-staff assignments to decrease risk of exposure from COVID-19. Blood samples to obtain serology status and emerging saliva-based PCR tests also have the potential advantage of being less burdensome to obtain than nasal swabs from ADRD patients.

Despite the evolving landscape in nursing homes with the arrival of COVID-19 vaccines, the objective is to continue to pilot test an intervention that leverages COVID-19 and PCR status to pair SNF staff with residents in the safest way possible. However, with vaccination, serologic tests may be less meaningful as either may afford adequate protection. For that reason, we will only seek serology from individuals with no vaccination or no confirmed prior COVID-19 infection. If an individual has received the COVID-19 vaccine, we will not seek serologic testing because a negative test does not indicate a lack of protection. (Current commercially available serologic testing does not detect antibody formation derived from being vaccinated.) Specifically, we propose to pair residents and staff based on the following three conditions: 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and 3) positive serology, if available. We will pair COVID-19 negative residents with antibody-positive/PCR-negative staff and COVID-19 antibody-positive/PCR-negative residents with antibody-negative/PCR negative staff. For our pairing strategy, having a completed vaccination is equivalent to prior positive PCR or positive serology. The main clinical outcome of this novel staff-assignment strategy will be a reduced COVID-19 incidence rate compared to SNF units not using this approach. The pilot project will be done in two facilities with high minority and ADRD representation—Terrence Cardinal Cooke and Mary Manning Walsh of New York City, NY. To ensure the highest likelihood of successful implementation, we propose a phased approach to this research, reflected in following three specific aims:

1. Develop a staff-resident assignment protocol based on vaccination, history of positive PCR COVID-19 test and positive COVID-19 serology testing (when applicable). This strategy will be feasible, scientifically sound, and acceptable to key stakeholders, particularly residents with ADRD and their families using the following approaches: 1) Semi-structured interviews (one-on-one interviews) including administrators, clinical leaders, front-line staff, residents and family members; additionally, because of the increase in staff stress—both work-related and personal—we are interested in understanding how mental health issues may influence attitudes about new programs and changes in usual practice. Therefore, we are including a brief mental health assessment for unit staff only and 2) Panel of experts familiar with the NH environment including: industry leaders, infection disease specialist, dementia expert, health equity expert, and bioethicist. We will develop protocols for: 1. Staff-resident assignments, 2. Serology (if applicable) or PCR testing and vaccination and 3. Implementation monitoring.

2. Employ a testing protocol based on vaccination, PCR, or serologic testing in each of the two SNFs among staff and residents to establish their baseline status and three and six months later using on-going surveillance testing.
3. Implement a SNF-unit staffing assignment strategy pairing COVID-19 negative and positive residents with staff based on protocols developed in Aim 1. To ascertain feasibility for a larger trial we will measure: i. COVID-19 resident incidence (primary outcome); ii. COVID-19 staff incidence; and iii. hospital transfers for COVID-19. We will assess implementation by: 1) % intended staff assignments achieved; 2) reasons for success/failure; and 3) intervention acceptability using exit interviews with staff, residents, and family members, with particular focus on the impact of the intervention on ADRD residents and their families.
IMPACT Establishing vaccine effectiveness in an older and frail population is an ongoing effort. In the meantime, more immediate strategies to address rapid spread and excessive mortality due to COVID-19 are greatly needed. We anticipate that this pilot study will set the stage for a larger trial that will ultimately set evidence-based policy for SNF staff-resident assignments that minimize risk of acquiring COVID-19, and directly improve the care of millions of Americans with ADRD.

B. SIGNIFICANCE
The COVID-19 pandemic has greatly impacted the United States. This public health and clinical crisis has been especially devastating for older persons, in particular, for those with ADRD where death rates have been among the highest.[8] Residents of skilled nursing facilities (SNF) where ADRD is highly prevalent have been most impacted, as a high-risk population living in close congregant quarters, requiring frequent need for personal care, with inadequate testing needed for thoughtful isolation practices and inadequate personal protective equipment to limit spread.[9,10] In particular, those with ADRD are more challenged, often unable to conduct self-prevention behaviors further increasing risk for themselves and others. Social isolation and wearing masks are certain to create confusion for those cognitively challenged. Moreover, communication through a mask is further exacerbated[11] when dementia is accompanied by hearing loss, a common co-occurring condition.[12] Other isolation strategies are needed. As of May 11th, over 30% nursing homes in 30 states had at least one documented case (2,949 of 9,395).[13] Urban location as well as greater percentages of African American residents significantly increased incidence.[13] More importantly, Five-Star rating, prior infection control citations, Medicaid dependency, and ownership were not associated with infection rates, which are clearly difficult to control.[9] In the absence of antiviral therapies, serologic testing is likely to be employed as a prevention practice, reflecting the history of efforts in hepatitis and HIV prevention. Serologic testing offers great promise for minimizing transmissions recognizing that there is still much to be learned about test accuracy and the relationship between antibody presence and reinfection.

