Ministry of Health
Zambia National Public Health Institute

Evaluating Covid-19 Vaccine Effectiveness Against Symptomatic Illness Among Health Care Workers During Early Phase Vaccination in Zambia, 2021

15 May 2021

Version 1.3

Contents

Investigators

Affiliation	Name and Title	Role in the Project
Principle Investigators		
Zambia National Public Health Institute	Victor Mukonka, MBChB, PhD	Protocol development, implementation, monitoring, data management and analysis, report writing
Zambia Ministry of Health	Kennedy Malama, MBChB, MPH	Protocol development, implementation, monitoring, data management and analysis, report writing
Co-Investigators		
Zambia Field Epidemiology Training Program	Oliver Mweso, MBChB	Protocol development, implementation, monitoring, data management and analysis, report writing
	John Simwanza, MBChB	
	Stephen Chanda, MBChB	
	Chilufya Mulenga, DVM	
	Grace Funsani, MPH	
	Lindiwe Tembo	
	Emmanuel Tembo	
	Danny Sinyange	
	Thelma Shinjeka	
	Cheepa Habeenzu	
	Oscar Nzila	
Zambia National Public Health Institute	Nyambe Sinyange, MBChB, MSc	Protocol development, implementation, monitoring, data management and analysis, report writing
	Muzala Kapin'a, MBChB	
	Kunda Musonda, MBChB, PhD	
	Peter Chipimo, MBChB, MPhil, PhD	
	Nkomba Kayeyi, PhD	
	Otridah Kapona, MSc	
	Mazyanga Mazaba Liwewe MSc	
	Dabwitso Banda, MBChB, MSc	
	James Exnobert Zulu, MBChB, MSc	
Zambia Ministry of Health	Lloyd Mulenga, MBChB, MMed, PhD	Protocol development, implementation, monitoring, data management and analysis, report writing
	Francis Dien Mwansa, MBChB, MSc	
	Fwoloshi Sombo, MBChB, MMed	
	Mwaka Monze, MBChB, PhD	
	Aaron Shibemba, MBChB, MMed	
University of Zambia School of Veterinary Medicine Laboratory	Ngonda Saasa, PhD	Protocol implementation, monitoring, data management and analysis, report writing
Tropical Diseases Research Center	Gershom Chongwe, MBChB, PhD	Protocol implementation, monitoring, data management and analysis, report writing
	Justin Chileshe, MSc, PhD	
PATH	Daniel Bridges, PhD	Protocol implementation, monitoring, data management and analysis, report writing
National Health Research Authority	Godfrey Biemba, MBChB, MSc	Protocol implementation, monitoring, data management and analysis, report writing
U.S. Centers for Disease Control and Prevention, Lusaka, Zambia	Jonas Hines, MD Surveillance Advisor yxj7@cdc.gov CITI GCP expires 2 January 2022	Protocol development, monitoring, data management and analysis, report writing
	Samuel Yingst, DVM PhD	

	Laboratory Branch Chief ofc7@cdc.gov CITI GCP expires 31 October 2022	
	Warren Malambo, MPH Public Health Specialist CITI expires 11 February 2022	
	Elizabeth Heilmann, MPH PHI fellow qng0@cdc.gov CITI GCP expires 25 June 2023	
	Adam Wolkon, MPH Associate Director for Epidemiology and Informatics aow5@cdc.gov CITI GCP expires 26 December 2021	

Funding source: This project is supported by CDC through a cooperative agreement with the Zambia Ministry of Health (CoAg ID number: GH002234; CoAg name: Ministry of Health; CoAg principle investigator: Lloyd B. Mulenga; CoAg funding period: 9/30/2020-9/29/2025).

CDC's role: CDC will not engage in data collection or have access to identifiable data; rather, CDC will provide technical leadership on protocol development, data collection procedures, data analysis, interpretation of results, and their dissemination. All data will be owned by the Zambia Ministry of Health and Zambia National Public Health Institute.

Conflict of interest: The primary investigators and co-investigators have no personal, financial, or other relationships that might pose a conflict of interest (or the appearance of a conflict) in their role in this activity. The contents in this protocol are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Adaptation from an existing protocol

This protocol is adapted from the CDC-cleared protocol, "Evaluating SARS-CoV-2 Vaccine Effectiveness Among Health Care Personnel During Early Phase Vaccination," Available at: https://www.cdc.gov/vaccines/covid-19/downloads/hcp-early-phase-protocol-508.pdf. This protocol differs from the original in the following ways:

- Project is being conducted in Zambia
- Added several additional secondary objectives, including performing genomic sequencing on positive specimens and assessing VE according to SARS-CoV-2 variant strain
- Sample size recalculated based on local epidemiologic picture
- Questionnaire updated to include several additional variables including HIV status and prior SARS-CoV-2 infection
- Elaborated on methods in some areas (definition of vaccination, data quality, data analyses, etc.)

Acronyms

ARDS	Acute respiratory distress syndrome
ART	Antiretroviral therapy
CDC	U.S. Centers for Disease Control and Prevention
CI	Confidence interval
COVID-19	Coronavirus disease 2019
CT	Computed tomography
CXR	Chest x-ray
HCW	Health Care Worker
HIV	Human immunodeficiency virus
ICU	Intensive care unit
IRB	Institutional review board
MoH	Ministry of Health
OR	Odds ratio
RCT	Randomized-controlled trial
SARS-CoV-2	Severe acute respiratory syndrome coronavirus type 2
WHO	World Health Organization
VE	Vaccine effectiveness
ZNPHI	Zambia National Public Health Institute

Introduction

Background

Since the World Health Organization was first notified of a cluster of respiratory infections in Wuhan City, China on December 31, 2019 (1), the novel coronavirus, severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), has caused more than 90,000 infections and 1,200 deaths in Zambia and more than 150,000,000 infections and 3,000,000 deaths worldwide as of 30th April 2021 (2). Although most persons with SARS-CoV-2 have mild illness (or are asymptomatic), some require hospitalization (3), and given the scope of the pandemic, the SARS-CoV-2 epidemic can place a substantial burden on health care workers (HCW) and health systems.

HCWs are at risk of contracting SARS-CoV-2 during their interactions with patients with suspected or confirmed infection with SARS-CoV-2 (COVID-19) or patients with unrecognized infection (4). A key component of controlling the pandemic and protecting the Zambian healthcare workforce is deployment of a safe and effective SARS-CoV-2 vaccine. Evaluating the performance COVID-19 vaccines post-licensure is critical as a number of factors can impact real-world vaccine effectiveness (VE), including transportation and storage conditions, how vaccines are administered, advanced age, presence of underlying medical conditions, and previous SARS-CoV-2 infection (5). In addition, post-licensure evaluations of COVID-19 vaccines can allow public health authorities to estimate the level of protection against severe disease and death; assess the relative effectiveness of different vaccine types and of single doses; evaluate VE against virus variants; and, understand the duration of protection of vaccines and thus the need (and frequency) for re-vaccination.

Multiple Covid-19 vaccines have been evaluated in clinical trials over the past year and, in Zambia, vaccines, the AstraZeneca became available in April 2021. The approach is to acquire and deploy different available vaccines (a basket approach) through 3 pillars which include: (i) the COVAX facility; (ii) vaccine diplomacy; and (iii) government and private sector procurement. Voluntary Covid-19 vaccination is being prioritized during early phases of introduction for frontline/essential workers, including all HCWs in Zambia. Through 2 May 2021, 12,459 HCWs in Zambia have been vaccinated with at least one dose of Covid-19 vaccine. This early phase distribution of the vaccine provides an opportunity to evaluate the effectiveness of these vaccines in preventing symptomatic Covid-19 and to learn how these vaccines work

in a real-world setting. This is of critical importance because of the emergence of the SARS-CoV-2 B.1.351 variant and circulation in Zambia (6).

