IMPACT-C:
Improving Vaccine Uptake in Skilled Nursing Facilities

Protocol

IMPACT-C: IMPROVING VACCINE UPTAKE IN SKILLED NURSING FACILITIES

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1 PRÉCIS

1.1 Study Title: IMPACT-C: Improving Vaccine Uptake in Skilled Nursing Facilities

1.2 Objective

SARS-CoV-2 vaccine, now being administered to SNF residents and staff, has highly variable acceptance between facilities. We need to develop and disseminate effective strategies to increase vaccination immediately. For SNF residents and staff we will develop and implement a scalable multi-pronged intervention that educates, builds trust and supports the informed consent process aimed to increase SARS-CoV-2 vaccination. We will compare the rates of vaccination in staff and residents in facilities that receive electronic messaging and education (i.e., ususal care) versus rates in facilities that receive an additional multi-pronged "high touch" intervention.

1.3 Design and Outcomes

Design

We will conduct a cluster randomized trial to compare the effect of electronic messaging and education (i.e., usual care) versus a multi-pronged "high touch" intervention to reduce vaccine hesitancy in SNF staff and residents among a random sample of facilities across four SNF chains. As part of the "high touch" intervention, we will identify and train local opinion leaders. We will offer these leaders assistance through real-time support for questions and provide consenting specialists. During the second wave of vaccination, we will provide the intervention facilities with positive reinforcement for staff and we will identify local champions to garner support and empowerment of staff. Finally, in the intervention facilities we will provide additional funds to support COVID-19 testing, in order that facilities have access to enough testing kits for patient or staff who develops symptoms following vaccination.

This trial will be randomized within 4 SNF chains in order to evaluate the effect of a multi-pronged strategy to improve SARS-CoV-2 vaccine acceptance among direct care staff and long-stay nursing home residents. In four chains, eligible facilities will undergo randomization between usual care versus adding the "high touch" intervention, implemented in two waves. Randomization and roll out of the intervention will occur at the facility level.

Outcomes

The following outcomes related to SARS-CoV-2 vaccination will be measured during the period of vaccine administration and followup:

PRIMARY OUTCOME:

A binary measure (Yes or No) indicating whether a long stay nursing home resident received any doses of a SARS-CoV-2 vaccine, identified by the electronic medical records (EMR)

SECONDARY OUTCOMES:

Number of direct care staff who received any dose of a SARS-CoV-2 vaccine

1.4 Interventions and Duration

The entire trial will take place over 11-15 weeks, each intervention facility will be involved in approximately 1-3 week start up activities, 6-8 weeks of vaccine administration (in all facilities, the vaccine will be offered on three dates approximately 3-4 weeks a apart), and an additional 4 weeks of data collection. Intervention homes will follow the same timeline for enrollment and data collection. During the start-up period in the intervention facilities, the research team works with the leadership and opinion leaders in each SNF to optimize program roll-out within each unique environment.

Numerous educational resources regarding vaccination already exist. Through the American Health Care Association (AHCA), our team plans to disseminate electronic messaging and educational material regarding the COVID-19 vaccine to 12 SNF chains with some 1,000 facilities including around 100,000 direct care staff and at least 60,000 long-stay residents. This quality improvement initiative represents typical care practices (i.e., usual care), and it will include all facilities in the four chains that will take part in the trial. Select facilities within the four chains will additionally receive the "high touch" intervention, offered in two waves.

1.5 Sample Size and Population

The study sample will include some 150 facilities including around 14,000 direct care staff and at least 8,500 long-stay residents across 4 SNF chains.

2. STUDY TEAM ROSTER

2.1 Principal Investigator

Vincent Mor, PhD
Florence Grant Price Professor School of Public Health, Brown University School of Public Health
Email: vincent_mor@brown.edu

Role: Dr. Mor is the PI for the IMPACT-C supplement and will be responsible for all aspects of the trial. Specifically he will oversee the recruitment of eligible NFs and the budget for Brown University and subcontract to Insight Therapeutics.

Sarah D. Berry, MD, MPH
Research Scientist, Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife,
Associate Professor of Medicine, Harvard Medical School
Address: 1200 Centre Street, Boston, MA 02131
Phone: 617-971-5355, Fax: 617-971-5339
Email: SarahBerry@hsl.harvard.edu

Role: Together with Dr. Mor, Dr. Berry will be responsible for all aspects of the trial. Specifically she will work with Dr. Gravenstein, McConeghy and Goldfeld on the trial design, and with Dr. Johnson, Dr. Jackson, and Insight Therpeutics on the development and implementation of the intervention. She will be responsible for budget management of the HSL site, and the management of the Project Director. She will be responsible for annual project reports to the NIH and IRB approval.

2.2 Co-Investigators:

Stefan Gravenstein, MD, MPH
David S. Greer Professor of Geriatric Medicine, Director Division of Geriatrics and Palliative Medicine, Brown University
401-369-4131; 401-444-5248 (w)
Email: Stefan_Gravenstein@brown.edu

Role: Dr. Gravenstein is an investigator at Brown University with several decades of clinical vaccine and antiviral trials experience in nursing home populations. For the proposed project, Dr. Gravenstein will be instrumental in developing the analytic approach and overseeing the implementation of the intervention.

Kevin McConeghy, PharmD, MS
Email: Kevin_McConeghy@brown.edu

Role: Dr. McConeghy is an investigator at Brown University with a background in pharmacoepidemiology and clinical trials, and has worked on large cluster-randomized clinical vaccine trials with Dr. Gravenstein for 4 years, participating in methods, and leading analytic work. For the proposed project, Dr. McConeghy will be responsible for overseeing data collection elements from the facilities, and participate in analytic work related to this trial.

