PROTOCOL TITLE:

Keeping rural minority 'essential' workplaces open safely during the COVID-19 pandemic: The role of frequent point-of-care molecular workplace surveillance for miners (Short title: The Miners' Pandemic Project)

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REGULATORY FRAMEWORK:

Please indicate all that apply (please note that the regulatory framework **does not** mean the funding source):

☐	DOD (Department of Defense)
☐	DOE (Department of Energy)
☐	DOJ (Department of Justice)
☐	ED (Department of Education)
☐	EPA (Environmental Protection Agency)
☐	FDA (Food and Drug Administration)
☒	HHS (Department of Health and Human Services)
☐	VA
☐	Other:

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CLINICAL TRIALS

PROTOCOL TITLE: Keeping rural minority 'essential' workplaces open safely during the COVID-19 pandemic: The role of frequent point-of-care molecular workplace surveillance for miners

Is this a clinical trial per the NIH definition of a Clinical Trial? ☒ Yes ☐ No

NIH Definition of a Clinical Trial:

"A research study in which one or more human subjects are prospectively assigned to one or more interventions. An "intervention" is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes."

Use the following four questions to determine the difference between a clinical study and a clinical trial:

1) Does the study involve human participants? ☒ Yes ☐ No
2) Are the participants prospectively assigned to an intervention? ☒ Yes ☐ No
3) Is the study designed to evaluate the effect of the intervention on the participants? ☒ Yes ☐ No
4) Is the effect being evaluated a health-related biomedical or behavioral outcome? ☒ Yes ☐ No

Note that if the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if…

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention

If yes to all 4 questions, please confirm that the research team is familiar with and agrees to comply with the investigator requirement to register the study on the ClinicalTrials.gov database. Additionally, the approved consent document(s) must be uploaded to the ClinicalTrials.gov database ☒ Yes ☐ No

For any assistance with registration of your trial or the requirements, please contact HSC-CTSCResearchConcierge@salud.unm.edu

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1. Objectives

The *long-term goal* of the study is to mitigate the spread of the pandemic in miners, a population of high-risk, rural essential workers who are susceptible and vulnerable to COVID-19, partly based on exposure to particulate air pollution, and who are predominantly racial/ethnic minorities in New Mexico (NM) (3, 11). The study *objective* is to provide proof-of-principle for frequent point-of-care molecular testing as a workplace surveillance tool to monitor and prevent the spread of SARS-CoV-2 infection in this unique population. The *central hypothesis* is that frequent workplace molecular surveillance is an effective method to reduce SARS-CoV-2 infection and discover novel host risk factors for the virus. The site of molecular surveillance (intervention site) will be a surface coal mine in McKinley County, NM, located just outside the Eastern Agency of the Navajo Nation, comprised of 66% minority miners. This site offers a unique opportunity for a community-based study of SARS–CoV-2 infection in this population. Miners at the intervention site will provide nasal swabs before beginning their work shift on alternate days that will be analyzed with a 'screening' molecular test (12). This test is ideal because it is low cost, simple, portable, point-of-care, rapid, and can be performed by minimally trained professionals in low-infrastructure settings. The control site is a similar coal mine in Campbell County, Wyoming (WY). Both mines, operated by the same company, have similar engineering, administrative, and personal protective measures in place. The *rationale* for this study is to establish the suitability of longitudinal molecular surveillance to prevent and control SARS–CoV-2 infection in this unique population by completing the following specific aims.

Specific Aim 1: To determine the acceptance rate to frequent point-of-care molecular workplace surveillance among miners. *Hypothesis 1:* Miners will have a cumulative acceptance rate of frequent testing at ≥85%, with the added objective of exploring difference in acceptance by miner characteristics.

Specific Aim 2: To determine the ability to detect the presence of SARS-CoV-2 by point-of-care molecular workplace surveillance in a real-world setting of miners.
Hypothesis 2: The sensitivity of the screening test in a real-world study setting is a) comparable to that described by others in controlled settings, and b) positively associated with viral load in upper respiratory specimens (latter measured in nose and nasopharynx using quantitative reverse transcriptase-polymerase chain reaction or RT-PCR).

Specific Aim 3: To determine the effectiveness and implementation costs of frequent point-of-care molecular workplace surveillance on reducing incident infection rates of SARS-CoV-2.
Hypothesis 3A: Frequent point-of-care molecular testing over up to twelve months in the intervention mine will result in lower incident seropositivity rates compared to the control mine. *Hypothesis 3B:* Frequent point-of-care molecular surveillance in the intervention mine is cost-effective compared to the control mine.

Specific Aim 4: To determine novel predictive factors associated with incident SARS-CoV-2 infection, tests, and vaccination in miners. *Hypothesis 4A*: Miners with incident infection demonstrate less frequent use of cloth face-coverings outside the workplace, greater mine dust exposure intensity, presence of dust-related lung

disease, and racial/ethnic minority status than those not infected. *Hypothesis 4B:* Test and vaccine uptake by miners is predicted by specific barriers and facilitators.

Hypothesis 4B involves a separate but related study, titled "Facilitators and barriers for COVID-19 testing uptake and its impact on vaccine uptake in a rural diverse essential workplace (Assaf/Sood, Co-PIs; NIH 1U23MD016258-01 RADx-UP Central Data Coordination Center Rapid Research Pilot Project)". The objective is to determine facilitators and barriers to COVID-19 test uptake, and the impact of the latter on vaccine uptake, at a surface coal mine. This study involves the administration of a questionnaire once between 6 and 12 months time point.

2. Background

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome-related coronavirus-2 (SARS–CoV-2) infection, is a novel disease, frequently transmitted at the workplace. Rural workers are increasingly affected, particularly racial/ethnic minorities (1-3). In New Mexico (NM), a rural, minority-majority, and medically underserved state, the greatest impact from COVID-19 is seen in McKinley County, in and around the Navajo Nation. The high risk of infection in minority communities could be due to genetic factors, immunological differences, social determinants of health (4), comorbidities, and/or high prevalence of concomitant co-exposures (1, 5, 6), in alignment with COVID-19 known risk factors (7-10). Despite sentinel studies in health care workers, meatpackers, and cruise ship workers, there are limited studies on the spread of SARS–CoV-2 infection in rural essential workers with health disparities. This critical *gap-in-knowledge* must be addressed to develop and implement novel pandemic strategies to keep rural minority essential workplaces open, particularly in environments such as coal mines, which are unable to use physical distancing, flexible schedules, or telecommuting interventions (3).

Scientific Premise

Essential workers: An estimated 15 million US workers provide essential services during the pandemic. 'Essential' services are deemed critical to societal infrastructure and are crucial for rural economies. Initial reports have highlighted the risk imposed on health care workers during the pandemic. However, essential work extends beyond health care. Despite being categorized as essential, many rural workers have not been adequately tested and studied for SARS-CoV-2 infection (13). Miners are rural essential workers with

Table 1: SARS-CoV-2 infection vulnerability and susceptibility factors in miners

Vulnerable workers: Workers at higher risk due to the greater likelihood of increased exposure	**Susceptible workers:** Workers at higher risk (or worse outcomes) at any level of exposure
Hazardous work characteristics: • Exposure to infected aerosols amongst essential workers unable to work from home • Enclosed, or poorly ventilated workplaces; difficulty distancing from virus-laden aerosols • Prolonged and close face-to-face or physical contact • Lack of access to flexible work schedule	Demographic characteristics: • Male sex • Rural residence • American Indian & Hispanics (particularly in intervention mine) Co-morbidities: • Obesity, hypertension, diabetes mellitus, cardiovascular disease Co-exposures: • Smoking/environmental tobacco smoke • Work in high particulate air pollutant environments
Cross-cutting factors for vulnerable and susceptible workers	
Enhanced Exposure to SARS-CoV-2: • Residence in homes that are overcrowded or multigenerational or without access to running water use (particularly in intervention mine) Predisposition to Poorer Health Outcomes: • Low socioeconomic status	

multiple vulnerability and susceptibility factors, as noted in Table 1, making them a unique population to test and study.

Table 2. Characteristics of NM miners (n=6685)

Characteristic	**%**
Male	97
Race/ Ethnicity	
Non-Hispanic white	28
Hispanic	37
American Indian	33
Age (years)	
< 40	14
40-59	44
≥60	42
Smoker	
Never	47
Former	35
Current	19
Self-Reported Diseases (n=5281)	
Chronic bronchitis	32
Current asthma	5
Dust-related lung disease	6
Cardiovascular disease	18
Diabetes mellitus	13

Community partners: Our engagement with key mining community stakeholders provides the *foundation* for the proposed project as well as *sustainability* for future partnerships. Our mobile screening program for NM and WY miners (14) was recognized as an innovation at the HRSA Rural Health Information Hub (Fig. 1). We have co-authored multiple research manuscripts with our partners (3, 15-20). Our Mining Advisory Council (MAC), chaired by a partner (Gore, LOS) allows stakeholders to review research materials and protocols. Our Miners' Wellness TeleECHO Program helps telementor rural professionals caring for miners (21), details for which are available at http://echo.unm.edu/miners-wellness/. The Advisory Council and the TeleECHO Program, recognized as rural COVID-19 innovations by HRSA's Rural Health Information Hub, exemplify our partnerships that will be leveraged for future pandemic mitigation efforts.