Literature review

Zambia is experiencing a SARS-CoV-2 epidemic. The first cases of SARS-CoV-2 were detected in March 2020 (7), and in July 2020, 10.6% of persons in six districts had been infected with the virus (8). At that time, HCWs had similar SARS-CoV-2 prevalence, although this could have been because the prevalence estimate was obtained during the upswing of the first wave in Zambia (9). Additionally, infections in HCWs could have been occurring in the community (9), as this is shown to also be a source of transmission for HCWs (10–12). No further prevalence studies of HCWs have been done in Zambia since July 2020.

Highly efficacious Covid-19 vaccines have been developed with unprecedented speed and, by the end of 2020, multiple vaccines were available and being administered in various countries around the world (13). Covid-19 vaccines utilize various technology/platforms to induce the adaptive immune system to respond to the virus or viral component (13). These include tried and true as well as novel approaches; the four main approaches include inducing immunity to SARS-CoV-2 through: 1) inactivated and live attenuated SARS-CoV-2 virus; 2) viral vectors (replication-incompetent, replication-competent, and inactivated); 3) nucleic acid (RNA and DNA); and 4) recombinant viral proteins (14).

The AstraZeneca (AZ) Covid-19 vaccine (AZD1222) is a modified chimpanzee replication-incompetent adenovirus vector vaccine with the spike protein of SARS-CoV-2. Given favorable logistic considerations and cost, this is the primary vaccine being distributed via the COVAX Facility, the international initiative aimed at creating equitable access to Covid-19 vaccines in low- and middle-income countries (including Zambia). The vaccine is administered in two doses 4 to 12 weeks apart (15).[*] This vaccine had a 70.4% (95% confidence interval [CI]: 54.8-80.6%) efficacy for preventing symptomatic Covid-19 at 14 days following the 2nd dose in a randomized controlled trial (RCT) in Brazil, United Kingdom, and South Africa (16). Similar findings were reported from an unpublished RCT in the United States, Chile, and Peru (17). In the trial, participants who inadvertently got a partial 2nd dose of AZ vaccine had greater protection than those who got the full 2nd dose (90.0% vs. 62.1%), although the difference was not statistically significant. Additionally, even a single dose of AZ vaccine appears to offer substantial protection from SARS-CoV-2,

[*] In Zambia, the dosing interval for the AZ vaccine is 8-12 weeks

and delayed receipt of the 2nd dose may also enhance effectiveness of the AZ vaccine (18). A large study from Scotland has shown an 88% (95% CI 75-94%) reduced hospitalization for the AZ vaccine (19).

SARS-CoV-2 variants may affect Covid-19 vaccine efficacy, including for AZ vaccine. Despite showing lower neutralizing activity against the B.1.1.7 variant, the AZ vaccine appears to remain efficacious against this strain (20). However, preliminary findings for a phase I/II trial of AZ vaccine in South Africa showed a 21.9% (95% CI: -49.9-59.8%) efficacy for mild to moderate disease, and the lower efficacy is believed to be related to the circulating SARS-CoV-2 variant called B.1.351 (aka N501Y2) (21). Laboratory evaluations have shown reduced antibody neutralization against variants with the E484K mutation (found in B.1.351) with serum from persons with wildtype SARS-CoV-2 infection and post-vaccination (22–24), although evidence is still sparse. Following the South Africa trial, the government halted use of the AZ vaccine. However, the efficacy of AZ against severe disease where B.1.351 is the dominant strain is not known. This question is of critical importance to Zambia because B.1.351 is currently the dominant strain in Zambia (and likely all of Southern Africa) (6,25,26).

Research question

"What is the vaccine effectiveness of a complete schedule of the SARS-CoV-2 vaccine in preventing laboratory-confirmed symptomatic Covid-19 among HCWs in Zambia?"

Objectives

Primary:

1) To evaluate post-introduction VE of a complete schedule of the SARS-CoV-2 vaccine in preventing laboratory-confirmed symptomatic Covid-19 among HCWs in Zambia

Secondary:

1) To evaluate post-introduction VE of the SARS-CoV-2 vaccine in preventing severe disease among HCWs with laboratory-confirmed symptomatic Covid-19
2) To evaluate VE by vaccine product (if more than one product is in use), combination of different products, for a single dose (if a 2-dose schedule is recommended), and the interval between doses (for two-dose vaccines)

3) To identify genomic sequences of SARS-CoV-2 among vaccinated HCWs and analyze for potential mutations that could lead to vaccine escape from immunity
4) To evaluate VE against specific SARS-CoV-2 variant strains

Methods

Design

This project will be completed using a case-control test-negative design in HCWs over 3-6 months, depending on vaccine uptake and sample size achieved. This study design has been well described in influenza vaccine evaluation, and it can be used in post-introduction vaccine evaluation for SARS-CoV-2 (27). The principle behind this design is to evaluate SARS-CoV-2 laboratory results among persons who meet a standard case definition and categorize those who test positive as "cases" and those with a negative test results as "controls". The project team will collaborate with participating healthcare facilities and public health agencies to identify HCWs at the time of SARS-CoV-2 testing or to receive line lists of HCWs who have already been tested. Potential participants will be identified through health facilities/providers and the SARS-CoV-2 testing results database maintained by the Zambia National Public Health Institute (ZNPHI). Cases and controls will be defined based on results of SARS-CoV-2 testing, and detailed information on demographics, illness, exposures for SARS-CoV-2, and medical and vaccination history will be collected via HCW interviews. All health facilities in Zambia are eligible for participation. Healthcare facility types that will participate in the project include public and private hospitals, health centres, and health posts across Zambia. Because of the constantly evolving COVID-19 situation locally, the plan is for the project to run for 6 months, although a pre-planned interim analysis will be conducted at 3 months.

Definitions of cases and controls

HCW refers to all paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to patients or infectious materials, including:

- Body substances
- Contaminated medical supplies, devices, and equipment
- Contaminated environmental surfaces
- Contaminated air

For example, this includes any employee or contractor of a healthcare facility such as staff physicians, resident physicians, clinical officers, nurse practitioners, nurses, mid-wives, nurses assistants, pharmacists, phlebotomists, laboratory personnel, social workers, respiratory therapists, physiotherapists, public health workers, clerks and administrative staff, guards, cafeteria staff, environmental services/custodial staff, managers and administrators, research staff, community-based volunteers, porters, and health sciences students (medical, nursing, pharmacy, dentistry, or others, as available). HCW of any job classification in any department will be eligible for enrollment, regardless of exposure to patients or vaccination status (as long as status is known).

HCW case:

A HCW case is defined as a HCW with Covid-19-like illness,[†] ≥1 positive SARS-CoV-2 test result and documented vaccination status during the project period, with or without known exposures in healthcare or community settings. During the HCW interview, clinical signs and symptoms of illness will be captured during the period ranging from 7 days before to 7 days after the positive SARS-CoV-2 test collection date to distinguish symptomatic from asymptomatic infections (this interval was chosen to minimize the likelihood of misclassification). If a HCW is asymptomatic but within the 14 days of testing positive, they will be followed up after day 14 to ascertain if symptoms developed (in which case they will be included as case). Only HCWs with a positive reverse transcriptase (RT)-PCR tests performed on nasal or oral swabs (or similar upper respiratory specimen types), sputum or other lower respiratory secretions will be included; a HCW is also eligible if they have positive rapid antigen test that is confirmed with a positive RT-PCR test within 4 days. HCW cases who are subsequently identified as having had collection of a positive SARS-CoV-2 RT-PCR test at least 60 days after the symptom onset date of a prior SARS-CoV-2 infection during the project period are not eligible for re-inclusion in this project.