Keith Goldfeld, DrPH
Email: Keith.Goldfeld@nyulangone.org

Role: Dr. Goldfeld is a senior statistician at NYU, and he has more than a decade of experience with clinical trials in frail, older populations. For the proposed project, Dr. Goldfeld will be responsible for the developing the analytic approach to the trial, handling missing data, and overseeing the interpretation of the analyses.

Susan Mitchell, MD MPH:
Senior Scientist, Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife,
Professor of Medicine, Harvard Medical School
Address: 1200 Centre Street, Boston, MA 02131
Phone: 617-971-5326, Fax: 617-971-5339
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Role: Dr. Mitchell is a senior investigator at the Institute for Aging Research, Hebrew SeniorLife and the co-Director of the Interventional Studies in Aging Center (ISAC). Dr. Mitchell has considerable experience in the design and implementation of pragmatic clinical trials in the nursing home setting, and in particular among persons with Alzheimers Disease and Related Dementias (ADRD). Dr. Mitchell will provide insight during the implementation phase of the trial.

Jonathan Jackson, MD
Email: jjackson31@partners.org

Role: Dr. Jackson is a senior investigator at Massachusetts General Hospital with expertise in understanding racial disparities in healthcare. In the proposed project, Dr. Jackson will serve to inform the implementation of the intervention, as well as to inform the analytic approach to understand within facility differences in the effect of the intervention

Edward Davidson, PharmD, MPH
Phone: 757-625-6040
Email: edavidson@inther.com

Role: Dr. Davidson is a Partner of Insight Therapeutics, with expertise in nursing home educational campaigns and implementing pragmatic clinical trials. He will be responsible for the implementation of the intervention. This includes identification of the facility champion, production of a series of educational videos, delivery of frequently asked questions, distribution of items to publicize vaccination, and facilitating education.

Lisa Han, MPH
Phone: 757-625-6040
Email: lhan@inther.com

Role: Ms. Han is a partner of Insight Therapeutics, with expertise in nursing home educational campaigns and implementing pragmatic clinical trials. She will be responsible for overseeing implementation tasks, including educational material production, project website development, material distribution, and champion education and support. She will provide strategy and operational oversight and support for the high touch intervention.

David Gifford, MD, MPH
Email: dgifford.ahca.org

Role: Dr. Gifford is the Director, Center for Health Policy Evaluation in LTC at American Health Care Association. He will provide access and facilitate participation to the SNF chains. He will additionally provide crucial feedback on the implementation process and requirements for consent that will be necessary for this proposal.

2.3. Consultants

Kimberly Johnson, MD
johns196@mc.duke.edu
(919) 660-7506

Role: Dr. Johnson is a Duke geriatrician and palliative care physician, and national expert on health disparities. In the proposed project, Dr. Johnson will serve as an expert to moderate some of the informational sessions for staff and as a consultant to advice on the implementation of the intervention.

Chris Rowley, MD
Crowley1@bidmc.harvard.edu

Role: Dr. Rowley will provide expertise and advice on COVID-19 testing, as well as emerging testing technology.

Michael Mina, MD
Email: mmina@hsph.harvard.edu

Role: Dr. Mina will provide expertise and advice on COVID-19 testing, as well as emerging testing strategies.

2.4. RESEARCH TEAM MEMBERS

Maggie Syme, PhD
Project Director, Hinda and Arthur Marcus Institute for Aging Research
Address: 1200 Centre Street, Roslindale MA 02131
Phone: 617-363-8000
Email: Maggie.l.syme@gmail.com

Role: Dr. Syme will work closely with Dr. Berry to oversee all aspects of the trial. This includes regulatory compliance with the award, organizational meetings, trouble shooting problems with the facility champions, and facilitating the collection and analysis of data.

Amy Recker, MPH

Project Director, Brown University School of Public Health
Email: amy_recker@brown.edu

Role: Ms. Recker will work closely with Dr. Berry and Dr. Mor to help coordinate and oversee all aspects of the trial. This includes organizational meetings, contact and support to facility champions, and facilitation the collection and analysis of data.

Laurie Herndon, NP
Email: lauriehерndon@hsl.harvard.edu

Role: Ms. Herndon will work with Drs. Berry and Johnson to facilitate the training sessions for the facility opinion leaders.

3. STUDY OBJECTIVES

3.1 Primary Objective

Aim 1: To conduct a cluster randomized controlled trial (~150 facilities across 4 SNF chains) to compare the number of SNF residents who receive the SARS-CoV-2 vaccine in facilities with usual care versus facilities randomized to the multi-pronged intervention.

H1: We hypothesize that the intervention will increase vaccination of SNF residents by at least 10 percentage points versus facilities usual care alone.

3.2. Secondary Objectives

Aim 2. To compare the number of direct care staff who receive any SARS-CoV-2 vaccination in facilities with usual care versus facilities randomized to the multi-pronged intervention.

H2. We hypothesize that staff of NFs with the intervention will have at least a 10 percentage point greater vaccine uptake of vaccine than staff in SNFs that do not participate in the high touch intervention

Aim 3. To determine whether the intervention will mitigate resident and staff disparities in SARS-CoV-2 vaccination by race/ethnicity.

H3. We hypothesize that within intervention SNFs, improvements in vaccine uptake will be similar across staff and resident race/ethnicities.

Aim 4. To assess the experiences of opinion leaders in intervention facilities in terms of their perceived barriers to intervention implementation, organizational culture, and overall experience with the intervention.

H4: We hypothesize that there will be a high variability in experiences across facility opinion leaders that will inform the results of the trial.