Figure 1: HRSA-funded mobile screening clinic for NM & WY miners, operated by NM & WY Black Lung Programs.

Table 3: Research attitudes in American Indian (n=112; Group 1) and non-American Indian miners (n=47; Group 2). Data from town hall meetings.

Question: How would you feel about….	Gp.	Yes, %	Maybe, %	No, %	P value
Participate in a long-term research study?	1	48.2	41.1	10.7	0.5
	2	38.3	48.9	12.8	
	Gp.	Comfortable	No feeling	Un-comfortable	
Provide blood samples for research?	1	60.7	16.1	23.2	0.14
	2	63.8	29.8	6.4	
Long-term storage of biospecimens?	1	47.3	21.4	31.3	0.02
	2	63.8	23.4	12.8	

Based upon data shown in Table 2, we serve 37% Hispanic, and 33% American Indian miners in NM, indicating robust participation from populations historically underrepresented in health research. NM data (19) indicate that minority miners are at greater risk for developing lung disease than non-Hispanic white miners (18, 22). The sex, race/ethnicity, and smoking distribution, and prevalence of lung and cardiovascular diseases, diabetes, and hypertension support our position that miners are a unique population for studying SARS-CoV-2.

The literature indicates that American Indians are reticent towards participating in research due to historic mistrust, resulting in some of the poorest health outcomes of any racial/ethnic group (21). However, our data from town hall meetings (Table 3) indicate that American Indian miners welcome participation in research to the same degree as those of non-American Indian descent, but maybe less comfortable with sharing biological specimens. To address this challenge, we will not store biological specimens for future research without consent for the same.

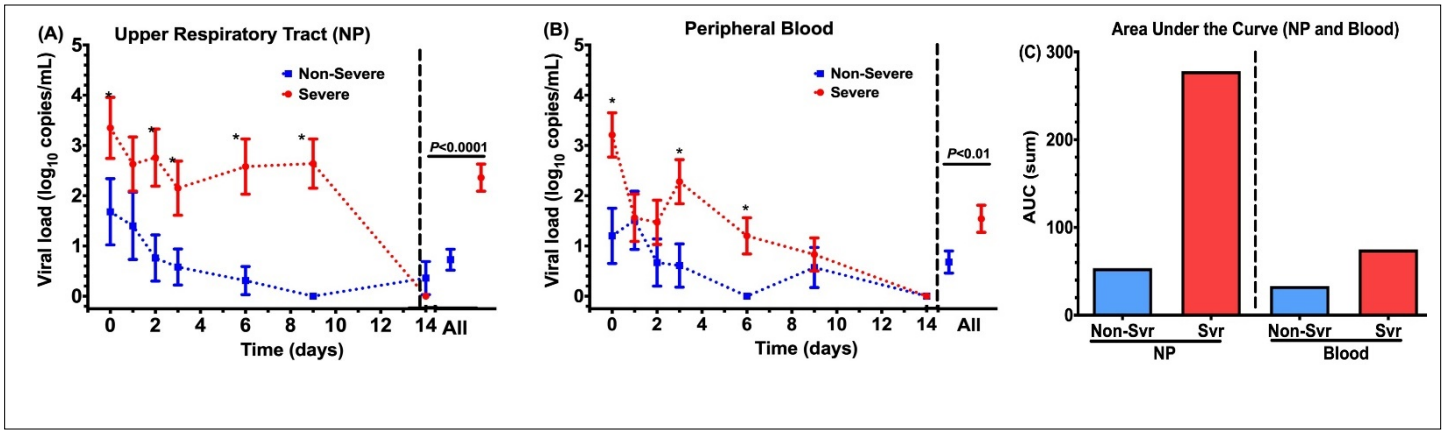
In a 2016 study at the intervention mine, we determined that 58% of miners used social media, 91% reported Internet access over their telephone, and 92% used the phone for texting. Miners reported using social media for 51 (mean) ± 142 (SD) minutes daily for 6±5 years, indicating adept and frequent usage. 52% of those surveyed indicated an interest in using social media to receive information about miners' projects from our group. The social media-savvy nature of rural NM miners, initially surprising to our group, is a novel way to reach out to the study population using phone/web apps, which will be developed by Ingenuity Software Labs, Albuquerque, New Mexico. Our mine safety officer partner, JC Williams, CMSP, helped establish our social media engagement and education plan, including a video tutorial.

Table 4: List of study SARS-CoV-2 tests

SARS-CoV-2 test	**FDA authorized**
Screening test (molecular)	Yes
Diagnostic test (RT-PCR)	Yes
Serologic antibody test	Yes
Viral burden (Quantitative RT-PCR or RT-qPCR)	Research test

Our capacity for SARS-CoV-2 testing: Molecular tests help establish a diagnosis by detecting SARS–CoV-2 nucleic acids using RT-PCR or nucleic acid amplification assays (23). Laboratory-based RT-PCR assays performed on nasopharyngeal (NP) swabs collected by trained professionals (i.e., diagnostic test) are the cornerstone of diagnostic testing. A recent study showed that unsupervised, self-collected, midnasal swabs for the detection of SARS-CoV-2 are comparable to clinician-collected nasopharyngeal swabs (Cohen K statistic = 0.81), offering a unique opportunity to scale-up workplace testing (24). The commercial choice of screening test for our study will be finalized, based on test availability, in collaboration with the NIH RADx-UP initiative, but will have the following characteristics (Regulatory status: All; Diagnostic target: Viral antigen; Analysis location: Self or Lab CLIA Waived; Platform: Lateral flow; Specimen collected: Nasal swab; Company: Any; Minutes to result: 30 minutes or less; Sensitivity and specificity: At least 80%)..

We have performed over 600 RT-qPCR measurements of patient samples for our ongoing projects using the CDC N1 and N2 assays and a published "Wuhan" spike protein (S) gene assay. The results showed that the CDC N1 assay is the most robust. As such, we present viral load dynamics (log_{10} copies/mL) for the N1 assay in non-severe (n=13) and severe (n=19) patients with COVID-19. As shown in Fig. 2, patients with severe disease have a higher and more protracted viral load in the upper respiratory tract (NP, $P<0.001$, panel A) and peripheral whole blood ($P<0.01$, panel B) compared to non-severe patients. Also, to capture viral load during the time-course measurements, area-under-curve (AUC) was calculated for the two groups. Patients with severe disease had a higher AUC than those with non-severe disease for both NP and peripheral blood (Fig. 3C). There was a significant positive relationship between severe disease and viral loads measured from the NP swabs ($P=1.2x10^{-4}$) and whole blood ($P=4.9x10^{-3}$), and between the NP and peripheral blood viral loads ($P=2.5x10^{-6}$).



3. Study Design

3.1. Specific Aim 1:

Frequent testing (i.e. alternate work shifts) using less sensitive molecular tests is proposed to keep workplaces open safely during the pandemic (26, 27), but its feasibility has not been studied. Our *objective* is to perform an experimental feasibility study to determine the acceptance of frequent point-of-care screening testing in our unique population. Our working *hypothesis* is miners will have a cumulative acceptance rate of frequent screening testing at ≥85%, with the added objective of exploring difference in acceptance by miner characteristics. The *rationale* for the proposed work is to establish worker acceptability for the proposed workplace surveillance. We expect that our findings will help design novel primary SARS-CoV-2 prevention strategies at rural workplaces, including future vaccination studies of essential workers.

Research design: This is a longitudinal surveillance study over up to twelve months, starting January 2021. We will utilize a fixed cohort of less than 250 at-risk miners at the intervention site, a surface coal mine in McKinley County, NM, with a population comprised of 66% minorities (American Indian and Hispanic), in partnership with the mine leadership.

3.2. Specific Aim 2:

Effective molecular surveillance may be only marginally affected by a test's lower analytical limits of detection (26). Although molecular tests may show false negatives (FN) early on or late in the infection cycle when viral load is increasing and decreasing, respectively, the viral burden corresponding to a positive screening test is not established (29). Interim results demonstrate that when compared to the diagnostic (laboratory-based qualitative RT-PCR), screening test in controlled settings (in urgent care clinic, hospitalized and nursing home patients) is ≥95% sensitive and ≥99% specific (30). In our study, the screening test utilizes samples collected: a) at the workplace, b) by the participant, c) using nasal swabs followed by point-of-care testing, d) in a low infrastructure community setting, e) by minimally trained professionals. The screening test was granted emergency use authorization without a detailed study on end-user needs in the real-world, but each of the above variables introduces a potential source of error in results.