HCW control:

A HCW control is defined as a HCW with Covid-19-like illness, who tested negative for SARS-CoV-2 with a documented vaccination status with or without known exposures in healthcare or community settings.

[†] Covid-19-like illness is defined as any of the following: fever, chills, cough, dyspnea, myalgia, chills, rigors, headache, anosmia, ageusia, sore throat, coryza/rhinorrhea, fatigue, general weakness, anorexia, nausea, vomiting, diarrhoea, altered mental status. Adapted from U.S. CDC (https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html) and WHO guidances (https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.2)

A negative test for SARS-CoV-2 is defined as an RT-PCR test performed on nasal or oral swabs (or similar upper respiratory specimen types), sputum or other lower respiratory secretions.

Participation criteria and recruitment

Inclusion criteria

- HCWs with COVID-19-like illness who are tested for SARS-CoV-2 by RT-PCR
- HCWs with documented history of vaccination for SARS-COV-2 (vaccinated HCWs only)
- Willing to participate in data collection

Exclusion criteria

- HCWs tested with rapid antigen tests, without confirmatory RT-PCR testing
- HCWs who's test result is unknown (by self-report and/or through review of testing data at ZNPHI)
- HCWs whose vaccination status is unknown
- HCWs whose SARS-CoV-2 test was collected >7 days after symptoms onset
- A HCW control who reported symptoms consistent with SARS-CoV-2 infection (despite having a negative test) during their interview is NOT ELIGIBLE to be included again in the project as a control until those symptoms from the first instance have been resolved for at least 4 weeks (i.e., there is a gap of at least 4 weeks of no symptoms between symptomatic episodes that results in SARS-CoV-2 testing).

Additional notes regarding including HCWs multiple times:

- Because a HCW may have multiple tests for SARS-CoV-2 over time, it is possible for a HCW control to be included in the study multiple times based on having received multiple negative tests during the course of the investigation.
    - If a HCW control is selected again for inclusion as a control later during the project period, project staff should first determine when the previous illness resolved before proceeding with the full interview. If there was not a gap of at least 4 weeks between illness episodes, the HCW control is not eligible for re-inclusion.
- HCWs who were included as controls and later test positive for SARS-CoV-2 may be included as cases. However, once a HCW has met the case definition by testing positive for SARS-CoV-2 infection, that HCW is no longer eligible to be included in the project as a control at a later time.

Recruitment of participants

Case and control finding will occur through two avenues: direct reporting from health facilities or providers and identification of potential participants from the database of SARS-CoV-2 tests maintained by ZNPHI. Project staff will work directly with health facilities to sensitize them to the project so that they will share the names, contact information and test results for HCW who have been tested for SARS-CoV-2 because of Covid-19-like illness. Project staff will seek to minimize the burden on health care facility staff to the extent possible. Additionally, project staff will review the ZNPHI testing database on a daily basis to identify positive and negative test results of persons identified through HCW surveillance, which is one of the routine surveillance strategies implemented in Zambia (28). HCWs who are identified via this approach will be contacted for invitation to participate in the project.

Controls will be matched to cases on timing of testing (+/- 14 days); if recruitment numbers permit, cases and controls will be matched, in this order: location (health facility, or if not possible, district), age (+/- 5 years), and sex. If the eligible controls exceeds 3 for a given case, an algorithm will be developed to enroll controls from among the eligible controls using random selection.

Sample size

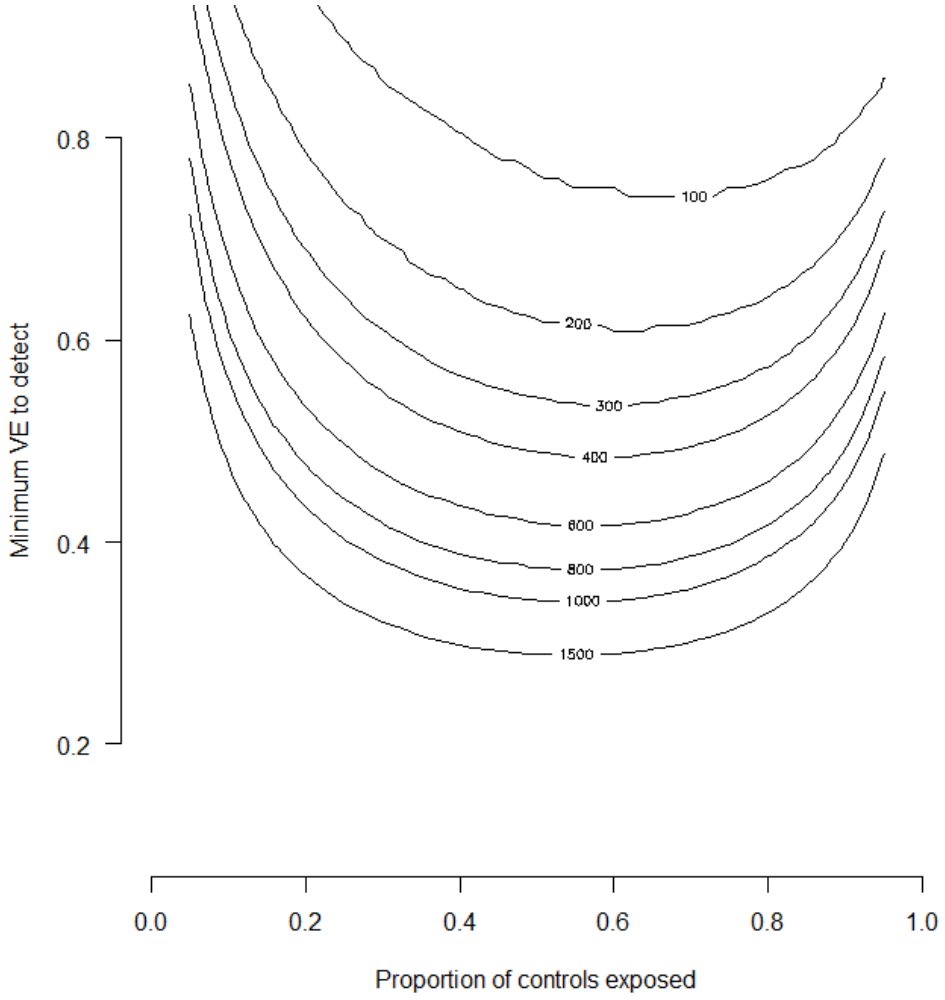
Sample size estimations were calculated in R using the EpiR package and are shown in Table 1. Parameters include matching number of controls to each case (from 2:1 to 4:1), alpha=0.95, beta=0.90, correlation between cases and controls=0.20, and a one-sided test (i.e., the later parameter is assuming vaccine will be more effective than no vaccine). We will attempt to match 4 controls to every case. With an estimated VE=60% for the primary outcome, the sample size will range 290-1110 participants depending on vaccine coverage (i.e., exposure prevalence in the control group). Given that the Covid-19 vaccine is already being administered in Zambia, a vaccine coverage among HCWs ranging from 30-80% is anticipated during the project period, with the higher sample size estimate for that range being 420 participants. Assuming a 30% refusal rate, we anticipate needing to recruit 550 participants (110 cases and 440 controls) for the primary outcome. Because multiple vaccine products may be available in Zambia during the study period, the sample size will be doubled to ensure ability to analyze data for the primary objective, so the final sample size is 1,110. The sample size estimation was conservative, hence an interim analysis will be performed at 3 months. Figure 1 demonstrates the minimum detectable VE for varying sample sizes at given vaccination coverage estimates.