4. BACKGROUND AND RATIONALE

Epidemiology of COVID-19 in SNFs. COVID-19 has disproportionately affected nursing facility (NF) staff and residents in the U.S., with the highest rates of infection and mortality in both groups.[1, 2] Facility outbreaks vary geographically and over time.[3] Aside from morbidity, COVID-19 has been extremely costly for NFs due to declining admissions, purchasing of personal protective equipment (PPE)[4-6] and testing. It is estimated the U.S. government may pay more than $15 billion to cover COVID-19 costs in SNFs alone.[7]

Vaccine availability. Three vaccine candidates are expected to be released in December 2020, with SNF direct care staff and residents scheduled to be in the first group in the country to be offered the vaccine. The first two vaccines (Pfizer and Moderna) use a novel microRNA technology. Phase two trials have already been conducted on over 50,000 and 30,000 persons for the Pfizer and Moderna vaccines, respectively, with demonstrated safety and efficacy against COVID-19.[8]

Staff barriers to vaccination. Despite the promise of these leading vaccine candidates in decreasing the rates of COVID-19 and serious illness, there are many barriers to having SNF staff receive the vaccine. First, because the vaccines will all be approved by an Emergency Use Authorization (EUA), employers will not be able to mandate that staff receive the vaccine. Second, in a recent survey of 1,250 Black and Latinx Americans, only 18% of Blacks and 31% of Latinx report that they would definitely get vaccinated if the vaccine were free.[9] This is consistent with historical differences in rates of influenza vaccination among Black and Latinx populations relative to non-Hispanic Whites.[10] A primary reason many Blacks/Latinx are hesitant to accept vaccination is a lack of trust that the vaccine is safe and in the authorities (including their employers) advocating vaccination.[9] This is alarming in the SNF setting where the largest group of direct care workers are nursing assistants (NA), and 50% of NA identify as Black/Latinx.[11, 12] A recent survey conducted by the National Association of Health Care Assistants (the major professional organization of NAs), confirmed that most NAs do not plan to be vaccinated for SARS-CoV-2.[13] Finally, staff may express vaccine hesitancy give a fear of side effects and concern they will be unable to work. Point-of-care COVID-19 testing offers a practical solution to determine whether staff who exhibit symptoms following vaccination are able to work; however, low resourced facilities are still having difficulty accessing an adequate supply of test kits.[14] Therefore, we believe that without a multi-pronged intervention to reduce vaccine hesitancy and dispel misinformation, vaccination rates among SNF direct care workers will be low, compromising efforts to protect SNF residents.

Resident barriers to vaccination. There are also major challenges to insuring that SNF residents are vaccinated. First, historically Black SNF residents are less likely to receive influenza and pneumococcal vaccines than are White residents.[5, 6] Most of this difference has been explained by inequities in offering the vaccine between facilities rather than within facility differences, although these still remain.[15, 16] SNFs are highly segregated along racial lines, with resource-poor facilities tending to have larger non-white populations. Second, the first two vaccines likely to be released require ultra-cold storage meaning SNFs are not equipped to store these vaccines. CMS has encouraged SNFs to overcome this barrier by partnering with pharmacy

chains (e.g. Walgreens) that will deliver the vaccine to staff and residents. Even though verbal informed consent will be allowed, knowing how many residents and staff will accept the vaccine, prior to the vaccine supplier being at the NH, will be critical to minimize waste and maintain maximal efficiency given the finite staffing resources available to ensure all NHs are offered vaccine in a timely fashion. We anticipate organizing the effort and coordination with the pharmacy provider will be an enormous barrier for facilities, but in particular, for the resource-poor facilities with larger Black and Latinx populations who may not have the capacity to systematically reach out to families to inquire about willingness to be vaccinated, obtain a verbal or written consent, and manage the documentation needed.

Interventions to reduce disparities in SNFs. Our team has extensive experience in implementing interventions to improve healthcare and reduce racial disparities in NFs, including experience with influenza vaccinations.[17-19] Based on our experience and a review of interventions targeting influenza vaccination in SNFs[20], we anticipate that a multi-pronged approach will be necessary to overcome these sizeable barriers and successfully implement the SARS-CoV-2 vaccine among SNF staff and residents. The multi-pronged approach should include the following components:

1. **Electronic Messaging and Education.** Messaging promoting prosocial motivations (i.e., protecting one's community from COVID-19) has been demonstrated to be a stronger predictor of willingness to practice preventive behaviors for COVID-19 as compared with messaging promoting personal motivations (i.e., protecting oneself from COVID-19).[21] This is consistent with systematic reviews of interventions to increase influenza vaccination in healthcare workers. [22] As part of a quality improvement initiative through AHCA, we will disseminate videos of staff from different SNFs stating their reason for choosing to be vaccinated. Messages may be disseminated by 12 SNF chains by email, text, and on social media. Messages will have links to Frequently Asked Questions (FAQs) on the web as well as broader Public Service Announcements (PSAs). This electronic messaging and education will be considered the 'usual care' of the cluster randomized controlled trial described herein. Only four of these 12 chains will participate in the trial itself.

2. **Facility Opinion Leader.** Our own experience in SNFs suggests that providing educational material by itself is less effective in changing behaviors than when a facility champion is identified among the direct care staff to reinforce the educational message.[23, 24] In one trial of influenza immunization among SNF staff, researchers noted that staff were typically siloed by job type,[25] and thus, multiple leaders should ideally be selected for each job type. We plan to identify up to four individuals within each facility who are trusted "opinion leaders," and can receive training so that they may more confidently address criticism or questions from their peers.