It should not be surprising that COVID-19 infections in SNFs are widespread and death due to infection is common. Death is likely to be even higher in residents with ADRD who are unable to report symptoms, thus delaying needed medical care. Long-term care facility deaths have been among the largest proportion of state reported deaths and several-fold higher when considered as a proportion of those infected who die.[5] Recognizing that the U.S. has now exceeded 100,000 deaths overall due to COVID -19, as of May 2020, nursing home residents accounted for more than one-third of the then 80,000 deaths in the U.S.[14] How many who have died and had ADRD is unknown. The best-known example was the first – a facility in King County, Washington when the first index case was identified on February 28th, 2020. By March 18th 167 persons were diagnosed and linked to this index case within two Washington Counties. Among 118 tested facility residents, 101 were positive for COVID-19 and 35 had died.[9] Over half of all residents were hospitalized. Fifty health care personnel, another constituency of great concern, had COVID-19. In New York State, the site for this pilot study, state officials identified 86 facilities with at least five COVID-19 related fatalities and over 300 New York facilities had at least one.[11] But because the federal government did not require reporting prior to May, underreporting is likely to be systemic and post-dates the period of high disease prevalence in March and April.[15]

Suspected asymptomatic spread also appears to be high in these settings,[8] which requires a more rigorous approach for isolation of affected residents from those who are not and removal of staff with identified infections. Some facilities such as those in this pilot (where ADRD prevalence is high) are engaged in frequent testing of residents and staff, a practice which leads to isolation of all affected residents, and reductions in personal care. This approach also results in cessation of meaningful activities and harmful social isolation, further compounded by greater staffing shortages. While the heightened risks for SNF residents are indisputable, less attention has

been focused on front-line nursing home staff, such as licensed vocational nurses who deliver the majority of personal care and are at greatest risk to infect themselves and the residents they care for. Infection rates have been high among nursing staff resulting in fear in delivering care and reluctance to even come to work. To address staff shortages, CMS has waived the requirements (42 CFR 483.35(d)[16,17] of nursing facilities to not employ anyone for longer than four months unless they have met training and certification requirements under 483.35(d).[17] To ensure the health and safety of nursing home residents, CMS will continue to require facilities to ensure that individuals are competent to provide nursing and nursing related services for nurse aides working full time for more than four months. This relaxation in training and certification may further compound the need for careful infection control. Moreover, an increase in prevalence of behavioral challenges for those with ADRD arise from changed routines, unfamiliar faces shrouded in masks, and more difficult communication due to hearing loss from a lack of facial expression/lip reading. An experienced staff to manage these challenges and who are not out of work due to COVID-19 illness becomes an even more critical need.

C. INNOVATION

This study is innovative for several reasons: 1) a resident-staff cohorting strategy based on a) completed vaccination; b) prior COVID-19 PCR positive testing; and c) positive serology has to our knowledge, never been utilized for infection control in any healthcare setting: 2) although stakeholder-influenced study designs have been increasingly utilized, employing a multi-stakeholder approach to design a facility-specific testing and cohorting strategy is highly innovative and ensures a greater engagement and fidelity across all involved sectors; 3) a detailed implementation design to capture values, changing attitudes, structural and cultural barriers to a testing and cohorting strategy is also innovative and will greatly serve larger trials and best practice disseminations; 4) comparing primary outcomes and infection rates between those with and without ADRD is novel; and 5) the use of smartphone based technology to facilitate proper cohorting while increasing fidelity is highly innovative and ensures greater capture of deviations from the intended approach. Additionally, this approach can benefit facilities in their effort to increase contact-monitoring amongst staff and residents.

D. METHODS AND APPROACH

D.1. Overview: This one-year cluster-randomized pilot study will be conducted in three phases. We have engaged two NYC facilities as the sites of the proposed study, where (Phase 1: AIM 1 – one month) we will convene all stakeholders (leadership, staff, residents, and their families) and engage a panel of experts to create a feasible, scientifically sound protocols for staff-resident assignments based on serology (if applicable), vaccination and PCR testing protocols, and Implementation monitoring. In the second phase (Aim 2 – two months), we will identify four units (average 40 residents per unit) in each facility. We will stratify the two NHs and then within each SNF, randomly allocate two units to the intervention arm and two units to the control arm (we have confirmed homogeneity across these four units in each SNF supporting no need for further stratification). We will conduct baseline serology and/or PCR COVID-19 tests from residents and staff on all four units in each SNF.