Our *objective* is to determine the ability of the screening test to correctly detect the presence of the virus in upper respiratory specimens in the real-world setting. This will be accomplished by evaluating screening test performance at the workplace by quantifying viral loads from self-collected nasal swab and health personnel-collected nasopharyngeal (NP) swab specimens, using quantitative RT-PCR (RT-qPCR). Our *working hypothesis* is that the sensitivity of the screening test in a real-world study setting is a) comparable to that described by others in controlled settings, and b) positively associated with viral load in upper respiratory specimens. Successful completion of this study will help determine the real-world performance of less sensitive screening tests in disease settings of mild severity.

Table 5: Test findings studied in Aim 2

Measurement	Biological specimen	N	Purpose
Screening test (qualitative)	Self-collected nasal swab	less than 250	Workplace surveillance
Diagnostic test (qualitative RT-PCR)	Healthcare personnel collected NP swab	less than 250	Establish sensitivity, specificity & diagnostic accuracy of screening test
Quantitative RT-PCR	Self-collected nasal swab	less than 250	Quantitate viral load vis-à-vis screening test
Quantitative RT-PCR	Healthcare personnel collected NP swab	less than 250	Quantitate viral load vis-à-vis screening test
Sputum biomarkers	Spontaneous home collected sputum samples	Less than 250	Quantitate inflammation

Research design: In this cross-sectional study, sensitivity, specificity and diagnostic accuracy (31) of the screening test on a self-collected nasal swab will be established by comparison with diagnostic test (qualitative RT-PCR), the latter conducted on an NP swab collected on the same day by trained health personnel, in a CLIA certified clinical laboratory (TriCore; Table 5). Also, since the diagnostic test is qualitative, we will also quantify viral load (log_{10} copies/mL) from repeat nasal (self-collected) and NP (collected by healthcare personnel) swab specimens using RT-qPCR established in the Perkins research laboratory (32). Viral load will be determined with primers and probes (N1 and RP) using the CDC 2019-nCoVEUA-01 diagnostic panel (33). Miners with any positive screening test (plus a sample of ~200 miners with a negative test) will undergo the above testing procedures. Database management and timelines will be similar to those described in Aim 1.

3.3. Specific Aim 3:

The role of frequent point-of-care molecular workplace surveillance to monitor and prevent the spread of SARS-CoV-2 is inadequately studied, particularly in rural essential workplaces. Our *objective* is to examine the effectiveness and costs of frequent point-of-care molecular workplace surveillance in rural essential workers. Our working *hypothesis 3A* is that frequent point-of-care molecular testing over up to twelve months in the intervention mine will result in lower incident seropositivity rates compared to the control mine. *Hypothesis 3B* is that frequent point-of-care molecular surveillance in the intervention mine is cost-effective compared to the control mine. The *rationale* for the

proposed work is that by establishing its effectiveness, implementation costs, and cost-effectiveness, our study will increase the real-world utility of workplace molecular testing, resulting in a novel primary prevention strategy targeted at rural essential workers.

Research design: We will conduct a up to twelve-month longitudinal surveillance study of miners at the intervention site (n=less than 250) in McKinley County, NM, and control site (n=less than 350) in Campbell County, WY. Both surface coal mines, operated by the same company, have similar engineering, administrative, and personal protective measures in place, including SARS-CoV-2 symptom & fever screening. While there will be frequent point-of-care molecular testing at the intervention site, seropositivity (baseline, 3, 6, and approximately12 m) will be measured at both sites.

3.4. Specific Aim 4:

Factors impacting SARS-CoV-2 spread is not well studied in rural essential workers outside healthcare. Our *objective* is to examine novel factors affecting the spread of infection in miners. A recent epidemiological study reported high COVID-19 mortality in communities exposed to ambient particulate air pollution (11). This novel risk factor is relevant for miners who are exposed to high levels of particulate air pollution at the workplace. Further, although the CDC encourages the public use of a cloth face-covering, its use by miners may vary, based upon individual and community factors (38), and has not been adequately studied. Our working *hypothesis* 4A is that miners with incident infection demonstrate less frequent use of cloth face-coverings outside the workplace, greater mine dust exposure intensity, presence of dust-related lung disease, and racial/ethnic minority status than those not infected. *Hypothesis 4B:* Test and vaccine uptake in miners is predicted by specific barriers and facilitators. The *rationale* for the proposed work is to prevent the spread of COVID-19 infection. We expect that our findings will result in novel primary prevention strategies for workers in dusty trades.

Research design: This is a up to twelve-month longitudinal surveillance study at the intervention (n=less than 250) and control (n=less than 350) mines.

4. Inclusion and Exclusion Criteria

All miners will be recruited at the mine site with the support of mine leadership.

4.1. Inclusion Criteria

- Male or Female Miner employed at the Peabody El Segundo mine in McKinley County, NM (i.e., intervention mine) or the Peabody Caballo and Rawhide mines at Campbell County, WY (i.e., control mine).
- $\geq$ 18 years of age.
- Willing and able to provide and sign Informed Consent Form.
- Willing and able to comply with study procedures.

4.2. Exclusion Criteria

- Unable or unwilling to provide and sign Informed Consent Form
- < 18 years of age.

We will not recruit or enroll pregnant women, incarcerated individuals, minors, or adults unable to consent.

5. Number of Subjects

Less than 600 subjects will be recruited at all mine sites in this longitudinal study. Of these, less than 250 miners will be recruited from the Peabody El Segundo mine in McKinley County, NM at the edge of Navajo Nation (i.e., intervention mine). The remaining less than 350 miners will be recruited from the Peabody Caballo and Rawhide mines at Campbell County, WY (i.e., control mine). Both surface coal mines, operated by the same company, have similar engineering, administrative and personal protective measures in place, including SARS-CoV-2 symptom & fever screening. While there will be frequent point-of-care molecular testing at the intervention site, seroprevalence (baseline, 3, 6, and 12 m) will be measured as an outcome at both sites.

6. Study Timelines

The duration of individual subject's participation in this research is estimated to be approximately 12 months from the time they give and sign informed consent. We anticipate that all study participants will be enrolled in the first month of the recruitment and enrollment. Below are milestones with estimated dates of completion. The dates may be adjusted as necessary depending on the completion of previous milestones.

Milestone 1: Completion of planning, contracts, purchase of tests and supplies, protocols and IRB approval: by January 2021.

Milestone 2: Recruitment and collection of data: January 2021 through March 2022 (anticipated).

Milestone 3: Data analysis and dissemination: July 2021 through November 2022 (anticipated).

7. Study Endpoints:

7.1. Specific Aim 1:

Predictor and Outcome variables: Screening test acceptance by miners is measured for each eligible work shift and cumulative acceptance rate (i.e., outcome) is calculated over the study timeframe (frequency of tests /number of eligible shifts worked, max=less than 60). Characteristics predicting acceptance include self-reported educational and racial/ethnic minority status (from baseline questionnaire), self-reported prior SARS-CoV-2 infection or vaccination (from app), evidence of prior infection (from a prior positive screening test), and daily county incidence and prevalence infection rates (from publicly available data). Focus group discussions and/or individual interviews will be performed in a sample of subjects at the intervention mine (in NM) to better understand 'testing hesitancy' towards the end of the study, using an interview script and trained interviewers. Only approved study members will be performing interviews.

Expected outcomes: We anticipate a higher testing acceptance rate among non-Hispanic whites and those with higher self-reported educational status. Conversely, we expect lower acceptance rates among those with prior infection (or vaccination), and during time

intervals in which incidence of infection in the County is either trending down or at a low level.

7.2. Specific Aim 2:

Predictor and Outcome variables: Predictor variable is the sensitivity of the screening test in our study conditions. Outcomes are a) the sensitivity of the screening test reported by others in controlled settings, and b) viral load measurements in upper respiratory specimens (i.e., repeat nasal and NP swab).

Expected outcomes: We anticipate that the screening test results can be confirmed by detecting the SARS-CoV-2 load, within the limit of RT-qPCR detection. Based on our preliminary data (Fig. 2), our detection limit is ≥100 viral copies per mL (32). This level of detection is contingent on obtaining enough sample material. It remains unclear if a self-collected nasal swab collected in a real-world setting will consistently yield enough sample material to detect SARS-CoV-2. Since we will incorporate a primer and probe for the detection of the human ribonuclease P gene in our assay, we can directly determine if there is sufficient sample material on the screening test for the detection of SARS-CoV-2. The study design will also allow us to determine if the level of the virus on the nasal swab, self-collected in a real-world setting, is comparable in its ability to detect SARS-CoV-2 as that of a health personnel-collected NP swab.