3. **Building Trust Locally.** Successful response models to prior epidemics including H1N1 and Ebola have required strong community engagement and a "bottom-up" approach.[26] We plan to work with the facility opinion leaders to identify a local well- respected member

of the community (e.g., minister, teacher, health care provider) who will help promote trust in the SARS-CoV-2 vaccine.

4. Positive Reinforcement. Health communication literature suggests that it is equally if not more important to address positive emotions (e.g., building altruism and hope) as it is negative emotions (e.g., combatting fear and anxiety) when addressing vaccine hesitancy.[27] Providing staff goodies (e.g., buttons, T-shirts, masks) as well as promoting positive images on social media have been successful strategies in increasing influenza vaccination[20] and improving other health behaviors among SNF staff.

5. Consenting Specialist. Low-resource SNFs will have very limited time or ability to counsel proxies on the risks and benefits of receiving the SARS-CoV-2 vaccine. A remote consenting specialist could overcome this barrier.

6. Testing Supplies. Phase III trials suggest that as many as 16% of persons will experience a fever and approximately half experience fatigue and headache, particularly after the second dose.[8] The CDC has recently provided guidance on the use of point-of-care COVID-19 testing following vaccination that may be helpful to determine if staff are able to work or if residents need to be isolated.[28, 29] We plan to provide additional funds ($10,000) for facilities to use to purchase COVID-19 testing kits, so that these facilities are able to follow CDC guidelines for residents and staff who have symptoms after vaccination.

Summary of significance.

The significance is summarized as follows: 1. COVID-19 has disproportionately affected SNF workers and residents; 2. Several SARS-CoV-2 vaccines are expected to be available starting December 2020, and facilities will only have a limited number of opportunities to receive the vaccine through a consulting pharmacy company; 3. Direct care staff, many of whom are Black and Latinx, have expressed considerable hesitancy regarding the safety of the vaccine; 4. There is a history of racial disparities in healthcare across SNFs, including a reduced tendency for Black residents to receive influenza vaccines; 5. Obtaining clinical consent for vaccination will be a second, major barrier to successful vaccination of residents along with obtaining a firm list of staff and residents willing to be vaccinated prior to pharmacy vaccinators coming into the NH to minimize vaccine waste and ensure efficiency; 6. Low resource facilities often house the largest numbers of non-white minority residents, and it will be challenging for these facilities to overcome these sizeable barriers to vaccination without additional support; 7. A multi-pronged approach that centers on building trust, empowering staff opinion leaders, providing positive reinforcement, easing the process of obtaining informed consent for the vaccine, aid in organizing the on-site clinic for staff and residents, and ensuring adequate testing supplies is a promising strategy to improve acceptance of SARS-CoV-2 vaccination among staff and residents.

5. STUDY DESIGN

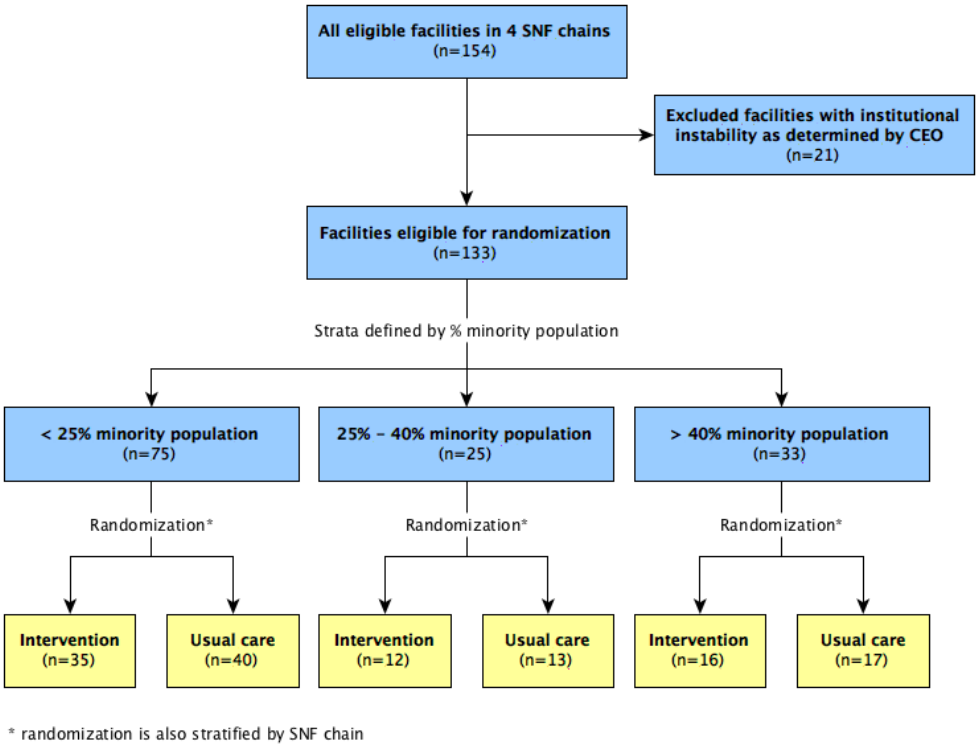
This will be a cluster randomized trial where the intervention is applied at the facility level. Our primary interest is the effect of this intervention on SNFs that are characterized by having a relatively high proportion of residents who are Black or Latinx. The 4 SNF chains that have been selected have already given assent to participate in this trial. Facilities that are ineligible (e.g., institutional instability) have been excluded from the list of facilities for randomization.