In phase 3 (Aim 3 – six months), we will introduce the staffing assignments based on 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and/or 3) positive serology in the two intervention units, while in control units will employ usual staffing assignments currently in practice in the facilities and only introduce the “concept of” a cohorting strategy. COVID-19 PCR testing will occur in all eight units with a regular frequency (testing frequency changes based on government guidelines) and whenever an individual is symptomatic. The primary outcome will be incidence of COVID-19 infection in residents and as secondary outcomes will include the incidence of COVID-19 infections in staff and hospital transfers due to COVID-19-related symptoms among residents. Implementation assessment will include: 1) proportion of designated staff assignments achieved and reasons for successes and failures; and 2) intervention acceptability using exit stakeholder interviews, with a focus on the experience of ADRD residents. Although the analyses will compare intervention and control units on the primary outcomes of infection incidence and hospitalization, we do not anticipate either event rate to be large enough to reach statistical significance at traditional levels of probability. As real-world management of COVID-19 is rapidly changing, we anticipate that the protocol will continue to evolve over time in terms of testing frequencies and the capacity to assign residents and staff consistent with our strategies. The protocol will be flexible to accommodate such changes. For example, both facilities are launching a SNF-wide resident testing strategy and are responsive to federal testing guidelines. Should a reliable PCR test emerge that is less invasive than the nasopharyngeal swab, we will adopt it into our protocol. Currently no staff member who tests positive

for COVID-19 is allowed to work. Thus, staff-resident assignments will be based on 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and 3) positive serology (when possible) among staff and residents.

D.2. Setting and Participants: We are conducting the proposed trial in two nursing facilities in NYC: Mary Manning Walsh (MMW) and Terrence Cardinal Cooke (TCC). Both facilities operate under the umbrella of the ArchCare Organization, a non-profit corporation that owns and operates five nursing facilities in addition to other older age care services. Dr. Chodosh and his team have been actively engaged in a research study (*SLUMBER* R01NR016461-01) in these facilities and others that involves staff education to promote better sleep, work that has led to smartphone-based educational reinforcements, which will support the proposed intervention. Both facilities care for a large proportion (>60%) of residents with dementia. Both facilities are also are diverse: 20% LatinX in MMW and 25% African American in TCC and there are 362 and 485 residents in these facilities, respectively. MMW recorded over 30 COVID-19-related deaths by the third week in April (the highest nursing home death rate in New York State at that time) and TCC had more than 20. Both facilities are currently mandating weekly testing of all staff and are conducting their first-wave resident tests for all residents and anyone with symptoms. Plans for repeated resident testing will follow CDC guidelines, which are expected to evolve over the next few months. Intervention participants include four groups: leadership, staff, residents and family. For leadership and family, they will participate in the institution's effort to develop a strategy for reducing COVID-19 infections by providing guidance to testing, staff assignment strategies and ongoing feedback based on periodic process data collection, analysis and reports. Staff and residents will follow the guidelines and requirements of the facility, which will be implemented on two units as a quality improvement initiative.

D.3. Methods for Aim 1:

Aim 1: *To develop a staff-resident assignment protocol based on 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and 3) positive serology (when possible) that is feasible, scientifically sound, and acceptable to key stakeholders, particularly residents with ADRD and their families using the following approaches: 1) Facility-specific semi-structured one-on-one interviews including administrators, clinical leaders, front-line staff, residents and family members; brief mental health survey for unit staff only, as an important potential covariable, and 2) Panel of experts familiar with the NH environment including: industry leaders, infection disease specialist, dementia expert, health equity expert, and bioethicist. We will develop protocols for: 1. Staff-resident assignments, 2. Serology (if applicable) and PCR testing, and 3. Implementation monitoring.*

D.3.a. Stakeholder meetings: All meetings will be recorded and transcribed with permission of meeting participants. At the earliest period of study, we will hold two leadership meetings that include both leaders at the organization level and individual facility level. Leaders will include Senior Vice President, Chief Medical Officer, Chief Information Officer, facility-level Medical Directors and Nursing Directors as well as any other individuals to be invited at the discretion of ArchCare. At the facility level, Chief Medical Officer, Director of Nursing, and unit-level leadership will attend two initial meetings and then will meet weekly, bi-weekly or monthly thereafter. These meetings will address: 1) unit selection; 2) viral testing (PCR and Serology) strategies; 3) marketing approaches for residents and families; 4) staff education strategies for implementation; 5) current in-facility data collection and staffing strategies; 6) data retrieval strategies (e.g., from electronic health records) for completed vaccination, PCR or serology tests 7) use of an external smartphone application to facilitate cohorting methods and monitoring; and 8) human subject consent strategies.