Table 1. Sample size estimates for a matched case control with alpha=0.05, beta=0.90, and correlation =0.2

Vaccine coverage	OR	VE	2:1 matching			3:1 matching			4:1 matching		
			N total	n cases	n controls	N total	n cases	n controls	N total	n cases	n controls
0.1	0.1	0.9	207	69	138	252	63	189	295	59	236
0.2	0.1	0.9	105	35	70	128	32	96	150	30	120
0.3	0.1	0.9	72	24	48	84	21	63	100	20	80
0.4	0.1	0.9	54	18	36	64	16	48	75	15	60
0.5	0.1	0.9	45	15	30	52	13	39	65	13	52
0.6	0.1	0.9	39	13	26	48	12	36	55	11	44
0.7	0.1	0.9	36	12	24	44	11	33	50	10	40
0.8	0.1	0.9	36	12	24	44	11	33	50	10	40
0.9	0.1	0.9	42	14	28	48	12	36	60	12	48
0.1	0.2	0.8	336	112	224	396	99	297	465	93	372
0.2	0.2	0.8	174	58	116	204	51	153	240	48	192
0.3	0.2	0.8	120	40	80	140	35	105	165	33	132
0.4	0.2	0.8	96	32	64	112	28	84	130	26	104
0.5	0.2	0.8	81	27	54	96	24	72	110	22	88
0.6	0.2	0.8	75	25	50	88	22	66	100	20	80
0.7	0.2	0.8	72	24	48	84	21	63	95	19	76
0.8	0.2	0.8	78	26	52	92	23	69	105	21	84
0.9	0.2	0.8	105	35	70	124	31	93	145	29	116
0.1	0.3	0.7	525	175	350	612	153	459	715	143	572
0.2	0.3	0.7	276	92	184	320	80	240	375	75	300
0.3	0.3	0.7	195	65	130	224	56	168	260	52	208
0.4	0.3	0.7	156	52	104	180	45	135	210	42	168
0.5	0.3	0.7	138	46	92	160	40	120	180	36	144
0.6	0.3	0.7	129	43	86	148	37	111	170	34	136
0.7	0.3	0.7	129	43	86	148	37	111	175	35	140
0.8	0.3	0.7	147	49	98	172	43	129	195	39	156

0.9	0.3	0.7	219	73	146	256	64	192	300	60	240
0.1	0.4	0.6	822	274	548	956	239	717	1110	222	888
0.2	0.4	0.6	438	146	292	504	126	378	585	117	468
0.3	0.4	0.6	312	104	208	360	90	270	420	84	336
0.4	0.4	0.6	255	85	170	296	74	222	340	68	272
0.5	0.4	0.6	228	76	152	264	66	198	300	60	240
0.6	0.4	0.6	219	73	146	252	63	189	290	58	232
0.7	0.4	0.6	228	76	152	264	66	198	300	60	240
0.8	0.4	0.6	267	89	178	312	78	234	360	72	288
0.9	0.4	0.6	423	141	282	492	123	369	570	114	456
0.1	0.5	0.5	1332	444	888	1540	385	1155	1785	357	1428
0.2	0.5	0.5	714	238	476	824	206	618	955	191	764
0.3	0.5	0.5	519	173	346	596	149	447	690	138	552
0.4	0.5	0.5	429	143	286	496	124	372	570	114	456
0.5	0.5	0.5	387	129	258	448	112	336	515	103	412
0.6	0.5	0.5	378	126	252	436	109	327	505	101	404
0.7	0.5	0.5	405	135	270	468	117	351	535	107	428
0.8	0.5	0.5	492	164	328	568	142	426	655	131	524
0.9	0.5	0.5	804	268	536	932	233	699	1075	215	860
0.1	0.6	0.4	2304	768	1536	2656	664	1992	3070	614	2456
0.2	0.6	0.4	1248	416	832	1440	360	1080	1660	332	1328
0.3	0.6	0.4	915	305	610	1052	263	789	1215	243	972
0.4	0.6	0.4	768	256	512	884	221	663	1015	203	812
0.5	0.6	0.4	705	235	470	812	203	609	935	187	748
0.6	0.6	0.4	699	233	466	808	202	606	930	186	744
0.7	0.6	0.4	762	254	508	876	219	657	1010	202	808
0.8	0.6	0.4	948	316	632	1092	273	819	1255	251	1004
0.9	0.6	0.4	1590	530	1060	1836	459	1377	2110	422	1688

Figure 1. Minimum vaccine effectiveness detectable according to vaccination coverage and sample size (for a 4:1 controls to cases matching ratio)



Data collection and analysis

HCW case report form (CRF)

Data collection will begin as soon as possible following receipt of HCW SARS-CoV-2 test results through telephone interviews with HCWs using an CRF (see Appendix 2) or through completion of a secure, electronic CRF by the HCW. For the purposes of this protocol, "interview" and CRF include telephone interview and CRF completion or completion of a self-administered electronic CRF. Each HCW will be contacted by project staff up to five times to schedule a future time for the interview or to conduct the

interview, unless the HCW participant requests a call back, or if the HCW returns the call from the project staff. In these instances, an additional contact attempt (i.e., a sixth call) is permissible. For example, if the project staff person makes contact with a HCW on the fifth call attempt, and the HCW requests a call back the next day, that will be permitted. Contact with HCW cases and controls may be via telephone, email or text message.

If a HCW is unable to be interviewed due to illness or incapacitation, or if the HCW is deceased, project staff will attempt to interview the HCW's primary caregiver or next of kin who will serve as the HCW's proxy (Appendix 3). Project staff will try to identify the person who is most familiar with the HCW's medical history to serve as the proxy, and the next of kin or primary health care provider will be asked to provide information on behalf of the deceased or incapacitated HCW. If appropriate, a proxy will be identified through review of medical records (including primary care provider records, where available) or contact with someone living at the HCW's residence.

Interviews will be conducted by trained project staff (unless an electronic tool is used). Interviewers will introduce themselves and the project using a standard, introductory script (see Appendix 4). The electronic questionnaire will include standard, introductory language about the project (Appendix 4). Any recruitment outreach via email or text to HCWs or their proxies will employ standard language about the project (see Appendix 5). HCWs or their proxies will be informed that their participation is voluntary.

Variable categories in the CRF include case status, demographics, underlying medical conditions, roles in healthcare facilities, workplace and community exposures, household income, education level, medical and vaccination history (including vaccines against SARS-CoV-2 and influenza), hospitalizations or outpatient visits related to the current illness episode (for symptomatic HCWs seeking care), clinical course, prior SARS-CoV-2 infection, and providers from whom the HCW has received vaccinations, including vaccines against SARS-CoV-2. Key dates to be collected include date of Covid-19 vaccination(s); date of first symptom(s); date of swab/specimen collection; date of admission (where applicable); date of discharge/death (where applicable).

Project staff will obtain verbal or electronic consent from HCW during the initial interview to participate in the project and review HCW medical records and vaccination records. The consent, survey, and interview will be available to HCW in English and local languages including Nyanja and Bemba.

Medical record

Medical record reviews may be completed by trained project staff for HCWs who report having sought medical care for the current episode of illness as reported on the CRF. Project staff will complete a supplemental review of hospital and/or outpatient medical records, as appropriate. A medical record review form (Appendix 6) will be used to abstract information from HCW medical records on clinical signs and symptoms of illness, laboratory tests for SARS-CoV-2 (test type, date, result), vaccination history, and underlying medical conditions. If there is a discrepancy between information in the HCW interview and the medical record, the information in the medical record (which is less subjected to recall bias) will be utilized for the study.