We will then stratify facilities into three categories based on racial composition of residents:

(1) < 25% Black and Latinx residents
(2) 25-40% Black and Latinx residents
(3) > 40% Black and Latinx residents

Facilities will undergo constrained randomization within each chain and stratum to ensure that the proportion of Black and Latinx residents is balanced across the intervention arms. We will randomize a total of 60 SNFs to the intervention, allocated proportionally across the strata. The SNFs that were removed due to institutional instability will be compared separately to the control arm to assess potential bias due to selection into the study.

The Figure below describes the random allocation of facilities:



Staff in facilities randomized to intervention arm will be informed by corporate leadership that they will be participating in a program to maximize COVID 19 vaccination among staff and residents. They will not be informed that this is part of a trial. Individual SNFs will be randomized to the intervention or usual care; randomization will be stratified by chain and by the proportion of minority residents based on three groups: <25%, 25%-40%, >40%. The research implementation team will not be masked to facility assignment. However, the PIs (Mor, Mitchell), the lead statistician (Dr. Goldfeld) and programmers will be masked.

6. SELECTION AND ENROLLMENT OF PARTICIPANTS

The four SNF chains that have been selected to participate in this trial include Vetter, Nexion, Mission, and Genesis (Northeast facilities only). The intervention will be rolled out facility-wide. Participation occurs at 3 levels. SNFs will be recruited and enrolled into the study. Site administrators who agree to participate in the study will serve as gatekeepers within their facility. Direct care staff will agree to serve as Opinion Leaders. Residents within the facility are eligible if they qualify as long-stay (defined below).

6.1 Facility inclusion criteria

1) Among Genesis corporation, location in the Northeast (PA, NJ, CT, MA, RI, NH, VT, ME) AND at least 15% of residents identify as Black or Latinx.

6.2 Facility exclusion criteria

1) Evidence of institutional instability at time of recruitment
2) Other reason (as determined by the SNF CEO) for inability to participate in the high touch intervention

6.3 Resident inclusion criteria

1) Long-stay will be defined as residence in the same facility for at least 100 days with no more than 10 days outside the facility on the date the first round of vaccines were delivered

6.4 Resident exclusion criteria

1) Living in the facility for less than 100 days
2) Resident died/transferred during baseline and before the date the first vaccine was delivered to the facility

6.5 Staff inclusion criteria

1). Staff (i.e., nurses, care aids, dietary, and housekeeping) should provide care in the facility during the time of any of the vaccine clinics.

6.6 Staff exclusion criteria

1) Not a "usual" provider within the NH (i.e. visiting hospice provider)

6.7 Study Enrollment Procedures

All SNFs in the four chains are prepared to receive electronic messaging and educational material (i.e., usual care) through the American Health Care Association (AHCA). Within the 4 SNF chains that have agreed to participate in the trial, we will ask the CEOs if there are any facilities that should be excluded due to leadership instability or other inability to participate in the multi-pronged intervention. Remaining facilities will be randomized to additionally receive the multi-pronged intervention versus continuing usual care.

7. STUDY INTERVENTIONS ADMINISTRATION AND DURATION

The entire trial will take place over 11-15 weeks: each facility in the high touch intervention will be involved in approximately 1-3 week start up activities, 6-8 weeks of vaccine administration (three scheduled deliveries for vaccine approximately 3-4 weeks a part), and 4 weeks of data collection. Facilities in the usual care group will follow the same timeline for enrollment and data collection. During the start-up period in the high touch facilities, the research team works with the leadership and opinion leaders in each SNF to optimize program roll-out within each unique environment.

7.1 Usual Care (Electronic Messaging and Education).

All facilities affiliated with the AHCA and IMPACT Collaboratory (12 SNF chains with at least 1,000 facilities) will be offered electronic messaging and education regarding the COVID-19 vaccine. This material stems from the CDC and AMDA resources and represents a suggested approach to reduce vaccine hesitancy in staff and residents/proxies (e.g., LARs, POAs). *This electronic quality improvement material will be developed as part of a QI initiative and disseminated by AHCA* to the SNF chains and using social media. Within the trial that includes 4 of the 12 SNF chains, this will be considered 'usual care' in the control arm. Specific examples of electronic messaging and education include:

a. *Electronic Messaging* – Direct care staff will be encouraged to post a selfie or short video encouraging others to get vaccinated. These messages will be disseminated through social media (e.g., Instagram). Messages will be linked with PSAs and FAQs regarding vaccination that reinforce the safety and efficacy of the vaccine.
b. *PSAs* – Our research team, in conjunction with AHCA, will produce a series of short (2-5 minute) video(s) designed to promote trust in the safety and efficacy of the SARS-CoV-2 vaccine, particularly among Black and Latinx direct care workers. The videos will include direct care staff (NA and or floor nurse) giving a short testimonial about their experience with vaccination and promoting altruistic feelings about vaccination for the safety of others. If possible, we will include a short testimonial from a well-respected member of society specifically encouraging vaccination in SNF staff and residents. SNF leadership will encourage all staff to watch these videos during the start-up period as part of regularly scheduled team huddles/meetings or individually. In addition, these links will be provided to all proxies via letter or email, when they receive the FDA mandated Fact Sheet regarding the vaccine.
c. *FAQs*- The AHCA will additionally disseminate suggested responses for frequently asked questions that staff and residents/proxies may have about the vaccine. This material has been reviewed by members of the National Association of Care Health Assistants (NACHA). SNF leadership will distribute these widely to staff during the start-up period. We will encourage SNFs to include the FAQ sheet to all proxies by letter or email as part of the material distributed with the vaccine Fact Sheet.