The rationale for two initial leadership meetings is: 1) the need for brevity (shorter meetings), ensuring logistical feasibility; 2) bidirectional information giving to ensure greatest collaboration and grounding in the intervention; and 3) anticipated need for follow-up based on questions that arise from the first meeting or subsequently needed revisions in the planned protocol. Weekly meetings with unit leadership including individual staff members, as needed will review most recent data on infection rates, hospitalizations, and process measures focused on intervention fidelity. Leadership will hold family informational meetings and solicit feedback prior to study initiation and resident meetings on the units where a staff- assignment strategy will be implemented. We anticipate that resident meetings will be conducted individually and not as groups given the likelihood that congregant meetings will not be allowed. Additional meetings with stakeholder groups will occur no less frequently than monthly and may be brief weekly "check-ins" as needed. We will (with permission) record all meetings if possible and take notes. No attendee identifiers will be included.

We will conduct semi-structured one-on-one interviews in-person or using a WebEx or Zoom meeting structure. When necessary or most expedient, we will conduct individual telephone-based interviews. Whereas our goals

for obtaining qualitative data are implementation-specific and not exploratory, strategies used in exploratory work are germane to this work including the use of open-ended questions and thematic analytic approaches. These methods increase the yield of valuable and actionable information where the interviewer or interviewee has incomplete knowledge, which is required for establishing most feasible and effective strategies. These methods also ensure greater democratization of knowledge and establish a collaborative spirit embodied in respect, mutual cooperation, and trust, all of which will be critical to success especially during these times of strong emotions and potentially grave consequences. We will audio record where permissible and regardless of that determination, we will take detailed notes. In addition to documenting key decisions, we believe that some of the deliberations will reveal and highlight key perspectives and sensitivities that will need to be considered and will inform not only this strategy but future SNF-level intervention strategies that require an abrupt departure from usual practice.

D.3.b. Expert Panel Meetings: We will convene a Panel of Experts familiar with the NH environment that will include two industry leaders, an infection disease specialist, a dementia expert, health equity expert, and a bioethicist. The bioethicist, dementia expert, and health equity expert will be drawn from the Cores and Teams of the IMPACT Collaboratory. We will meet with our Expert Panel prior to study initiation and quarterly over the year of study.

D.4. Methods for Aim 2:

Aim 2: *Employ a protocol based on 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and 3) positive serology (if applicable) in each of the two SNFs among staff and residents to establish their baseline status and three and six months later using on-going surveillance testing.*

D.4.a. Testing Protocol and Data Entry: The facility will conduct periodic PCR testing based on CDC guidance and will test additionally based on individual symptom or exposure-related concerns. Modifications to the testing strategy will be based on collaboration between facility leadership and our infectious disease expert. Given the discomfort of a deep nasopharyngeal swab, we will use, if deemed acceptable at the time the pilot study is conducted, a saliva-based PCR test to identify active infection and the frequency of testing will be based on a collaborative decision between our infection disease expert (Dr. Shopsin) and facility leadership. Collection of completed vaccination and/or prior COVID-19 PCR positive testing records or positive serology testing will occur at baseline and at three and six months but the frequency may be modified based on new discoveries as our understanding of this virus evolves. The laboratory providing results will present testing results to the facility in a timely manner, if possible, and those results will also be transmitted to our study team. Although it is best that the facility maintain responsibility for populating their health records, we will confirm their interest in using our REDCap database and we will closely monitor those entries to ensure accuracy and present timely feedback using a standard audit and feedback process. We have successfully used this approach in other nursing home studies focused on depression care.[18] For any resident moving into an intervention unit, the default status will be 'COVID-19 negative' until vaccination completion records or prior COVID-19 PCR positive status is known, or if serology testing is performed. We also anticipate completed vaccination, prior COVID-19 PCR positive testing and serology results will be collected at baseline, three and six months but a different set of frequencies for testing will also be considered. Test results will be maintained at the level of the individual resident and labeled for easy recognition by facility and unit. Weekly meetings between study team, the facility designated data manager, and staff leadership for each intervention unit (n=4) will ensure data accuracy and quality.