Covid-19 vaccination history

Accurate and complete vaccination documentation is critical. To ensure complete capture of SARS-CoV-2 vaccination history for HCWs, project staff will query various sources of information, as appropriate and available, including the national Covid-19 immunization registry maintained on DHIS-2. Vaccination history will be recorded in the CRF and if additional data is captured from other sources, using a vaccine record review form (Appendix 7).

COVID-19 vaccination status ascertainment

For every HCW, vaccination history (yes/no), date(s) of vaccine administration, and type of vaccine and brand name for every dose of COVID-19 vaccine will be documented. The source of documentation of vaccine history should be recorded as well. Sources of information for COVID-19 vaccination status may include:

- Vaccination registry (preferred option)
- Consultation of the HCW's vaccination card
- Interview with the HCW's health care provider or in review of HCW's hospital notes
- Review of records at facility that administrated the vaccine
- HCW self-report (alone, this is the least preferred option)

Definition of vaccination status

- Fully vaccinated: HCWs will be considered fully vaccinated if they have received the one dose (for one-dose vaccine) or the two doses (for two-dose vaccine) at least 14 days before symptom onset
- Partially vaccinated (for two-dose vaccines only): HCWs will be considered partially vaccinated if they have received only the first of two doses at least 14 days before onset
- Vaccinated, indeterminate immunity status: HCWs who are in the 13 days between vaccine administration and partial or full immunization
- A HCW will be considered unvaccinated if s/he did not receive COVID-19 vaccine or if s/he was vaccinated after symptoms onset

Laboratory methods

Because they are high-risk for SARS-CoV-2 infection, HCWs are recommended to be tested if they develop symptoms. Furthermore, respiratory specimens are routinely collected from HCWs as part of the Covid-19 surveillance system in Zambia. Therefore, additional respiratory specimens will not need to be collected as part of this project. As is the practice for routine Covid-19 surveillance, trained health personnel collect respiratory specimens from patients respecting safety standards for COVID-19 and following WHO biosafety guidelines (29,30). Biological materials will only be collected and stored in collaboration with hospitals and local health authorities according to current laboratory safety procedures.

According to national guidelines, HCWs who have positive test results should undergo genomic sequencing (31). Furthermore, WHO recommends genomic characterization as part of a country's routine surveillance program (5). RT-PCR specimens with cycle threshold (Ct) values of ≤30 are eligible for sequencing in Zambia. Specimens will be stored at -20°C while awaiting genomic sequencing. Genomic sequencing will be performed at the University of Zambia School of Veterinary Medicine laboratory according to a standard protocol. For WGS, complementary DNA was prepared using random primers from viral RNA extracted from SARS-CoV-2 real-time RT-PCR–positive specimens. Multiplex PCR will be performed using custom primers to generate overlapping amplicons for nanopore sequencing on a MinION (Oxford Nanopore Technology, United Kingdom).[‡] Consensus sequence reads will be generated using the standard ARTIC Network bioinformatic pipeline.[§] HCW participants will be consented for

[‡] https://www.protocols.io/view/ncov-2019-sequencing-protocol-v3-locost-bh42j8ye
[§] https://artic.network/ncov-2019/ncov2019-bioinformatics-sop.html

genomic sequencing as part of this project. Additionally, HCW participants will be consented to store specimens for potential testing at a future date.

Data management

All data collected through this protocol are the property of the Zambian Ministry of Health. All data will be maintained on encrypted servers at the MOH. Data will be backed up as per the protocol for MOH servers; additionally, the data manager will weekly download the project data and store the dataset on a password-protected and encrypted hard drive. The data manager (authorized by MoH) will routinely generate datasets for project-related analysis, with the client identification number removed and a new unique identifier created. No personally identifying information (PII) will be contained in project datasets. The CRF will be produced in hard copy and available electronically in KoboCollect (ODK). Completed CRFs and HCW line lists will be maintained in the project team's office in secure locations according to applicable MoH regulations. The project staff will enter data from hard-copy CRF into the electronic KoboCollect form, which will be maintained on the encrypted MoH server. All reviews and decisions regarding data sharing, for example at the request of a journal at the time of publication, will be made by the MOH as the owners of the primary data according to NHRA policies and procedures. Electronic data will be retained, disposed, and/or archived according to established MOH policy.

Data quality

Routine data quality assessments will be performed by the project staff. During data collection, key variables will be interrogated for data completeness on a frequent basis, with investigation of any discrepancies and remedial action as indicated. Summary and frequency tables as well as visual representations of appropriate variables will be used to find implausible or missing values within the dataset. Checks for inconsistencies will be carried out (e.g., date of discharge from hospital before date of onset of symptoms). These checks will be included as warnings in the electronic questionnaire to avoid inconsistencies in the data entry. Any changes to the data will be documented and stored separately from the crude database. Any recoding of data (e.g., age) will be documented.

Staff training

All project staff will be trained in the procedures of the protocol. Data collectors will be trained in interviewing skills, completing the questionnaire, and medical records and vaccination documents review.

All staff will be trained in privacy, security, and confidentiality. Selected staff (project manager, health facility in-charge) will be trained in case/control identification.

Data analysis

Data will be aggregated and analyzed by MoH with support from CDC using R, SAS, or other appropriate statistical software. For the primary objective, only HCW cases who developed any symptoms of Covid-19-like illness during a period from 7 days prior to 7 days after test collection date will be included in the VE analysis. Primary sensitivity analyses will include HCW cases who meet criterion 1 or 2 below, which were adapted from the WHO COVID-19 surveillance case definition (32).

Table 2. Criteria for sensitivity analyses of the primary outcome variable based on the WHO Covid-19 case definition

Criterion 1. At least TWO of the following respiratory signs/symptoms	Criterion 2. At least THREE of the following
• Fever • Cough • Dyspnea (shortness of breath or difficulty breathing) • Acute respiratory distress syndrome (ARDS) • Anosmia or ageusia (new olfactory or taste disorders)	• Fever • Chills • Cough • Dyspnea • Myalgia • Rigors • Headache • Sore throat • Coryza • Rhinorrhea • Fatigue • General weakness • Anorexia • Nausea • Vomiting • Diarrhoea • Altered mental status

The primary population is symptomatic HCWs. Secondary outcomes will assess VE by SARS-CoV-2 variant strains, duration since vaccination, interval between doses (for two-dose vaccines) and severe Covid-19. Markers of severity of disease may include hospitalization, length of stay, oxygen therapy, intensive care unit admission, mechanical ventilation, death, clinical signs of pneumonia (fever, cough, dyspnea, and/or tachypnea), severe tachypnea (respiratory rate > 30 breaths/min), severe respiratory distress, acute respiratory distress syndrome (ARDS), and oxygen saturation <90% on room air, sample size permitting.

Descriptive analyses will be performed (Table 3). Characteristics of HCW cases and controls will be compared using chi-square tests or Fisher's exact tests (for categorical variables) or t-tests or Wilcoxon rank-sum tests (for continuous variables). Bivariate logistic regression will be performed on the outcome variables according to the different objectives. Additionally, a multivariable logistic regression analysis will be conducted to control for negative and positive confounding. Variables will be tested for multicollinearity. Interactions will be tested using the likelihood ratio test or Wald's test and will be included in the model if significant at the 5% level. Factors other than statistical significance (prevalence of exposure, magnitude of OR) will also be used as criteria for inclusion of a variable or an interaction term. A variable for sex, age and for onset time will be included in all multivariable models. Analyses will adjust for clustering by health facility (or district) and repeat participation (for those HCWs who have two interviews).