7.3. Specific Aim 3:

Predictor and Outcome variables: The predictor variable is the mine status (intervention vs. control). The primary outcome is any *new* seropositivity for SARS-CoV-2 IgM or IgG at 3, 6, or approximately 12 months relative to baseline. The serologic test (depending upon availability, finalized using NIH recommendation) allows for the qualitative detection of IgG or IgM antibodies (separately) against SARS-CoV-2, indicating recent (IgM: 3-5 days) or prior infection (currently unknown). We will also study the presence of symptoms or fever, irrespective of infection status, as an alternative study outcome for hypothesis 3A. Costs of the test-based surveillance program, employee absenteeism patterns, and mine coal production will contribute towards defining the outcome variables for hypothesis 3B. At a minimum, a valuable outcome is to determine surveillance program costs, which have not been previously established for this rural industry setting, organization size, or proposed surveillance frequency. Additionally, variance in outcome measures—defined as employee days lost due to incident infection, mine productivity, and reduction in worksite infection rate—across the two sites will be used to estimate the cost-effectiveness of the intervention. Database management and timeline are similar to that for Aim 1.

Expected outcomes: We anticipate that as compared to the control mine, the intervention mine demonstrates lower incident seropositivity, and that workplace surveillance is cost-effective over twelve months.

7.4. Specific Aim 4:

Predictor, and outcome variables: The outcome variable for hypothesis 4A of incident seropositivity, is defined as in Aim 3. Predictor variables include frequency of cloth face-covering use outside the mine, occupational dust exposure intensity, presence of lung

disease (historically or measured by sputum inflammation), and race/ethnicity status. Additional predictor variables for hypothesis 4B are specific barriers and facilitators. Additional outcomes for hypothesis 4B are test and vaccine uptake.

Expected outcomes: We anticipate that low levels of use of cloth face-coverings in public settings outside the mine, high levels of occupational dust exposure intensity, baseline dust-related lung disease, and racial/ethnic minorities are each associated with a greater relative risk for incident seropositivity than those without these characteristics. We anticipate that additional predictor variables, as outlined in the previous paragraph, affect test and vaccine uptake.

8. Research Setting

Recruitment, enrollment, and data collection will be conducted at the Peabody El Segundo mine in McKinley County, NM (i.e., intervention mine) and the Peabody Caballo and Rawhide mines at Campbell County, WY (i.e., control mine). Both surface coal mines, operated by the same company, have similar engineering, administrative and personal protective measures in place, including SARS-CoV-2 symptom & fever screening.

Baseline survey will be collected from both intervention and control mine sites but the additional questionnaire (and sputum collection) will be limited to the NM mine site only.

Confirmatory diagnostic tests, which are standard of care RT-PCR tests, will be conducted at TriCore Reference Laboratories from samples collected at the Peabody El Segundo mine or at the Cibola General Hospital (where TriCore Reference Laboratories currently provide reference laboratory services). The results from the standard of care test will be provided by TriCore to the study investigators. This does not require a data user agreement.

Since the confirmatory diagnostic standard of care test is qualitative, we will also quantify viral load ($\log_{10}$ copies/mL) from nasal (self-collected) and NP (collected by healthcare personnel) swab specimens using research diagnostic RT-qPCR tests established in the research laboratory of Dr. Douglas J. Perkins at the Center of Global Health in the University of New Mexico's Department of Internal Medicine. The specimens for the research diagnostic tests will be collected at the Peabody El Segundo mine or at the Cibola General Hospital. Any specimens collected will be transferred to the Perkins laboratory using a Materials Transfer Agreement (MTA)

Statistical analysis will be completed at the University of New Mexico Health Sciences Center.

We will engage and work with the Mining Advisory Council, chaired by a partner, Bobbi Gore. This council allows stakeholders to review research materials and protocols.

9. Resources Available

This study is based on the collective experience, expertise and infrastructure put together by a respected team of researchers, and community and clinical experts from the University of New Mexico and the Peabody mine sites in the states of New Mexico and Wyoming. This collaborative team, from the University of New Mexico (UNM) Health Sciences Center (HSC), Miners Colfax Medical Center, the Peabody El Segundo Mine, and the Peabody Caballo and Rawhide Mine, combine expertise in miner epidemiology, infectious disease, clinical care, and community-based prevention and care. The team at UNM will include Dr.

10. Prior Approvals

UNM HSC IRB approval will be obtained before beginning any study activities.

11. Multi-Site Research

This is a single site study (i.e., at UNM HSC), with recruitment at two mine sites. This does not qualify as multi-site search. This study will take place and recruit participants at the (1) Peabody El Segundo Mine in McKinley County, NM at the edge of Navajo Nation (i.e., intervention mine), and the (2) Peabody Caballo and Rawhide mines at Campbell County, WY (i.e., control mine). Laboratory diagnostic testing will be conducted at TriCore Reference Laboratories. Since the diagnostic test is qualitative, we will also quantify viral load (log_{10} copies/mL) from nasal (self-collected) and NP (collected by healthcare personnel) swab specimens using RT-qPCR established in the research laboratory of Dr. Douglas J. Perkins at the Center of Global Health in the University of New Mexico's Department of Internal Medicine. Data storage and analysis will be conducted at the University of New Mexico Health Sciences Center. The PI will have regular communication with the locations to confirm all research staff are competent, properly trained; they will have the most current version of the protocol, consent documents, and HIPAA authorization; any modifications will be communicated to sites and implemented only after IRB approval; they will safeguard all research data; any non-compliance with the study protocol or applicable requirements will be reported immediately to the PI; all adverse events, interim results and study closure determinations will be communicated via email and/or teleconference between the PI and study staff.

12. Study Procedures

During the baseline study visit, former miners and never-miners will complete a comprehensive baseline survey. Additional study procedures are outlined below

Overview of study procedures

Measurement	**Intervention mine, NM, n=less than 250**	**Control mine. WY, n=less than 350**
Baseline survey: Demographics (age or DOB, gender or sex, race and ethnicity, education, household income, insurance, height, weight, Mailing residential address and if PO Box, physical mailing address, phone number, medical history including hypertension, diabetes, COPD, asthma, pneumoconiosis, immunocompromised state, cardiovascular disease, smoking, environmental tobacco smoke exposure, home access to running water, use of household wood or coal smoke, d tobacco, , current medications, history of prior COVID hospitalization, shared transportation	At the time of study enrollment, using paper and/or REDCap	
Additional questionnaire: Demographics (age or DOB, gender or sex, race and ethnicity, education, household income, insurance, Mailing residential address and if PO Box, physical mailing address, phone number, medical history, smoking, history of prior COVID hospitalization, Testing and vaccination history	Once between 6 and 12 months, using paper, or electronic (e.g. REDCap)	**None**

Web-based phone app questionnaire: Symptoms; frequency of cloth face-covering use outside the mine ; vaccination history, infected contacts, & history of prior COVID infection	Each work shift via the phone app	
Measured fever screen	Each work shift measure, recorded via REDCap (normal vs. abnormal)	
Nasal swab (self-collected) screening test	Alternate shift collection plus test acceptance data entered into REDCap	**None**
Nasopharyngeal swab (trained professional or TP-collected) diagnostic test (RT-PCR, TriCore labs)	All abnormal screening tests (collected at TriCore Cibola) & sample (n=approximately 200) of normal screening tests (collected at mine site) plus test acceptance data entered into REDCap	**None prescribed**
Nasal (self-collected) and nasopharyngeal swab (TP-collected) research test (RT-qPCR, Perkins labs)	All abnormal & sample of normal tests as above	None prescribed
Serology	Blood sample at baseline, 3, 6, and approximately 12 months plus test acceptance data entered into REDCap	
Occupational dust exposure intensity	Every work shift via job-exposure matrix created by occupational safety team via REDCap	
Daily county incidence and prevalence data	Recorded daily by study coordinator from public health records entered into REDCap	
Focus group discussions and/or individual interviews to study "testing hesitancy"	Yes	No
Spontaneous home collected sputum sample	Yes once at approximately 12 months	No

12.1. Specific Aim 1:

Miners work one of two twelve-hour shifts daily, in repeated patterns of 4 days on followed by 4 days off work. At the beginning of each alternate work shift, each miner, irrespective of symptom status, will provide supervised self-collected midnasal swabs to trained mine safety personnel at the mine entrance. The safety personnel will run the screening test on swabs at the mine site. Miners with a positive screening test will undergo a confirmatory diagnostic test, and will be: 1) referred to their healthcare provider; 2) offered telemedicine evaluation at UNM, for those interested, and 3) removed from the workplace per CDC guidance (28). The final assay for the screening test will be decided based on advice from the NIH RADx-UP Coordinating and Data Collection Center. Acceptance data will be entered at the mine site by the safety personnel into a Research Electronic Data Capture (REDCap) database. Focus group discussions and/or individual interviews will be performed in a sample of subjects at the intervention mine in NM to better understand 'testing hesitancy' towards the end of the study.

12.2. Specific Aim 2:

Miners with any positive screening test (plus a sample of ~200 miners with a negative test) will undergo trained professional collected NP swab (for RT-PCR diagnostic testing), self-collected nasal swab (for RT-qPCR) and trained professional collected NP swab (for RT-qPCR). Database management and timelines will be similar to those described in Aim 1.