7.2 HIGH TOUCH MULTI-PRONGED INTERVENTION

Among four SNF chains, we will randomize eligible facilities to receive an additional "high touch" intervention. *These high touch facilities will receive the electronic messaging and educational material described above.* In addition these facilities will work with our research team on the following:

1. **Facility Opinion Leader.** At each intervention facility, our research team will work with the facility administration to identify local opinion leaders among nursing assistants (NA), nursing, dietary, and housekeeping. The opinion leaders will participate in the following activities: 1) Participate in an initial informational meeting with the research team and other facility opinion leaders; 2) Identify a local champion who could help participate in educational materials; 3) Participate in the social media messaging described in the Electronic Messaging section above; 4) Engage the research team for support and problem solving.

   We will invite all of the opinion leaders to participate in a one hour virtual informational meeting with members of our research team and other facility leaders. Meetings will be organized by discipline (e.g., nursing, dietary) and SNF chain. We will offer a few make-up sessions for staff who are unable to attend. During these meetings we will cover basic information on vaccine safety and efficacy, leaving the majority of time for an open question and answer session. These sessions will NOT be recorded. Opinion leaders who participate in these meetings will be given a $50 gift card for their time.

   Our research team will provide opinion leaders with direct contact information (email and phone number) of the study team so that they may ask questions during implementation. Insight Therapeutics will also work to identify a support team that can offer guidance and problem solve during implementation.

2. **Consenting Specialist.** Through Insight Therapeutics, our research team will employ external staff members to facilitate the clinical consent for vaccination process. Each facility will make up to ten referrals of residents who were not vaccinated during the first of the three available vaccine dates to our consenting specialists. Consenting specialists will contact each proxy, review risks and benefits of the vaccine, and answer questions. We will provide a 1-800 number for proxies who have additional questions/hesitancy, and we will offer a group zoom call for interested proxies to review risks and benefits. <u>As indicated, this consenting process will be a clinical consent for the vaccination itself</u> – not a study-specific informed consent process to participate in research. We are seeking a waiver of informed consent for the overall intervention study.

3. **Building Trust Locally.** The facility opinion leaders will be encouraged to identify well respected persons in the community (e.g., minister, teacher, government leader) who are willing to provide a message promoting trust in the vaccine. Through Insight Therapeutics, our research team will reach out to these leaders and coordinate the video messages and implementation plan. Messages will be distributed widely within a facility by email, website, text and/or social media. Further, our research team will prepare the community leaders to serve as an additional support for the facility opinion leaders during implementation.

4. **Positive Reinforcement.** Our research team will create and distribute buttons, T-shirts, and masks that promote awareness about vaccination (e.g., Ask me about the COVID-19 vaccine! OR Vaccinated for You!). These items will be distributed through facility leadership at each facility, with recommendations to give each staff member these goodies when vaccinated.

5. **Testing Supplies.** Our research team will provide funds ($10,000) to each facility in the high touch intervention arm, that the facility may use to acquire additional COVID-19 testing kits. This will enable frequent testing of any residents and staff that experience symptoms following vaccination. Given that the cost of most point-of-care testing kits is around $50, these funds will support the cost of approximately 200 test kits. We will suggest that facilities follow the CDC recommendations for testing following vaccination.[28, 29] Our research team will additionally facilitate kits for facilities that are experiencing difficulty securing the test kits.

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The high touch intervention will be implemented in two waves. For the first cycle of vaccine administration we will focus on identifying opinion leaders and positive reinforcement. During the second round we will add building trust locally, a consenting specialist, and testing supplies.

8. DATA COLLECTION ELEMENTS AND PROTOCOL

8.1 Facility Data

Nursing home data are collected prior to the start of the study for descriptive purposes and to inform the development of a list of eligible facilities for recruitment. These include elements from Nursing Home Compare, including: the number of beds, hospital-based, special care dementia unit, nursing and nursing assistant hours/resident/day, and number of deficiencies on state inspections.

8.2 Resident Data

Resident data is already being collected for all facilities within the 4 chains as part of the RADx-UP supplement. Existing data transfer agreements from all 4 chains have been signed and authorized. We plan to use data from the electronic medical record, as well as data from the Minimum Data Set (MDS) for this study. Resident characteristics will be obtained during baseline only (that is during the 3 months before the vaccine is first delivered to the facility) whereas vaccination data will be obtained during the 6-8 weeks of implementation and 4 weeks of followup..

Demographic: age, gender, race, ethnicity, proxy contact information (for "high touch" facilities only in need of consenting specialist) and relationship to resident.

Medical co-morbidity: All active medical diagnoses. History of COVID-19 infection from testing results and diagnoses in EMR.
Functional status: Katz Activities of Daily Living Scale from MDS; Dementia severity (Cognitive Functional Scale)

Influenza Vaccination: Using EMR and MDS data we will also determine if each resident received the influenza vaccine during the 2020-2021 season

SARS-CoV-2 Vaccination: Using the EMR we will determine if each resident received any dose of the SARS-CoV-2 vaccine within the vaccine implementation period and 4 weeks from the last date the vaccine was delivered to the facility.

8.3. Staff data

Each facility will provide our team with a log of aggregated staff vaccination (counts of number of staff vaccinated). We will calculate the number of eligible staff in a facility using the Kronos time and effort reports along with Payroll-Based Journal data.

For Genesis facility only, we will receive additional person level information on staff demographics (job description, race/ethnicity) from Human Resources.

In addition, the facility opinion leaders will be surveyed with regards to their experience of the intervention components. This anonymous data will be collected via a Qualtrics survey sent directly to all opinion leaders.

9. STATISTICAL ANALYSIS

9.1 **General Design**: The hypothesis that will be tested is whether facilities that receive the high touch multi-pronged intervention will achieve a greater number of staff and residents vaccinated as compared with facilities randomized to usual care.