Table 3. Example of descriptive table for cases and controls

Variables	Number of symptomatic laboratory-confirmed COVID-19 cases /total n (%)	Number of symptomatic test-negative controls /total n (%)
Median age (IQR*)	X	X
Missing	X	X
Age groups		
0–14	x/x (x)	x/x (x)
15–44	x/x (x)	x/x (x)
45–64	x/x (x)	x/x (x)
≥ 65	x/x (x)	x/x (x)
Missing	X	X
Sex		
Female	x/x (x)	x/x (x)
Missing	X	X
Days between onset of symptoms and swabbing		
0	x/x (x)	x/x (x)
1	x/x (x)	x/x (x)
2	x/x (x)	x/x (x)
3	x/x (x)	x/x (x)
4–7	x/x (x)	x/x (x)
COVID-19 vaccination by documentation	x/x (x)	x/x (x)
Unvaccinated	x/x (x)	x/x (x)
Fully Vaccinated	x/x (x)	x/x (x)
Partially vaccinated	x/x (x)	x/x (x)
Unknown	x/x (x)	x/x (x)

	Etc.			

*IQR: inter-quartile range

To measure VE, we will calculate the odds ratio for vaccination (receipt of SARS-CoV-2 vaccine compared to no vaccine) among cases vs. controls, adjusting for potential confounders (including matched variables) (33). Because it is a test-negative design, time (of onset or testing) will be included in analyses. VE will be estimated as follows:

$$Vaccine\ effectiveness\ =\ (1\ -\ aOR\ for\ vaccination)\ x\ 100\%$$

A 95 % CI will be computed around the point estimate as 1 − CI_{OR}, where CI_{OR} is the confidence interval of the odds ratio estimates (34). For the primary VE analysis, a conservative approach will be taken to minimize the risk of misclassification bias: a complete recommended series of SARS-CoV-2 vaccine (e.g., 2 doses) will be compared to no vaccine. Any HCW with symptoms onset during the 14 days following receipt of the 2nd dose will be excluded from the analysis of complete vaccination because their vaccination status is unknown (5). Likewise, any HCW with symptoms onset during the 14 days following receipt of the 1st dose will be excluded from the analysis of partial vaccination. We will adjust VE estimates for important covariates (Table 4). Sensitivity analyses evaluating VE will be conducted (Table 5). Controls who are negative by RT-PCR but have chest imaging results suggestive of COVID-19** (gleaned from medical record review), and those with prior SARS-CoV-2 infection in the 3 months prior to recruitment, may be excluded as controls in sensitivity analyses. Analyses will be stratified by vaccine type.

Table 4. Example of table showing vaccine effectiveness against COVID-19 adjusted for various covariables by sex and age group

Type/subtype	Population included	Analysis scenarios/adjustments made	CVE (%)	(95%CI)
Symptomatic COVID-19	All ages	N (cases/ vaccinated; controls/ vaccinated)		
		Crude		
		Adjusted for onset week (cubic spline)		
		Adjusted for sex		

** According to WHO: Chest radiography: hazy opacities, often rounded in morphology, with peripheral and lower lung distribution. Chest CT: multiple bilateral ground glass opacities, often rounded in morphology, with peripheral and lower lung distribution. Lung ultrasound: thickened pleural lines, B lines (multifocal, discrete, or confluent), consolidative patterns with or without air bronchograms.

	Adjusted for chronic condition
	Adjusted for age (cubic spline)
	Adjusted for onset week, age (cubic spline)
	Adjusted for onset week, chronic condition
	Adjusted for onset week, age (cubic spline), chronic conditions, sex
0–49 years	N (cases/ vaccinated; controls/ vaccinated)
	Crude
	Adjusted for onset month, age (cubic spline)
50 years and over	N (cases/ vaccinated; controls/ vaccinated)
	Crude
	Adjusted for onset week, age (cubic spline), chronic condition, sex

Table 5. Planned sensitivity analyses of vaccine effectiveness

Sensitivity analyses planned
- HCWs meeting more restrictive clinical criteria (outlined in Table 2)
- Interval between doses (for two-dose vaccines)
- Time since complete vaccination is done
- Inclusive of HCWs with self-reported vaccination without documentation/details
- Exclusion of HCW controls who have probable Covid-19 (based on radiography findings)
- Inclusion of persons with indeterminate vaccination status (as defined earlier)
- By variant strain (sample size permitting)
- Other analyses, where indicated

We will conduct interim analyses after approximately 3 months of enrollment to evaluate vaccine coverage among controls. If these analyses suggest that we will not have adequate sample size to meet our primary objective, we will consider conducting the evaluation for a longer period.

For genomic sequencing, consensus sequence reads will be analyzed to identify virus clade and genotype according to PANGO nomenclature.[††] Overall proportions will be reported and, sample size permitting, VE estimates will be calculated according to variant strain type.

[††] https://github.com/cov-lineages/pangolin/

Impact of previous SARS-CoV-2 infection in cases or control and potential inclusion of asymptomatic controls

Individuals who have been previously infected may have a greater response to the vaccine or be less likely to be reinfected even if unvaccinated. It is possible that some of the controls (those testing negative for SARS-CoV-2) may have themselves been positive for SARS-CoV-2 some time before but were asymptomatic. Knowledge of prior infection could affect one's likelihood to be vaccinated. This, in turn, would lower vaccination coverage among controls and increase VE. Ascertainment of which controls may have had previous SARS-CoV-2 infection will be attempted by asking about previous SARS-CoV-2 tests and results, as well as prior clinical symptoms. However, among the controls, there could still potentially be several patients with prior SARS-CoV-2 infection. Sensitivity analyses will be conducted excluding any HCW with previous SARS-CoV-2 infection confirmed and/or suspected.

Results dissemination

Results dissemination to stakeholders of any analyses completed under the auspices of this protocol will occur through five main mechanisms: 1) local presentation to the MOH COVID-19 response team or relevant sub-group; 2) local presentations to CDC-Zambia; and; 3) a report which can be disseminated to all levels of MOH and the public; 4) presentations at regional and international scientific conferences; and 5) manuscripts published in international, peer-reviewed journals.

Ethics

Patient risks and benefits

This investigation poses minimal risk to participants. The main risk of participating in this project is a potential for breach of confidentiality, namely the disclosure of personal medical information collected as part of this activity, such as HIV status. No names or personal identifiers will be used in reports, presentations, or publications from this project. Project staff will implement human (training), physical, and electronic protections to ensure security of personally identifiable information. To prevent inadvertent identification of participants due to fine stratification (e.g., small cell size related to residence), any stratification units resulting in less than 10 participants will not be released. No other risk are anticipated as a result of participation in the project. The primary benefit of the project is indirect in that data collected will help improve and guide vaccination efforts and policy against SARS-CoV-2 infection

and may prevent further transmission of the virus in Zambia. The study includes participants in the following potentially vulnerable populations: pregnant women, persons living with HIV.

Informed consent

Informed consent will be obtained for CRF's (electronic and telephone), for which a consent section is part of the interview process (Appendices 2-4). The purpose of the investigation will be explained to all HCWs identified for recruitment into the investigation. Verbal informed consent will be obtained by a trained member of the project team from all HCWs willing to participate in the investigation before any information is collected as part of the investigation. Each participant must be informed that participation in the project is voluntary and that s/he is free to withdraw, without justification, from the investigation at any time without consequences and without affecting professional responsibilities. Informed consent will seek approval to genetically sequence nasopharyngeal specimen. HCW participants will also be asked about storage and future testing of their test specimen. With HCW participant permission, an informational card will be emailed (encrypted) or texted to with contact information for the project manager for questions or follow-up.