12.3. Specific Aim 3:

In brief, at the beginning of each work shift, trained mine safety personnel will obtain the following: 1) 24-hour history of SARS-CoV-2 symptoms, provider diagnosis of infection, close contact with any infected, vaccination, and use of cloth face-covering in public settings outside the mine, using a web-based phone app, also available using a computer connected to the Internet; and 2) body temperature measurement using a no-touch forehead infrared thermometer. The web-based phone app, created by Ingenuity Software Inc., will be accessed by the subjects with password protection. The information will be encrypted during data transfer to a secure server that resides at the UNM HSC and will auto-populate the REDCap database. The phone app has been approved by UNM HSC IT.

At the beginning of each alternate shift, the mine safety team will collect a supervised self-collected nasal swab from each worker for point-of-care screening testing, as described in Aim 1. Fingerstick or venipuncture blood samples will be obtained at the mine site from all study participants at the time of enrollment, and at 3, 6, and approximately 12 months (no more than 24 ml or 4.9 teaspoons each visit) to determine seropositivity, using the COVID-19 IgG/IgM antibody test. Employee absenteeism (both general and screen test results-driven) and coal production records will be analyzed.

12.4. Specific Aim 4:

Predictor variables are listed in Table titled Overview of Study Procedures. Database management and timeline will be similar to that for Aim 1.

13.Data Analysis

13.1. Specific Aim 1:

Predictor and Outcome variables: Test acceptance by miners is measured for each eligible work shift and cumulative acceptance rate (i.e., outcome) is calculated over the study timeframe (frequency of tests /number of eligible shifts worked, max number estimated at less than 120). Characteristics predicting acceptance include self-reported educational and racial/ethnic minority status (from baseline questionnaire), self-reported prior SARS-CoV-2 infection or vaccination (from app), evidence of prior infection (from a prior positive screening test), and daily county incidence and prevalence infection rates (from publicly available data).

Statistical approach: Cumulative acceptance rate will be compared between groups, defined by predictive characteristics. Poisson regression with indicator variables will be used to assess the effects of miner characteristics on cumulative acceptance rates. Analyses will use the number of shifts in which tests were available to miners for the rate denominator (offset) to account for absenteeism. Longitudinal analysis of shift-level acceptance by miners will be examined using mixed model regression for binary outcomes that account for repeated measures. Within-miner factors will include time-varying SARS-2-COV-2 exposure (personal and community) and vaccination status, and linear and nonlinear time trends.

Power calculations: If we recruit less than 250 miners, we have the power to estimate 85% acceptance rate ± 4.6%. For a comparison of acceptance rates between predictor groups, we assume, for example, non-Hispanic white and minority miners (1/3 and 2/3 of the study population respectively) have 85% and 80% acceptance respectively. We used simulation to assess power for Poisson regression analyses where the rate denominator (offset) is the number of miner workdays, assumed to be 95% of possible days. For these conditions, power is 94% for a 5% lower acceptance rate for minority miners. We also used simulation to assess the planned longitudinal analysis of miner acceptance by assuming that miners attended work 95% of the shifts, that initial acceptance is 85% and that there is a linear decline in acceptance over the study to a final acceptance rate of 80%. For repeated measures on about 200 miners, the power to detect a linear decrease to 80% is 95%.

13.2. Specific Aim 2:

Statistical analysis: We will compare screening test performance measures between our real-world study setting and controlled settings (as published by others). We will use a one-sample Exact test for a binomial proportion to test whether sensitivity for the screening test is the same as that published. We will correlate screening test results with quantitative viral loads, and perform Bland-Altman plots to reveal systematic differences between viral loads collected by the two sampling methods.

Power Calculations: If we conservatively estimate identifying 25 true positive miners, using a one-sample Exact test for a Binomial proportion equal to the comparison test, we have the power (>90%) to detect a difference between the screening and the comparison test if the screening test sensitivity is 90% or lower.

13.3. **Specific Aim 3:**

Predictor and Outcome variables: The predictor variable is the mine status. The primary outcome is any new seropositivity for SARS-CoV-2 IgM or IgG at 3, 6, or 12 months relative to baseline. The test allows for the qualitative detection of IgG and/or IgM antibodies (separately) against SARS-CoV-2, indicating recent (IgM: 3-5 days) or prior infection (currently unknown). The tests have positive percent agreements of 97% and 87% and negative percent agreements of 98% and 99% for IgG and IgM, respectively, compared to oropharyngeal swab RT-PCR. We will also study the presence of symptoms or fever, irrespective of infection status, as an alternative study outcome for hypothesis 3A. Costs of the test-based surveillance program, employee absenteeism patterns, and mine coal production will contribute towards defining the outcome variables for hypothesis 3B. At a minimum, a valuable outcome is to determine surveillance program costs, which have not been previously established for this rural industry setting, organization size, or proposed surveillance frequency. Additionally, variance in outcome measures—defined as employee days lost due to incident infection, mine productivity, and reduction in worksite infection rate—across the two sites will be used to estimate the cost-effectiveness of the intervention. Database management and timeline are similar to that for Aim 1.

Covariates: Baseline seropositivity, vaccination status, other host susceptibility and vulnerability factors outlined in Table 1, and daily community prevalence and incidence, will be studied as covariates in multivariable models (35).

Statistical analysis: Chi-square tests will examine whether relative frequencies of incident seropositive miners are the same at 3-months, 6-months, and 12-months for the two mine types, using α=0.025 to account for the two tests. Generalized linear models for repeated binary outcomes will be used to assess how covariates are associated with seropositive status over time.

Power calculation: Based on representative seroprevalence/molecular prevalence rates for similar communities (36), we anticipate a 10% baseline seropositivity with incident seropositivity at 6 months at 5% for the intervention mine and a baseline seropositivity of 5% in the control mine. We anticipate similar power calculations to apply up to 12 months. We explored a range of control miner incident seroprevalence values that would have 80% power when comparing frequencies at the two mines using chi-square tests. We expect 80% power if incident seropositivity at the control mine is ≥9% (α =0.025).

13.4. Specific Aim 4:

Statistical analysis: Chi-square and logistic regression analyses will be used to explore how miner characteristics are associated with baseline seropositivity. Generalized linear models for repeated binary outcomes will be used to assess how predictor variables (noted in Table 7) and covariates (as noted in Aim 3) are associated with incident seropositivity at 3, 6, & approximately 12 months. Both analysis strategies will include mine type as a covariate and will add predictor and outcome variables noted in Table 7.

Table 7: List of predictor and outcome variables for Aim 4

Predictor and outcome variables	Time of measurement	Procedure for ascertainment
Frequency of cloth face-covering use outside the mine	On the day of the screening test; Mean summary variable over the one week before the test	Self-report, via the app, every work shift
Occupational dust exposure intensity	On the day of the screening test; Mean summary variable over the one week before the test	Mine safety team, via job-exposure matrix, every shift
Presence of lung disease	Baseline	Baseline survey
Race/ethnicity status	Baseline (at study enrollment)	Self-report via questionnaire
Facilitators and barriers	Between 6 and 12 months	Self-report via questionnaire
Test and vaccine uptake	Between 6 and 12 months	Self-report via questionnaire

Power calculation: We assessed power, using simulation for incident seropositivity at 6 months with mine type as covariate and a predictor miner variable, such as high dust exposure. We anticipate similar power calculations up to 12 months. We assumed the miner variable, present in 1/3 sample, will increase the probability of incident seropositivity by 0.10. For a logistic regression analysis and this setup, power is >96%.

14. Provisions to Monitor the Data to Ensure the Safety of Subjects

Data and Safety Monitoring Plan (DSMP)

Overview: The proposed study is an NIH-designated clinical trial. The Mining Advisory Council (recognized in 2020 by HRSA as rural COVID-19 innovation) will serve as the

"Human Subjects Unit" which will work to monitor ethical and social implications and human subjects concerns in testing implementation. This work is essential in monitoring implementation efforts are not exacerbating health disparities in our underserved and vulnerable populations. A data and safety monitoring board will not be needed for the study, since the intervention in the clinical trial is low-risk.

Purpose: to ensure the safety of research participants and protecting the validity and integrity of study data in the clinical trial.

The clinical trial will be monitored by the Principal Investigator (PI), Institutional Review Board (IRB), and members of the Mining Advisory Council. Monitoring of our clinical trial includes the following activities.

- Description of any specific events that would preclude a participant from continuing the intervention
- Description of the potential risks and the measures in place to protect participants against foreseeable risks
- Description of the consent procedures
- Description of the mechanisms in place to protect subject privacy
- Description of the trial stopping rules for the study
- Description of the plan for management of incidental findings
- Description of the process for the disclosure of any conflicts of interest that may potentially challenge participant safety or bias the data and how the conflict will be managed
- Description of the data security in place to protect the confidentiality of the data

The roles and responsibilities for the individuals participating in the DSMP are outlined below. No DSMB is needed since the intervention is low risk.