D.4.b. Subject Consent and Regulatory Issues: <u>All human subjects concerns will be reviewed and approved by the IMPACT Collaboratory's Advarra Central Institutional Review Board and Data Safety and Monitoring Board. To meet our timeline, these approvals need to be sought as soon as possible</u>**.** For Aim 1, we will obtain consent from participants to take notes and audio record while clearly stating that there will be no subject identifiers. Aim 1 will help direct our approach to consent and human subject protections for Aims 2 and 3. Residents and staff PCR testing fall under current usual care and are already used to cohort residents. Any resident room relocations based on infection status will follow existing SNF institutional policies. However, we will need to consider consent processes to obtain serologic tests from staff and residents, use of testing information to create staff-resident assignments, and utilizing all data for research purposes. We will request a modified consent process (e.g., opt-out, verbal consent) from Advarra IRB but recognize that this may also require individual written consent. We will follow all rules and sensitivities with regard to the need for legally authorized representatives in the absence of subject capacity to consent.

D.5. Methods for Aim 3:

Aim 3: *Implement a SNF unit staffing assignment strategy pairing COVID-19 negative and positive residents with staff based on protocols developed in Aim 1 in intervention units and introduce a "concept of" cohorting strategy in the control units, meaning these units will follow regular facility policy and will not receive staff-resident assignments.* To ascertain feasibility for a larger trial we will measure: *i. COVID-19 resident incidence (primary outcome); ii. COVID-19 staff incidence; and iii. hospital transfers for COVID 19. We will assess implementation by: 1)* % intended staff assignments achieved; 2) reasons for success/failure; and 3) intervention acceptability using exit interviews with staff, residents, and family members, with particular focus on the impact of the intervention on ADRD residents and their families.

D.5.a. Randomization of Units: 40-bed facility units are the unit of randomization and we will randomize within individual SNFs to select each intervention unit. Should we identify specific unit-level characteristics that are not consistent across units (we have been assured there are none) and may influence our outcomes (such as median age, other demographics or unit size) we will conduct a stratified randomization. We recognize there may be some contamination between staff/residents between intervention/control units but will do our best and monitor this "contamination" as one of our implementation fidelity outcomes.

D.5.b. Staff-Resident Assignment Strategy: Within individual intervention units, we will pair care-partners (staff) with individual residents, based on 1) completed vaccination; 2) prior COVID-19 PCR positive testing; and 3) positive serology (if applicable). For serology testing, antibody negative will be paired with antibody positive as well as antibody-positive with anti-body positive if the frequency of antibody-positive residents and staff is high. Prior known COVID-19 infection and recovery in the absence of vaccination will still require serology testing as we do not yet know how to anticipate antibody development and resilience. Contact between two or more antibody-negative and unvaccinated individuals (and no history of positive PCR) will be restricted such that no antibody negative, unvaccinated individual (and no history of positive PCR) will intentionally interact with another antibody-negative, unvaccinated person (and no history of positive PCR), regardless of individual type (resident or staff). We anticipate that high staffing ratios (more residents with fewer staff) that require the responsibility of one staff person to care for several residents will present considerable challenges to achieving full fidelity, particularly on overnight shifts. Although strict cohorting is a primary implementation goal, we anticipate less than perfect fidelity. Nonetheless, we believe that any reduction in unnecessary exposure will reduce the risk of disease transmission and may lead to meaningful outcomes. Ensuring greatest fidelity will require full engagement of clinical leaders (nursing leads) at the unit level but these leaders will require real-time data for making staffing decisions. These data should also be available to front-line staff so that there is less opportunity for misinformation or lack of information to inform decisions.

D.5.c. Staff-Resident Assignment Decision-Making Tool: Dependent on stakeholder meetings we will propose a data-driven decision-making tool built on a smartphone compatible REDCap platform. We have built REDCap applications for registry enrollment (NIH/NIA ELM) Research Collaborative 1R24AG063725; Chodosh-MPI), educational event feedback and community-based research recruitment (NIH/NIA ADRC P30-AG008051-26; Chodosh-ORE Core Leader), and a nursing staff behavioral support decision-aid (*SLUMBER* R01NR016461-01). Our detailed cohort data is smartphone compatible and interfaces with Tableau© for best data visualization to support in-the-moment decision-making. Data capture will be either direct linkage to the laboratory testing site or a facility-identified data manager for data entry. Our tool will identify residents and staff by unit, type date of test, and test results. We will create a stratification strategy that will include a list of residents by COVID-19 status and a connected list of staff who are "cleared" to care for those individuals based on mutual test-derived classifications. Data from the two intervention units will be combined to increase the flexibility of cross-unit staffing when shortages require staff to work on units that are not their usual work location. We will also consider additional serologic testing for staff members who might "float" onto the intervention units. During the study period we will pursue an independent software application that does not require a University-based software system (REDCap) with an eye towards broader feasibility and dissemination should our findings warrant a larger multi-site clinical trial and national dissemination.