Local review with an institutional review board (IRB)

The protocol will undergo local review by an IRB in Zambia and the protocol will be registered with the relevant authorities in country.

Sponsor monitoring

CDC is the primary sponsor for the activities described herein. As the sponsor, the CDC may conduct monitoring or auditing of activities to ensure the integrity of the data collected and to ensure the rights and protection of individuals. Monitoring and auditing activities may be conducted by:

- CDC staff ("internal")
- Authorized representatives of CDC (e.g., a contracted party considered to be "external")
- Both internal and external parties.

Monitoring or auditing may be performed by means of on-site visits to government facilities or through other communications such as telephone calls or written correspondence. The visits will be scheduled at mutually agreeable times, and the frequency of visits will be at the discretion of CDC. During the visit, any

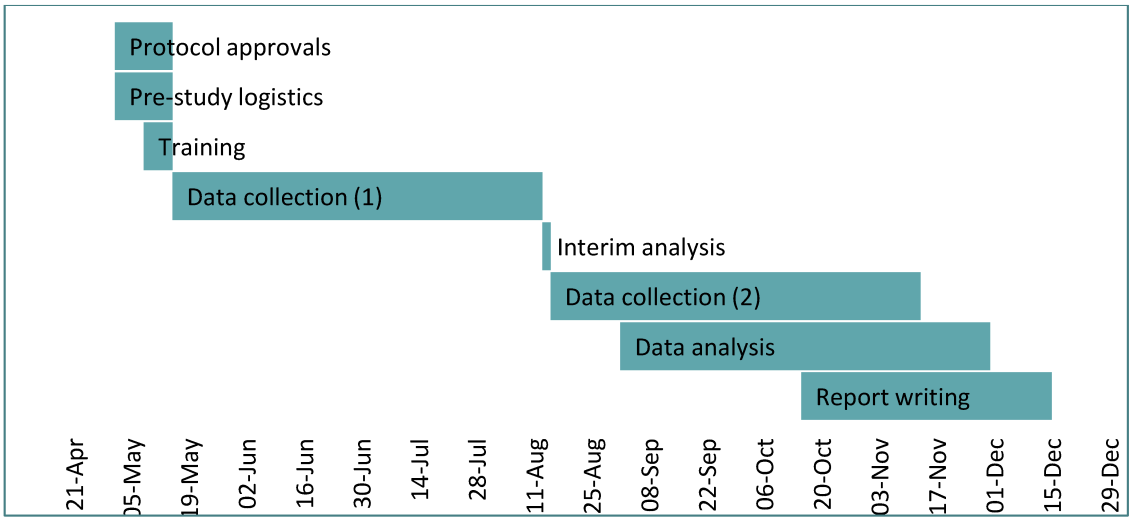
related materials may be reviewed and the Co-Agreement managers along with the relevant staff should be available for discussion of findings.

To ensure compliance with national and international regulatory guidelines, the activities outlined in this proposal may be subject to inspection or review by authorized Zambian or international regulatory authorities, including the UNZA BREC, NHRA, and US IRBs.

1Project timeline

- May 15,2021: Enrollment and data collection for HCW cases and controls begin
- July-August 2021 (if enrollment started in May): Interim analysis of vaccine coverage among VE controls; revise sample size estimates and enrollment timelines as needed
- December 2021 (or after 6 months of enrollment or when sample size is reached): Complete VE analysis; report results

Figure 2. Gannt chart of Covid-19 vaccine effectiveness project



Budget

Expense	Unit cost (Kwacha)	Number	Days	Total (Kwacha)
IRB fees	5,000	1	-	5,000
Training – hall hire	4,400	1	5	22,000
Training - Transport allowance	200	20	5	20,000
Site visits (fuel oil)	700	20	1	14.000
Research assistants	20,000	3	6	360,000

Airtime	50	250	-	12,500
Translation services	1,000	5	-	5,000
Genomic sequencing	1,100	90	-	99,000
Tracing specimen and transport	200	100	-	20,000
Total				*557,500*

References

1. Phelan AL, Katz R, Gostin LO. The Novel Coronavirus Originating in Wuhan, China: Challenges for Global Health Governance. Vol. 323, JAMA - Journal of the American Medical Association. 2020.
2. Zambia National Public Health Institute. Zambia COVID-19 Statistics; Daily Status Update [Internet]. Available from: https://www.facebook.com/ZMPublicHealth/
3. Bialek S, Boundy E, Bowen V, Chow N, Cohn A, Dowling N, et al. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(12).
4. McMichael TM, Currie DW, Clark S, Pogosjans S, Kay M, Schwartz NG, et al. Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington. N Engl J Med. 2020;382(21).
5. World Health Organization (WHO). Evaluation of COVID-19 vaccine effectiveness [Internet]. 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1
6. Mwenda M, Saasa N, Sinyange N, Busby G, Chipimo PJ, Hendry J, et al. Detection of B.1.351 SARS-CoV-2 Variant Strain — Zambia, December 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2021;70(8):2020–2. Available from: http://www.cdc.gov/mmwr/volumes/70/wr/mm7008e2.htm?s_cid=mm7008e2_w
7. Chipimo PJ, Barradas DT, Kayeyi N, Zulu PM, Muzala K, Mazaba ML, et al. First 100 Persons with COVID-19 — Zambia, March 18–April 28, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(42):1547–8.
8. Mulenga LB, Hines JZ, Fwoloshi S, Chirwa L, Siwingwa M, Yingst S, et al. Prevalence of SARS-CoV-2 in six districts in Zambia in July , 2020 : a cross-sectional cluster sample survey. Lancet Glob Heal [Internet]. 2021;(21):1–9. Available from: http://dx.doi.org/10.1016/S2214-109X(21)00053-X
9. Fwoloshi S, Hines JZ, Barradas DT, Yingst S, Siwingwa M, Chirwa L, et al. Prevalence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) among Health Care Workers-Zambia, July 2020. Clin Infect Dis [Internet]. 2021 Mar; Available from: https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab273/6204763
10. Çelebi G, Pişkin N, Çelik Bekleviç A, Altunay Y, Salcı Keleş A, Tüz MA, et al. Specific risk factors for SARS-CoV-2 transmission among health care workers in a university hospital. Am J Infect Control. 2020 Oct;48(10):1225–30.
11. Lai X, Wang M, Qin C, Tan L, Ran L, Chen D, et al. Coronavirus Disease 2019 (COVID-2019) Infection Among Health Care Workers and Implications for Prevention Measures in a Tertiary Hospital in Wuhan, China. JAMA Netw open. 2020 May;3(5):e209666.
12. Contejean A, Leporrier J, Canouï E, Fourgeaud J, Mariaggi A-A, Alby-Laurent F, et al. Transmission Routes of Severe Acute Respiratory Syndrome Coronavirus 2 Among Healthcare Workers of a French University Hospital in Paris, France. Open forum Infect Dis. 2021 Mar;8(3):ofab054.
13. Shrotri M, Swinnen T, Kampmann B, Parker EPK. An interactive website tracking COVID-19 vaccine development. Lancet Glob Heal. 2021;9(5).
14. World Health Organization. Draft landscape and tracker of COVID-19 candidate vaccines [Internet]. 2021. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
15. World Health Organization. Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19. 2021;19(3):1–9. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1
16. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269).