Name of DSMP member	Qualification	Role
Akshay Sood (PI)	Physician	Plan for management of incidental findings & conflict of interest
Nour Assad	Physician	Adverse event monitoring
Kevin Vlahovich	Physician	Adverse event monitoring
Orrin Myers	Biostatistician	Trial stopping rules & data security
Xin Shore	Biostatistician	Trial stopping rules
William "Cotton" Jarrell	Mine safety officer	Consent and procedures/privacy
Bobbi Gore	Community manager	Community perspectives
Diane Gail Johnson	Community manager	Community perspectives

Bruce Wissore	Miner lawyer	Legal perspective

Reportable Events: The team will follow the protocols and timelines laid down by the IRB (UNM HRPO) for collecting and reporting Adverse Events (AEs), Serious Adverse Events (SAEs), and Unanticipated Problems Involving Risks to Subjects or Others to appropriate monitoring and regulatory entities. The ITB also has rules regarding protocol violations, non-compliance, suspensions, and terminations.

Data Management, Analysis, and Quality Assurance: The team will identify all data sources (e.g., questionnaires, biospecimen collections, app data, data entered by mine safety team into REDCap), outline the security measures to protect data sources including how the data will be labeled and stored, and determine quality assurance measures for subject recruitment, enrollment, enrollment targets, and for the validity and integrity of the data.

15. Withdrawal of Subjects

Subjects are free to withdraw from study participation at any time during this clinical study. The Investigator may withdraw a subject if continued participation is not in the interest of the subject's health and welfare, for noncompliance with protocol-specified procedures, or because of a protocol violation. This will be evaluated on a case-by-case basis by the Investigator. Overall, because this is a study with a low risk to participants, no other stopping rules apply. Data collected from participants up to the point of withdrawal will not be destroyed, but no additional data will be collected.

The primary reason for discontinuation or withdrawal will be documented as one of the following:

- AE
- Noncompliance
- Protocol violation
- Consent withdrawn

16. Data Management/Confidentiality

Data transfer between study personnel and for test results from TriCore Reference laboratory will use an HIPAA- compliant encrypted fax system managed by the HSC's RightFax system. Data will be stored and managed on a REDCap database on a secure server at the UNM HSC. The database will be populated using both electronic and paper source systems. Once entered into REDCap, electronic and paper source documents will be destroyed. At the study site, password protected mobile and fixed computer devices will be utilized to collect study data utilizing the REDCap Mobile system. Data will be coded with a digital study number. Identifying information will be stored in a separate REDCap database. When off-site the database will be secured and accessed via secure https:// connection provided by UNM HSC. Control of users and privileges, as well as local and remote backup of the database will be in accordance with UNM HSC management procedures. All documents and paperwork will be stored in locked file cabinets at UNM and individual medical records will be electronically stored in HSC secure electronic drives. All personal data and identifiers will be maintained in accordance with HIPAA regulations. Study records and data will be kept for 6 years at the local site after study closure per federal regulations.

De-identified data resulting from this study may also be presented at meetings, published in journals/books, used in classrooms for training/teaching purposes, and may be shared with other researchers including scientists at other universities and institutions.

Study information will be shared with: 1) local investigators at the CEAL-WEAVE study at the UNM HSC, PI Lisa Cacari-Stone (HRRC ID 21-371) of the data from the additional questionnaire administered between 6 and 12 months in a deidentified data format. The CEAL-WEAVE study has a similar objective related to vaccine uptake. 2) NIH (of the data from the additional questionnaire in a deidentified data format, by the CEAL-WEAVE study) and 3) the NIH-funded RADx-UP databases at the Duke Clinical Research Institute (DCRI). RADx-UP stands for Rapid Acceleration in Diagnostics (in) Underserved Populations. RADx-UP is a health research program to learn more about COVID-19 disease. DCRI is a research group chosen by the NIH to combine the data collected from everyone taking part in RADx-UP studies. The purpose of sharing of data with DCRI for future studies is to allow the medical community to learn more about COVID-19, in particular, and better health, in general. The data will be shared by secured internet connection and stored in secure electronic files.

The DCRI will build two RADx-UP databases. The first database will only hold identifiable information. Examples are subject name, address, email, and gender.

- These data will be kept at the DCRI. The DCRI will not share these data with the NIH.
- Subject information will be linked with information from other sources, such as the Centers for Medicare and Medicaid Services and subject's electronic health record, among others.
- These data will stay in a password-protected secure electronic system and only staff responsible for maintaining the security of subject data at the DCRI will be able to see this information.

The second database will not hold information to identify the subject. It will hold all the non-identifiable information the subject agrees to give.

- The subject will be assigned a code and will only be identified in this database by this code.
- It will not contain subject name or other information that could easily identify the subject.
- The DCRI plans to transfer and keep these non-identifiable data in a secure database for COVID-19 research at the NIH. Other researchers may use these data for studies, other than the ones stated in this consent form.
- When using the data from this second database, researchers will only have access to subject non-identifiable data and cannot link the data back to the subject.

For all data sets, preliminary analyses will include checking for missing values, range checking, and outlier checking.

Only IRB approved study team members will be able to view and have access to research related data.

Please note that a DUA will be put into effect with Duke Clinical Research Institute (please see sections 47 and 48) and the SPO will be utilized for the same. Please note that a MTA

will be put into effect with any future researchers before material is transferred (please see sections 47 and 48).

DUA and MTA are part of the contract with Peabody mines. DUA is part of the contract with Ingenuity Software (for phone app creation).

17. Data and Specimen Banking

We will utilize the approved data and biological specimen repository study (HRRC ID 14-058). Blood and respiratory specimens will be indefinitely banked in the approved tissue repository at UNM HSC for future studies, if allowed by the study subject. The specimens will be stored in the IRB and HTOC-approved MEL Repository with HRRC ID 17-422. The existing study 14-058, will be amended to account for samples from this study being added to it.

18. Risks to Subjects

Potential Risks: The proposed protocol involves minimal risk only. However, we will continuously monitor the study related procedures and data collections. We have established mechanism to protect the confidentiality of participant information. Nevertheless, accidental disclosure of study data may occur. There are no alternative treatments appropriate for this protocol and no circumstances for terminating the study other than declining to participate in the study. Only trained and certified staff will perform and administer the procedures to minimize the risk of following:

Loss of privacy: Participation in a research study may result in some loss of privacy. The risk of loss of privacy and confidentiality will be minimized. Information about a subject will be handled as confidentially as possible. Representatives from the University of New Mexico Health Sciences Center Human Research Review Committee that oversees human subject research and the National Institutes of Health will be permitted access to a subject's records. Also, a subject's participation in the study and information in a subject's study records may be disclosed to a subject's doctors and nurses, and may be disclosed as otherwise provided by law. However, a subject's name will not be used in any published reports about this study. Please also see the section on data management.

Injury from fingerstick or venous blood draws: Temporary local discomfort accompanies virtually all needle sticks. Potential injury from venous blood draws includes occasional (<10%) bruising, sweating, dizziness and rarely (<1%) fainting and infection.

Nasopharyngeal (NP) and Nasal Swabs: Occasional and temporary mild discomfort and bleeding from repeated efforts of obtaining NP swabs. Nasal swabs can be performed without discomfort or risk.

Precautions will be exercised in order to maintain the highest standard of anonymity. Each patient data/blood samples will be given a unique study number that will not be linked in any way to standard HIPAA identifiers, and importantly, the datasets we will work with are Limited Data Sets in accordance with HIPAA guidelines (stripped of standard identifiers). The

PI will store the database linking the medical record and study numbers in a separate secure REDCap database. No reference to subject name or other personal identifiers that could jeopardize their privacy will appear in the main database, blood samples, in abstracts, scientific papers or other documents that emanate from this study. Importantly, random anonymous identifiers will be used to label blood samples.

Survey and Questionnaires: Answering some questions may cause stress and/or emotional discomfort.

Spontaneous home collected sputum: The risks related to spontaneous sputum expectoration are minimal and include cough, chest discomfort or shortness of breath but this is anticipated to be short lasting. At home, taking a shower before collecting the sample may help.

There may also be side effects or risks to study participation that are unforeseen and not known at this time.

19. Potential Benefits to Subjects

There will be no direct benefit to participants of this study. The risks involved do not pose a significant threat to the health of the participants. However, the prevalence of COVID-19 in rural essential workers and minorities can be very high. Thus, participants in the proposed study may benefit from early diagnosis and treatment of COVID-19.