E. ANALYSES:

Data Elements Overview: Data includes both quantitative and qualitative measures. Our quantitative main outcome measures are the number of new COVID-19 detected infections over time, and number of hospitalizations over time. PCR data will be collected at baseline and compared to determine incidence (although we expect that this number/ proportion to be quite low). Incident infection data will be entered and collected through the REDCap tool described above as will serologic data. We will collect data on hospital admissions at the end of each month during the intervention period. We will also collect data on fidelity with respect to testing compliance and cohorting. All test results will be maintained in a database that is available to facility and unit leadership with identifiers to enable an active and flexible staffing strategy. These same test results will be available to our study team but without identifiers. We will collect qualitative data using notes from stakeholder meetings and transcribed recordings where permissible. We will gather additional data from exit interviews with representatives of each stakeholder group.

We will collect incidence rates for PCR and serologic results as detailed in Section D.4.a. Other variables we will collect include using Minimum Data Set (MDS) 3.0 for: resident age, race/ethnicity, gender, function (ADL),comorbidities as well as measures that look into anxiety, depression levels, functional disabilities, cognitive performance, among others. Data will be requested from three time points 1) pre-COVID-19 (1 year before) 2. COVID-19 (as of February 2020) and 3) post-COVID (present time). Staff data will include: age, race/ethnicity, gender, and zip code of residence. We will examine differences in outcomes comparing those with and without ADRD within intervention and control units. A protocol for obtaining laboratory data either from the facility-related clinical lab or directly from the facility will be established following our first leadership meeting. Should rapid tests with on-site interpretation become available, we will create a protocol to ensure accurate and timely data capture working with leadership at the unit level. We will use unique identifiers to ensure resident/staff confidentiality within our database, but the facility managers will require identifiers to achieve their staffing strategy using the database and for making best and timely decisions about resident staffing. We will include in our REDCap database a tool for listing, by each unit, daily staff/resident assignments. Should unit managers want to use another method for monitoring assignments, we will request a daily fax or email of those assignments. Each facility medical director at will ensure compliance with data capture.

E.1. Quantitative Analyses: The ultimate goal of developing a serologic strategy is to reduce COVID-19 infection rates and hospitalizations. In this pilot phase, where the focus is informing the design of a larger pragmatic RCT, a key focus will be on the ability to measure the outcomes, incident cases of COVID-19 and hospitalizations, in a pragmatic way using administrative data only. Once we have successfully collected these data, we will estimate incident rate ratios using Bayesian Poisson models that include resident length of stay in the nursing home. The Bayesian model provides a posterior probability distribution of the effect of serologic strategy on incidence and hospitalizations. A strength of this analytic approach is that we will be able to conduct ongoing interim analyses to understand if and how the strategy is working as we conduct the study.

The COVID-19 analysis will be conducted at the level of the nursing home unit using this model:

$$Y_i \sim Poisson\ (\lambda_i)$$
$$log\ (\lambda_i) = \beta_0 + \beta_1 T_i + log\ (R_i)$$

Y_i is the number of incident cases for nursing home unit i, $i \in [1, 2, \ldots, 8]$. T_i is an intervention indicator, $T_i = 1$ if unit i is using the serologic strategy, $T_i = 0$ otherwise. R_i is the total number resident-days for unit over the 6-month observation period. The parameter λ_i represents the modeled mean for site, and λ_i / R_i is the incidence rate, represented as the number of infections per resident-day. β_1 is the effect of interest: the incidence rate ratio. We will assume an uninformative prior distribution for β_1. The model for hospitalizations will be developed in the same manner. Both analyses will be conducted using the latest version of R, which is currently 4.0.0 (R Foundation for Statistical Computing, Vienna, Austria).

E.2. Qualitative Analyses: Overview of Qualitative Methodology: This project includes qualitative data from key stakeholder meetings and interviews about: 1) perceptions of the testing program and implementation strategies; 2) perceptions about staff-resident assignment strategies; 3) barriers/facilitators toward program implementation and sustainability including the impact of staffing changes on resident behaviors for those with ADRD. Because much of this work is implementation and feasibility-specific, meetings will often be both information giving and soliciting of other details, e.g., how is testing being conducted currently. We will use focus

group and semi-structured interview guides for these meetings consisting of open-ended questions and probes to focus while allowing participants to speak freely. The meeting guides will be adapted from tools used in the formative phase to assess acceptability of the intervention and feasibility of strategies.