9.2 Sample Size and Randomization:

9.3 Outcomes

Primary Outcome – The primary outcome will be a binary measure (Yes or No) indicating whether an eligible resident received any doses of the vaccine during the study period.

Secondary Outcome – The secondary outcome will be the number of staff that received any dose of the vaccine during the study period. This will be the count of all eligible staff who received one or more doses of the vaccine.

We will examine the primary outcome separately by race/ethnicity (defined as White, Black, Latinx, and Other). In one SNF chain (Genesis) we will examine the secondary outcome separately by race/ethnicity.

9.4 Approach

The treatment effect based on the primary binary outcome will be the estimated odds ratio (OR). The primary outcome will be analyzed at the individual resident level using a mixed effects generalized linear model with a binomial distribution that includes both network fixed effects, race/ethnicity strata-specific fixed effects as well as nursing home-specific random effects:

$$log\left(\frac{P(Y_{ijk}=1)}{1-P(Y_{ijk}=1)}\right) = \beta_0 + \beta_1 T_{jk} + \beta_2(S_{jk}=2) + \beta_3(S_{jk}=3) + \alpha_k + b_{jk},$$

where Y_{ijk} is an indicator variable for resident *i* in nursing home *j*/network *k*, where $k \in (1,2,3,4)$; $Y_{ijk}=1$ if the resident received the vaccine and $Y_{ijk}=0$ otherwise. T_{jk} is an indicator variable for nursing home *j*/network *k*; $T_{jk}=1$ if the nursing home is in the intervention arm and $T_{jk}=0$ if in the control arm. S_{jk} is the strata indicator, $S_{jk} \in (1,2,3)$. α_k is the network-specific fixed effect for network *k*. b_j is the nursing home-specific random effect, which has a normal distribution with mean 0 and standard deviation σ_b. The parameter β_1 is the log-OR of vaccination, comparing the odds of vaccination for those in the intervention arm with the odds of vaccination for those in the control arm.

We will estimate an odds ratio ($\hat{\beta}_1$) along with a 95% confidence interval. We will conduct a two-sided hypothesis test based on $H_0: \beta_1 = 0\ vs.\ H_1: \beta_1 \neq 0$ using an α-level 0.05. All analyses will be conducted using the latest version of R (currently 4.0.3, R Foundation for Statistical Computing, Vienna, Austria).

We will use an intention-to-treat approach as our primary analytic approach, including all facilities that were randomized to the intervention regardless of implementation of the intervention components. Additional exploratory analyses will estimate a complier average causal effect to assess the effect of the intervention on those SNFs who fully engage in the intervention.

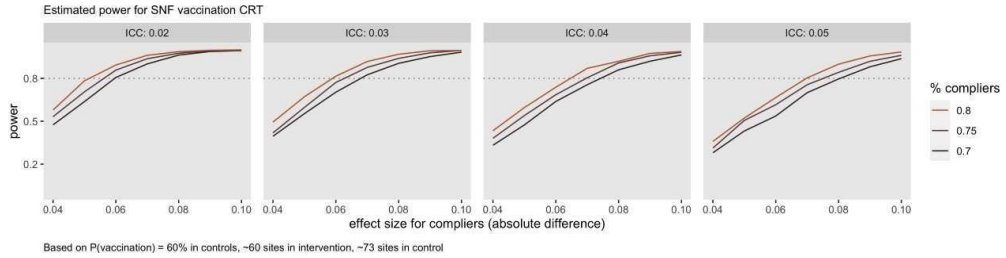
Because the components of the "high touch" intervention will be rolled out sequentially in waves (e.g., first facility champion and positive reinforcement, then building local trust, consenting specialist and additional testing supplies) we will examine the individual and additive effects of program components, if possible.

A similar approach will be used to determine the effect of the high touch intervention on staff vaccination.

The logistic model described for the primary analysis will be extended to include race and ethnicity indicators as well as interaction terms, to better understand if the treatment effect is heterogeneous across different subgroups of residents.

9.5 POWER ESTIMATE

Using the **crtpwr.2prop** function in the R package **clusterPower** (version 0.6.111), we estimate that with **60** facilities in the intervention group, we will have 90% power to observe a difference of 10 percentage points and 80% power to observe a difference of 8 percentage points, under the assumption that the probability of vaccination is 70% in the intervention facilities, an intraclass correlation of 0.05, and average cluster size of 60. This is likely a conservative estimate of the intraclass correlation, and we will have 80% power to observe a difference of just 6 percentage points if the intraclass correlation is 0.02 and other assumptions remain unchanged (see Figure).



10. HUMAN SUBJECT PROTECTIONS

10.1 Sources of Data

Resident EMR: The residents' EMR medical is already being transferred at regular intervals to secure servers at Brown University as part of this RADx-UP supplement. This will include information the information regarding vaccination and history of COVID-19 infection.

Minimum Data Set: We already have DUAs in place to allow use of MDS data for all 12 SNF chains. This will be used to provide descriptive information about residents in the trial.

Facility logs: Facilities will provide staff COVID-19 vaccination logs (binary counts of the number of staff vaccinated).

Kronos and time and effort reporting: We already have data transfer agreements in place for Kronos, and we will be using this data to identify the number of eligible staff in each facility.

Payroll-Based Journal data: This publicly available dataset via the Centers for Medicare and Medicaid Services will provide staffing estimates from total hours worked per day for all study facilities.

Genesis Human Resources Data: We already have data transfer agreements in place to share demographic information on staff within the Genesis facility, including age, length of time of employment, and race/ethnicity.