20. Recruitment Methods

Less than 600 subjects will be recruited at all mine sites in this longitudinal study. Of these, less than 250 miners will be recruited from the Peabody El Segundo mine in McKinley County, NM at the edge of Navajo Nation (i.e., intervention mine). The remaining less than 350 miners will be recruited from the Peabody Caballo and Rawhide mines at Campbell County, WY (i.e., control mine). Both surface coal mines, operated by the same company, have similar engineering, administrative and personal protective measures in place, including SARS-CoV-2 symptom & fever screening. While there will be frequent point-of-care molecular testing at the intervention site, seroprevalence (baseline 3, 6 and approximately 12 m) will be measured as an outcome at both sites.

All miners will be recruited at the mine site with the support of mine leadership (see attached letters). Recruitment methods include 1) flyers and emails (attached) and 2) miner videos, placed on 'theamericanminer.org' website and played on mine TV monitors.

21. Provisions to Protect the Privacy Interests of Subjects

The research study will require IRB approval.

The risk of loss of privacy and confidentiality will be minimized. Information about a subject will be handled as confidentially as possible. Representatives from the University of New Mexico Health Sciences Center Human Research Review Committee that oversees human subject research and the National Institutes of Health will be permitted access to a subject's records. Also, a subject's participation in the

study and information in a subject's study records may be disclosed to a subject's doctors and nurses, and may be disclosed as otherwise provided by law. However, a subject's name will not be used in any published reports about this study. Please also see the section on data management.

The mines have walled-off sections that give privacy to study participants and for making them feel at ease and in control of with whom they interact and prevents 'eavesdropping' or observation by non-study team members. Privacy will be protected during recruitment, consent, and data collection.

Additionally, all tests will be similarly performed by qualified personnel using standard protocols and appropriate test settings to minimize the risks related to study procedures.

22. Economic Burden to Subjects

Subjects are not responsible for their participation in the research. There are no costs to participants. If there are any adverse events or complications, the cost of treating those adverse events or complications will be borne by the participant and their insurance.

Research Procedures	Number of Samples/Procedures	Responsible Party	
		Study	3rd Party Payer or Participant
Screening COVID-19 Testing	Multiple	☒	☐
COVID-19 qualitative RT-PCR and quantitative RT-PCR Testing	Multiple Possible	☒	☐
Phlebotomy/Serology IgG/IgM Test	4	☒	☐
Spontaneous home collected sputum	1	☒	☐
_____	_____	☐	☐
_____	_____	☐	☐
_____	_____	☐	☐
Standard of Care Procedures	**Number of Samples/Procedures**	**Responsible Party**	
		Study	**3rd Party Payer or Participant**
_____	_____	☐	☐

23. Compensation

There is a $10 reimbursement via a merchandise card (generic merchandise or CTSC-CLIN card) sent by email or by mobile phone text or by mail or hand delivered for providing each biological specimen (i.e., each nasal swab, each nasopharyngeal swab, each blood specimen, including fingersticks, and each spontaneous home collected sputum sample) while participating in the study, in addition to study tests being provided without charge.

Eligible subjects will be provided telemedicine consultation upon request via UNM, which will be charged to their insurance.

Subjects will be provided an additional $5 reimbursement, using a merchandise card as described above, for completing the phone app survey every work shift, until the end of the project (estimated at less than 120 work shifts). Since this information was not provided in the

consent, all participants will be informed by email (or phone text), using the message below (sent approximately every four days till the end of the project- estimated at approximately 26 times). This message will also be 1) mailed to their mailing address once, with a phone app users guide; 2) placed at the worksite messages area (with copies of app users guides); 3) placed on the phoneapp in the Reminders section; and 4) placed in a flyer handed over to miners at the guard shack (at the mine entry) frequently.

Subjects will be provided a $100 reimbursement via a merchandise card as described above for completing the additional questionnaire once between 6 and 12 months.

Message to NM mine site: Please complete the Miners' Pandemic Project Phone app survey (hyperlink leads to https://miners.health.unm.edu) before each work shift and receive a $5 merchandise card for each completed survey. For questions, please contact Cotton Jarrell.

Message to WY mine site: Please complete the Miners' Pandemic Project Phone app survey (hyperlink leads to https://miners.health.unm.edu) before each work shift and receive a $5 merchandise card for each completed survey. For questions, please contact Kelly Zimmerscheid.

24. Compensation for Research-Related Injury

If a participant becomes sick or injured as a direct result from the study, they may receive emergency treatment, however, there is no commitment by the UNM HSC to cover the costs related to research related injuries. The subject and/or their third party payer will be charged in the usual way.

25. Consent Process

Consent will be obtained following local IRB SOP titled, "SOP: Informed Consent Process for Research (HRP-090)." Parts of the informed consent process may be conducted virtually, over the phone, or in person as allowed by the UNM Human Research Protection Office due to COVID-19 related restrictions. The in person consent process will take place in a private area at the mine site and be conducted by an IRB approved study team member. Participants will be given time, and encouraged, to discuss the study with friends and family before making an informed decision. Ongoing verbal consent will be obtained at each study visit. The protocol requests a waiver of written documentation of consent. This is reasonable since the research is no greater than minimal risk. However, signature will be obtained on the consent form within two weeks of the virtual consent.

All participants will be reconsented for their continued study involvement between 6 months and up to 12 months. The reconsenting will occur at or after six months, using the approach outlined above. Participants who have or have not consented at baseline may consent at or after six months.

Participants not fluent in English

Participants not fluent in English will not be consented or enrolled into the study. This is due to the questionnaires being only in English. Additionally, we may not have access to qualified interpreters.

26. Documentation of Consent

To document our consenting process we will be following "SOP: Written Documentation of Consent (HRP-091)." The protocol requests a waiver of written documentation of consent. However, signature will be obtained on the consent form within two weeks of the virtual consent.

27. Study Test Results/Incidental Findings

Test results of clinical significance will be shared with the patients and they will be instructed to follow-up with their primary care physicians, as necessary.

We do not expect any incidental findings, as we are specifically testing for COVID-19 and IgG/IgM antibodies to COVID-19 only.

28. Sharing Study Progress or Results with Subjects

Consented subjects will not be provided with a summary of the trial progress while the study remains underway nor will they be provided with study results. Results of positive screening test or positive RT-PCR diagnostic test will be shared with the study subject and occupational health and safety team. Results of the positive RT-PCR diagnostic test will be shared with public health authorities, as necessary.

29. Inclusion of Vulnerable Populations

N/A – No vulnerable populations will be recruited for this study.

30. Community-Based Participatory Research

Community partners: Our engagement with key mining community stakeholders provides the *foundation* for the proposed project as well as *sustainability* for future partnerships. Our Mining Advisory Council (MAC), chaired by a partner (Gore, LOS) allows stakeholders to review research materials and protocols. Our Miners' Wellness TeleECHO Program helps telementor rural professionals caring for miners (21), details for which are available at http://echo.unm.edu/miners-wellness/. The Advisory Council and the TeleECHO Program, recognized as rural COVID-19 innovations by HRSA's Rural Health Information Hub, exemplify our partnerships that will be leveraged for future pandemic mitigation efforts.

Table 3: Research attitudes in American Indian (n=112; Group 1) and non-American Indian miners (n=47; Group 2). Data from town hall meetings.

Question: How would you feel about….	Gp.	Yes, %	Maybe, %	No, %	P value
Participate in a long-term research study?	1	48.2	41.1	10.7	0.5
	2	38.3	48.9	12.8	
	Gp.	Comfortable	No feeling	Un-comfortable	
Provide blood samples for research?	1	60.7	16.1	23.2	0.14
	2	63.8	29.8	6.4	
Long-term storage of biospecimens?	1	47.3	21.4	31.3	0.02
	2	63.8	23.4	12.8	

Based upon data shown in Table 2, we serve 37% Hispanic, and 33% American Indian miners in NM, indicating robust participation from populations historically underrepresented in health research. NM data (19) indicate that minority

miners are at greater risk for developing lung disease than non-Hispanic white miners (18, 22). The sex, race/ethnicity, and smoking distribution, and prevalence of lung and cardiovascular diseases, diabetes, and hypertension support our position that miners are a unique population for studying SARS-CoV-2.

The literature indicates that American Indians are reticent towards participating in research due to historic mistrust, resulting in some of the poorest health outcomes of any racial/ethnic group (21). However, our data from town hall meetings (Table 3) indicate that American Indian miners welcome participation in research to the same degree as those of non-American Indian descent, but maybe less comfortable with sharing biological specimens. To address this challenge, we will not store biological specimens for future research for participants who do not provide consent for the same.

31. Research Involving American Indian/Native Populations

We anticipate enrolling approximately 66% racial/ethnic minorities, including approximately 33% American Indians, at the NM-based intervention mine. Since we will not collect tribe-specific data on American Indian subjects and since the intervention mine is located outside the Navajo nation and University IRB rules apply, we do not need tribal IRB permissions. We anticipate enrolling 5% racial/ethnic minorities in the WY-based control mine, reflecting the demographic population of that mining community.