E.2.a. Qualitative Analysis Plan: The qualitative data will be analyzed using content thematic analysis.[19] When possible, meetings and interviews will be audiotaped and transcribed verbatim, with accuracy confirmed, and coded using ATLAS.ti version 8.0,[20] a powerful analytical tool for qualitative analysis. When taping is not possible, these discussions will be captured through extensive notetaking. Dr. Dickson, an expert in qualitative and mixed methods research will oversee all phases of the qualitative analysis including the data integration phases. Preliminary analysis will include a line-by-line review yielding clusters of data that we will label into brief headings. We will derive codes from these data linked to meeting/interview questions and coding categories. We will summarize coding categories within-cases, then across cases, subsequently cross-classified to yield a rich descriptive analysis.21 Finally, we will identify emerging themes both within and across coding categories; and verify a review of data fit. For the key stakeholder meetings/interviews, we will analyze data site by site and then across sites to identify site-specific data as well as overarching themes. In the final analysis stage, we will integrate qualitative and quantitative site/unit-specific data to describe implementation barriers and facilitators. We anticipate that the qualitative data will also reveal factors that influence understanding (e.g., interpretation of serology results, what constitutes meaningful and at-risk contact). In the final analytic phase, we will use informational matrices, a type of joint display22 to integrate the stakeholder qualitative data and the resident outcome data to describe the mechanism of testing and cohorting effectiveness. Methodological rigor[23] throughout all phases of this analysis will be assured by training of research staff who will do initial coding, assessing inter-coder reliability, an audit trail of analytic decisions, regular meetings with experts and member checking, the process by which findings are validated as representative of the experience of the participants.

F. PROJECT MANAGEMENT PLAN AND TIMELINE

Please see Biosketches for qualifications of co-investigators. A GANTT chart is included here. Dr. Chodosh will have responsibility for all aspects of study design and execution. We have already established meetings with ArchCare leadership in developing this proposal. This will serve as an excellent conduit to a rapid launch should this study be funded. His senior research coordinator, Diana Hernandez is bilingual and has an excellent rapport with facility staff at both MMW and TCC. Ms. Hernandez will work closely with ArchCare leadership and facility staff to coordinate all meetings and will serve as the go-between for the research team and facility staff. Dr. Shopsin has expertise in serologic and PCR testing and will facilitate that process and data interpretation. His close working relationship with his NYU colleagues ensures that new discoveries will more readily be integrated into pilot work where appropriate and deemed to be of benefit. Our team is also benefitted by the counsel and expertise of the NIA IMPACT Collaboratory including, bioethics, dementia, health equity, implementation, stakeholder concerns, and pragmatic statistical design. We will meet periodically with Collaboratory experts for ongoing advice and specific direction where needed.

GANTT Chart - COVID-19 SEROLOGIC SNF STRATEGIES	Month											
Tasks	1	2	3	4	5	6	7	8	9	10	11	12
Schedule and hold stakeholder meetings												
IRB application to Advarra												
Conduct additional focus groups, interviews												
Convene Expert Panel												
Establish testing protocol and subject consent												
Build and test REDCap cohort-support tool												
Randomize units and train staff												
Conduct and collect PCR and Serology testing												
Maintain audit and feedback with staff and leadership												
Conduct qualitative analyses												
Conduct quantitative analyses												
Complete final report, manuscripts and large trial application												