Proxy name and contact: In the intervention homes only, our study team and credentialing specialists (through Insight Therapeutics) will receive referrals with the name, contact number and relationship of proxies who have not responded to the electronic informed consent request in the first round of vaccination. This information will be stored securely either in locked cabinets or behind a secure server and will NOT be distributed or used in any of the analysis.

Opinion leader survey data: We will collect anonymous data from opinion leaders via a Qualtrics survey that will examined at an aggregate level. The information will be stored securely via a secured server.

11. POTENTIAL RISKS OF STUDY PROCEDURES

The study meets criteria for minimal risk. Our intervention to reduce vaccine hesitancy is based on suggestions from experts and recommendations from leading organizations, the risk of harm is low.

We will request both a waiver of informed consent under the Common Rule and a HIPAA waiver of authorization under the HIPAA Privacy Act for resident and staff participation in this study.

11.1 Potential Medical Risk to Study Participants

Data from the Pfizer vaccine Phase III studies suggests that the risk of adverse events from vaccination is low, even in residents over the age of 65.[8] The most common side effects are arm pain, followed by fatigue, headache, chills and fever. Although side effects of the vaccine

itself are not directly related to our intervention, we do plan to collect and report information on adverse events among residents in all facilities (see description below).

We do not anticipate any potential psycho-social risks discomforts or inconveniences of study procedures beyond those encountered in usual care practices. The intervention provides information for proxies and staff about the safety and efficacy of the vaccine. The intervention will be rolled out at a facility level. Staff and proxies do not have to view any of the electronic material or participate in any training sessions that we will provide.

The risk of loss of confidentiality is low. Our team is already collecting this data as part of existing data transfer agreements with provisions to keep identifiable data safe. Staff who participate in the Opinion Leader training sessions will need to provide their name and facility, in order to receive reimbursement with an e-gift card. This list of names will be kept behind a secure server and will NOT be distributed or used in any of the analysis. The consenting specialists will receive referrals with confidential information including patient and proxy name. This information will be kept behind a secure server and will NOT be distributed or used in any of the analyses.

One additional potential burden of this study is the time commitment of the SNF staff in to address questions raised by the electronic material we will provide. We will provide staff will a list of FAQs that may be helpful. In addition, for the intervention facilities we will offer some training and support for facility opinion leaders.

11.3 Adverse Events and Serious Adverse Events

This is a study to reduce vaccine hesitancy and we do not anticipate any study related adverse events to occur in this study. Separately, members of our team are monitoring adverse side effects of the vaccine in residents within one SNF chain (Genesis).

AE/SAE Definitions:

The study will adhere to the definitions for AEs and SAEs stipulated in the NIA Adverse Event and Serious Adverse Event Guidelines as outlined below.

AE Definition: AE is any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

SAE Definition: SAEs consist of any adverse event that results in death; requires hospitalization; or anaphylaxis/ meets the Centers for Disease Control definition of serious adverse events potentially associated with the vaccine (CDC weblink)

Reporting Procedures

The study team will collect information on SAEs (deaths, hospitalizations, and CDC defined potential serious related adverse events) among residents using the Electronic Medical Records (EMR). This information is sent securely to Brown University from some facility daily, for other data is transmitted weekly or monthly.

We propose the following reporting schedule for AEs and SAEs:

- All **adverse events that are both serious (SAE) and unexpected** (i.e., have not been previously reported for the study's intervention) should be reported to the IRB, NIA PO and to the NIA-Appointed Safety Officer (SO) within 48 hours of the study's knowledge of SAE.
- The summary of all other SAEs should be reported to NIA PO and to the SO along with recruitment and retention milestones, quarterly (unless otherwise requested by the SO). The SO will make recommendations to the DSMB and the NIA PO particularly regarding the *related* SAEs and recruitment and retention milestones. Expected SAEs unrelated to the trial intervention are listed in DSMP and include death, hospitalization, and vaccine-related adverse reactions as per CDC (i.e., anaphylaxis). There are no expected SAEs related to the trial intervention which aims to reduce vaccine hesitancy.
- The DSMB provides overall data and safety monitoring oversight for the study and makes recommendation to the NIA regarding study continuation.
- All deaths will be reported to the Safety Officer, IMPACT-C Collaboratory Regulatory and Data Team Leader (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya) within 24 hours of study's knowledge of death.
- AEs will be reported per IRB policies and also to IMPACT Collaboratory Regulatory and Data Team Leader (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer at minimum every 6 months, or at a frequency requested by NIA and/or by the DSMB.

11.2 Safety Monitoring

As agreed upon by the NIA and overseeing project officer, Dr. Partha Bhattacharyya, safety monitoring will be the responsibility of a Data Safety Monitor (DSM). Additionally, the project officer will appoint a Safety Officer. Given the urgent need to begin this study immediately, we will review any issues raised by the data safety monitoring officer simultaneously with IRB review. Similarly, given the very short timeline for vaccine administration in SNFs, we will not plan an interim DSM meeting, but we will provide the project officer and SO the SAE reports quarterly, or sooner if available, and they will notify DSMB of related SAEs. The DSM may determine the need to stop the continuation of the study based on examination of these reports.

12. INTERVENTION DISCONTINUATION

The study may be discontinued at any time by the IRB, the NIA, OHRP or other government agencies as part of their duties to ensure that research participants are protected. Individual SNFs in the intervention arm may withdraw from study participation at any time at the discretion of their senior management or corporate supervisors. Staff and proxies or residents can opt out of

viewing any of the electronic material we will provide. Facilities may choose to implement only some of the intervention. Variation in implementation is expected in clinical practice and as part of this pragmatic trial.

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