32. Transnational Research

N/A

33. Drugs or Devices

Diagnostic device studies (i.e., screening test in this study) are exempt from the IDE requirements as long as the sponsor complies with the requirements of 21 CFR 809.10(c) for labeling, and if the testing: (1) is noninvasive; (2) does not require an invasive sampling procedure that presents significant risk; (3) does not by design or intention introduce energy into a participant; and (4) is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

34. Principal Investigator's Assurance

By submitting this study in the Huron IRB system, the principal investigator of this study confirms that:

☒ The information supplied in this form and attachments are complete and correct.

☒ The PI has read the Investigator's Manual and will conduct this research in accordance with these requirements.

☒ Data will be collected, maintained and archived or destroyed per HSC Data Security Best Practices, including:

1. **Best Practice for data collection** is for it to be directly entered onto a data collection form that is in a secured access folder on an HS drive behind a firewall, or in a secure UNM Data Security approved system such as REDCap.

2. **Data collection of de-identified data**, if done in a clinical setting or other setting that does not allow direct entry into a secured system, may be done temporarily using a personal or university owned electronic storage device or hard copy document. **The important security safeguard is that no identifiers be include if the data is entered or stored using an untrusted device or storage.**
3. **Permanent (during data analysis, after study closure**) storage must reside on HSC central IT managed storage. Processing of data (aggregation, etc.) are to be carried out in such a way as to avoid creating/retaining files on untrusted storage devices/computers. Trusted devices are HSC managed and provide one or more of following safeguards: access logs, encryption keys, backups, business continuity and disaster recovery capabilities.

Alternate storage media must be approved by HSC IT Security as meeting or exceeding HSC central IT provided security safeguards.

47. Data Transfer/Sharing (Checklist) (required –do not delete even if the answer is "No")

Provide all information requested if the research involves transferring/sharing of data with an external entity (institution, company, etc.).

A. Will data be transferred/shared with an external entity (institution, company, etc.)?

☒Yes

☐No. **The remainder of this section does not apply.**

B. Indicate if the data is incoming and/or outgoing: *Outgoing*
C. Provide the name of the entity that data will be transferred/shared with: *Outgoing Data: Duke Clinical Research Institute (DCRI), Duke University, NC, USA, which serves as the Coordination and Data Collection Center (CDCC) for the NIH-funded program entitled: "Rapid Acceleration of Diagnostics for Underserved Populations Coordination and Data Collection Center" also referred to as "RADx-UP CDCC", under the direction of Duke's investigator, Michael Cohen-Wolkowiez, MD.*

D. Provide the contact name, email and phone number with whom data is being transferred/shared with: *Outgoing Data: Michael Cohen-Wolkowiez, MD, 300 West Morgan Street, Box 3850, Durham, NC 27701, phone: (919) 668-8812, email: michael.cohenwolkowiez@duke.edu*

E. Who is responsible for transmission of the data? *Outgoing Data:* Akshay Sood, MD at UNM HSC

F. Who is responsible for receiving the data? *Outgoing Data:* Alka Srivastava, J.D.

G. Describe how the data will be transferred/shared. Please note data cannot be transferred/shared without assistance from UNM HSC IT. **Requesting HSC Central IT Transfer is detailed on the Sponsored Projects website:** *Outgoing Data: All data will*

be transferred from our secure REDCap databases to the secure Duke Network using Duke approved secure remote access via Duke provided solutions. All transfer activities during remote access may be monitored by Duke and UNM HSC IT, as necessary. At the time of data transfer, the UNM HSC project team will download the CSV file of the project data from the UNM HSC project database in REDCap. This file will then be uploaded by a designated project team member into the secure RADxUP CDCC data portal by logging in to the CDCC system through a web browser (portal to be created – the link will be shared with HSC IT when available for further approval). The secure, cloud-based portal will require individual credentials and log-in to access to data upload feature. Credentials will be assigned by the CDCC, or if the institution has federated credentials via In Common, their access will be granted via that method. No external users will have access to the UNMHSC REDCap database.

H. For data being transferred/shared with outside locations or entities, describe the following:

- Where is data storage and how will it be maintained in a secure manner (i.e. encryption, password protection, use of Qualtrics or REDCap, etc)? *Outgoing Data: Data will be stored on protected, secure computer systems with approved secure password.*

- What is method in which data will be collected and stored (i.e. electronic, hard copy, etc)? *Outgoing Data: Data will be stored on protected, secure computer systems. DCRI will limit and keep track of who can see these data. Anyone who can see these data will have to use a password. DCRI will take steps to protect the information from others that should not be able to see it. When data are shared with other researchers, they will not have information that can identify participants. This project has a Certificate of Confidentiality from the United States government.*

- How long will the data be stored? *Outgoing Data: The data will be stored indefinitely.*

- Who will have access to data? *Outgoing Data: The staff at DCRI and researchers approved by DCRI will have access to data, as described below in subsection I.*

I. Please list all specific data elements, variables, etc. to be sent out and/or received. Indicate if the data contains identifiers and health information. Please note that identifiers that MUST be removed to make health information de-identified are as follows: Names, All geographic subdivision smaller than a State, All elements of year (except year), Telephone, Fax numbers, E-mail addresses, Social Security, Medical record number, Health plan beneficiary, Account numbers, Certificate/license numbers, Vehicle identifiers and serial numbers, Device identifiers and serial numbers, Web URLs, IP address numbers, Biometric identifiers, full face photographic images, and Any other

unique identifying number, characteristic or code.) *Outgoing Data:* The DCRI will build two RADx-UP databases. The first database will only hold identifiable information, which include participant name, address, county, date of birth, telephone, email, and gender but will not include any medical information. These data will be kept at the DCRI. The DCRI will not share these data with the NIH. Participant information will be linked with information from other sources, such as the Centers for Medicare and Medicaid Services and participant electronic health record, among others. Only if participant agrees, as per the consent form, the DCRI will keep information that can identify participants in order to contact them for future research studies. These data will stay in a password-protected secure electronic system and only staff responsible for maintaining the security of your data at the DCRI will be able to see this information. The second database will not hold identifiable information. It will hold all the non-identifiable information the participant agrees to give. This information will include COVID test results as well as the results of all surveys and questionnaires completed by the participant. Participants will be assigned a code and will only be identified in this database by this code. It will not contain participant name or other information that could easily identify him or her. The DCRI plans to transfer and keep these non-identifiable data in a secure database for COVID-19 research at the NIH. Other researchers may use these data for studies, other than the ones stated in the consent form. When using the data from this second database, researchers will only have access to non-identifiable data and cannot link the data back to study participants. Because the data cannot be linked back to participants, DCRI will not contact the participants to inform them or ask their permission before sharing the data with researchers.

J. If the research requires the access, use, or disclosure of any of the 18 individually identifiable protected health information (PHI) identifiers that can be used to identify, contact, or locate a person (e.g., name, medical record number, etc.), are the subjects going to consent to or authorize the disclosure of their individually identifiable health information? *The research requires the access, use, or disclosure of one or more of the 18 individually identifiable protected health information (PHI) identifiers, as noted in 47I and the subjects will consent to or authorize the disclosure of their individually identifiable health information.*
    a. ***Or*** is HIPAA authorization altered or waived? *No. HIPAA authorization is not altered or waived.*
K. What is the classification of the data (de-identified, limited data set, protected health information, other). *protected health and identifiable information*
L. Does the request to transfer/share data include clinical data that belongs to the UNM Health Systems? *Yes*

M. Does the data to be transferred/shared include information about patients seen at external health system or at a third party medical provider? *No*
N. Is the external entity a "covered entity"? *Yes*
O. Is the data that is going to be transferred/shared owned or partially owned by another party or have any type of restrictions including regulatory restrictions (i.e. HIPAA, FERPA, etc.)? *No*

P. Is the data publically available? If yes, please provide details: *No*
Q. Does the data include information about substance abuse treatment, sexually transmitted diseases, genetic testing results, HIV/AIDS testing results, and/or mental health? *No*

48. Specimen Transfer/Sharing (Checklist) (required –do not delete even if the answer is "No")

Provide all requested information if the research involves transferring/sharing of specimens with an external entity (institution, company, etc.).

A. Will specimens be transferred/shared with an external entity (institution, company, etc.)?

☐ Yes

☒No. **The remainder of this section does not apply.**

B. Indicate if the specimens are incoming and/or outgoing: *NA*

C. Provide the name of the entity that specimens will be being transferred/shared with: *NA*

D. Provide the contact name, email and phone number with whom specimens are being transferred/shared with: *NA*

E. Who is responsible for sending out the specimens? Please note specimens cannot be sent out without a fully executed material transfer agreement.

NA

F. Who is responsible for receipt of the specimens? Please note specimens cannot be received without a fully executed material transfer agreement.

NA

G. For specimens being transferred/shared with outside locations or entities, describe the following:

Where is specimen storage and how will it be maintained in a secure manner? *NA*

- What is method in which specimens will be collected and stored? *NA*
- How long will the specimens be stored? *NA*

Who will have access to the specimens? *NA*