References

1. Wang H, Li T, Barbarino P, et al. Dementia care during COVID-19. The Lancet 2020; 395:1190-1.
2. U.S. Centers for Medicare & Medicaid Services. Nursing Home Data Compendium 2015 Edition. Available at: https://www.cms. gov/Medicare/Provider-Enrollment-and-Certification/ CertificationandComplianc/Downloads/ nursinghomedatacompendium_508-2015.pdf. Accessed June 17, 2020.
3. Iaboni A, Cockburn A, Marcil M, et al. Achieving Safe, Effective, and Compassionate Quarantine or Isolation of Older Adults With Dementia in Nursing Homes. The American Journal of Geriatric Psychiatry [Internet] 2020. Accessed 2020 Jun 10. Available from: https://www-sciencedirect-com.ezproxy.med.nyu.edu/science/article/pii/S1064748120303262
4. Grabowski DC, Mor V. Nursing Home Care in Crisis in the Wake of COVID-19. Accessed 2020 Jun 10. Available from: https://jamanetwork.com/journals/jama/fullarticle/2766599 *JAMA.* Published online May 22, 2020. doi:10.1001/jama.2020.8524
5. True S, Claxton G, Chidambaram P. COVID-19 and Workers at Risk: Examining the Long-Term Care Workforce [Internet]. KFF. 2020. Accessed 2020 Jun10. Available from: https://www.kff.org/report-section/covid-19-and-workers-at-risk-examining-the-long-term-care-workforce-tables/
6. Lippi G, Simundic A-M, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clinical Chemistry and Laboratory Medicine (CCLM) 2020; 58:1070-6.
7. Harris-Kojetin L SM, Lendon JP, Rome V, Valverde R, Caffrey C. Long-term care providers and services users in the United States, 2015-2016. Washington, DC: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics [Internet]. 2019. Accessed 2020 Jun 10. Available from: https://www.cdc.gov/nchs/data/series/sr_03/sr03_43-508.pdf
8. Cipriani G, Fiorino MD. Access to Care for Dementia Patients Suffering From COVID-19 [published online ahead of print, 2020 Apr 17]. *Am J Geriatr Psychiatry*. 2020; S1064-7481(20)30293-1. doi: 10.1016/j.jagp.2020.04.009
9. McMichael, Temet M et al. Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington. The New England journal of medicine 2020; 21:381
10. Kimball A, Hatfield KM, Arons M, et al. Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. MMWR Morbidity and Mortality Weekly Report 2020; 69:377-81.
11. Chodosh J, Weinstein BE, Blustein J. Communicating with patients through medical masks. *Submitted BMJ* June 2020.
12. Hardy CJ, Marshall CR, Golden HL, et al. Hearing and dementia. *J Neurol*. 2016;263(11):2339-2354. doi:10.1007/s00415-016-8208-y
13. Abrams HR, Loomer L, Gandhi A, Grabowski DC. Characteristics of U.S. Nursing Homes with COVID-19 Cases. Journal of the American Geriatrics Society [Internet]. 2020. Accessed 2020 Jun 10. Available from: https://www.mdlinx.com/journal-summary/characteristics-of-us-nursing-homes-with-covid-19-cases/VFRpE9YUiVJMbjtMUjvUI
14. Yourish K, Lai KKR, Ivory D, Smith M. One-Third of All U.S. Coronavirus Deaths Are Nursing Home Residents or Workers [Internet]. The New York Times 2020. Accessed 2020 Jun 10. Available from: https://www.nytimes.com/interactive/2020/05/09/us/coronavirus-cases-nursing-homes-us.html
15. Chidambaram P. State Reporting of Cases and Deaths Due to COVID-19 in Long-Term Care Facilities. [Internet]. Kaiser Family Foundartion (KFF). 2020. Accessed 2020 Jun 10. Available from: https://www.kff.org/coronavirus-covid-19/issue-brief/state-reporting-of-cases-and-deaths-due-to-covid-19-in-long-term-care-facilities/
16. Levitt AF, Ling SM. COVID-19 In the Long-Term Care Setting: The CMS Perspective [published online ahead of print]. Journal of the American Geriatrics Society. 2020; 10.1111/jgs.16562.

17. COVID-19 Emergency Declaration Blanket Waivers for Health Care Providers [Internet]. Centers for Medicaid and Medicare Services. Accessed 2020 Jun 10. Available from: https://www.cms.gov/files/document/summary-covid-19-emergency-declaration-waivers.pdf
18. Chodosh J, Price RM, Cadogan MP, et al. A Practice Improvement Education Program Using a Mentored Approach to Improve Nursing Facility Depression Care-Preliminary Data. Journal of the American Geriatrics Society 2015; 63:2395-9.
19. Sandelowski M. Combining Qualitative and Quantitative Sampling, Data Collection, and Analysis Techniques in Mixed-Method Studies. Research in Nursing & Health 2000;23(3):246-55.
20. GmbH AtSSD. ATLAS.ti: The Qualitative Data Analysis & Research Software. 2017.
21. Ayres L KK, Knafl KA. Within-case and across-case approaches to qualitative data analysis. Qualitative health research 2003;13(6):871-83.
22. Creswell JW, Clark VLP. Designing and Conducting Mixed Methods Research: SAGE Publications, Inc 2017.
23. Creswell JW. Qualitative Inquiry and Research Design: Choosing Among Five Approaches: SAGE Publications, Inc 2012.