17. AZD1222 US Phase III primary analysis confirms safety and efficacy [Internet]. 2021. Available from: https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/azd1222-us-phase-iii-primary-analysis-confirms-safety-and-efficacy.html
18. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet. 2021;397(10277).
19. Vasileiou E, Simpson CR, Shi T, Kerr S, Agrawal U, Akbari A, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet (London, England). 2021 Apr;
20. Emary KRW, Golubchik T, Aley PK, Ariani C V., Angus B, Bibi S, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Lancet. 2021;397(10282).
21. Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. N Engl J Med. 2021;
22. Jangra S, Ye C, Rathnasinghe R, Stadlbauer D, Krammer F, Simon V, et al. SARS-CoV-2 spike E484K mutation reduces antibody neutralisation. The Lancet Microbe. 2021;
23. Greaney AJ, Loes AN, Crawford KHD, Starr TN, Malone KD, Chu HY, et al. Comprehensive mapping of mutations in the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human plasma antibodies. Cell Host Microbe. 2021;29(3).
24. Andreano E, Piccini G, Licastro D, Casalino L, Johnson N V., Paciello I, et al. SARS-CoV-2 escape in vitro from a highly neutralizing COVID-19 convalescent plasma. bioRxiv [Internet]. 2020; Available from: https://www.biorxiv.org/content/10.1101/2020.12.28.424451v1.full.pdf
25. Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. medRxiv [Internet]. 2020;2. Available from: https://www.medrxiv.org/content/10.1101/2020.12.21.20248640v1.full.pdf
26. Mashe T, Takawira FT, Gumbo H, Juru A, Nyagupe C, Maeka KK, et al. Surveillance of SARS-CoV-2 in Zimbabwe shows dominance of variants of concern. The Lancet Microbe. 2021;
27. Fukushima W, Hirota Y. Basic principles of test-negative design in evaluating influenza vaccine effectiveness. Vaccine. 2017;35(36).
28. Zambia Ministry of Health. Implementation Strategy – Active Screening for COVID-19 in Health Facilities. Lusaka; 2020.
29. World Health Organization. Laboratory biosafety guidance related to coronavirus disease (COVID-19) [Internet]. 2020. Available from: https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-(covid-19)
30. World Health Organization. Laboratory biosafety manual 3rd edition [Internet]. World Health Organization. 2004. 1–178 p. Available from: http://books.google.com/books?hl=en&lr=&id=qVHfjFlNjzwC&oi=fnd&pg=PP9&dq=Laboratory+biosafety+manual&ots=Qw_FLuZChi&sig=xgd8x9nOBNLlDE5wsH-WAZP6Kw0
31. Zambia National Public Health Institute. Zambia's SARS-CoV-2 Genomic Surveillance Strategy. Lusaka; 2021.
32. World Health Organization. COVID-19 Case Definition [Internet]. 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.2
33. Pearce N. Analysis of matched case-control studies. BMJ. 2016;352.
34. Tenforde MW, Olson SM, Self WH, Talbot HK. Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Among Hospitalized Adults Aged ≥ 65 Years —. Morb Mortal Wkly Rep. 2021;70.

Appendices

Appendix 1: Example of a weekly line list for HCW cases and controls

Week reporting: _____ Start date: ____ / ____ / _____ End date: ____ / ____ / _____

Reported by: (Name)_____

Healthcare Facility: _____

Last name	First name	DOB	Phone number	Email	Job	Test collect date	Test type	Specimen type	Reason for test	Test result
Smith	John	01/01/1981	404-793-1234	abc@xyx.com	RT		PCR		Symptomatic	Positive
Jackson	Rosy	10/10/1970	470-923-8765	efg@abn.com	RN		Antigen		Screening	Negative

Appendix 2: Case report form (Exposure assessment form) (see attachments)

Appendix 3: Proxy form (see attachment)

Appendix 4: Introductory script for telephone interview

INSTRUCTIONS: THIS SCRIPT HAS MULTIPLE SECTIONS. USE THE SECTION APPROPRIATE FOR THE CALL YOU ARE MAKING.

BEFORE CALLING: Complete the information on the call log sheet. List the district of residence, national ID number (if known), HCW name, and telephone number(s).

Section A: Answering Machine

TO THE ANSWERING MACHINE: Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. I am calling to talk with you about an important public health project. Please call me at _____. If I am unable to answer the phone when you call, please leave a message with your name, phone number, and a time I may call you back. Thank you.

Section B: HCW Cases

Q1 TO THE PERSON WHO ANSWERS THE PHONE, IF ADULT; OTHERWISE, ASK TO SPEAK TO AN ADULT: Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project about COVID-19. May I please speak to [HCW CASE]?

___YES: PERSON WHO ANSWERED IS HCW CASE; GO TO Q4.

___YES: COMING TO THE PHONE; GO TO Q3.

___NO: PERSON IS NOT AVAILABLE NOW; GO TO Q1.1.

___NO: PERSON IS DECEASED: I'm sorry. I was not aware of your loss. I would like to offer my condolences to you and your family. We are still able to include [HCW CASE] in the project using an interview from you or others who know about him/her, if you would like – Is this a good time to talk or should I call back another time? IF A GOOD TIME TO TALK, GO TO Q6; IF NOT, RECORD CALL-BACK DAY/TIME ON PHONE LOG.

___NO: PERSON IS INCAPACITATED; I'm sorry to hear that. GO TO Q1.2

___NO: REACHED WRONG NUMBER; ASK IF YOU HAVE DIALED THE NUMBER NOTED ON **CALL LOG**.

Sorry, I must have the wrong number. Good-bye. =STOP=

___DOES NOT SPEAK ENGLISH; RECORD LANGUAGE IN COMMENT SECTION OF **CALL LOG**. We will try to call back with someone who speaks [preferred language].

Q1.1 When would be a good time to reach him/her or is there another phone number to reach him/her? RECORD PERSON'S NAME TO ASK FOR, AND DAY/TIME TO CALL AND ALTERNATIVE NUMBER ON CALL LOG. Thank you very much for your time. Good-bye. =STOP=

Q1.2 Can I call back in 7 days to see if [HCW CASE] will get better and be able to talk?

___YES; RECORD ON **CALL LOG** TO CALL AGAIN IN **7 DAYS**. Thank you very much for your time. I wish [HCW CASE] a quick recovery. GO TO Q1 WHEN CALL IN 7 DAYS; IF [HCW CASE] IS STILL INCAPACITATED ON DAY 7 AFTER INITIAL CALL, GO TO Q1.2 (IF HCW CASE IS STILL INCAPACITATED AFTER 5 ATTEMPTS, GO TO Q6)

___NO; Thank you very much for your time. I wish [HCW CASE] a quick recovery. [RECORD DAY/ TIME ON **CALL LOG**]. =STOP=

Q2 May I speak with him/her?

___YES; COMING TO THE PHONE; GO TO Q3.

___NO; BUT NOT HOME; GO TO Q2.1.

Q2.1 Is there another phone number at which I could reach him/her?

___Yes; RECORD ALTERNATE PHONE NUMBER ON **CALL LOG**. Thank you very much for your time. =STOP=

___No; When would be a good time to call back to reach him/her? [RECORD DAY/ TIME ON **CALL LOG**]. Thank you very much for your time. =STOP=

Q3 Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project on COVID-19. Are you [HCW CASE]?

___Yes; GO TO Q4. ___No; GO BACK TO Q2.

Q4 I am helping to investigate the outbreak of coronavirus infection (known as COVID-19) in Zambia. The Ministry of Health/Zambia National Public Health Institute is notified whenever there is a person with COVID-19. Public health officials are trying to better understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well vaccine to prevent COVID-19 is working among healthcare workers.

You have been identified as a healthcare worker who tested positive for the coronavirus that causes COVID-19. Would you be willing to answer some questions to help us describe the types of exposures that healthcare workers have had to COVID-19, and if you have received the new vaccine to prevent COVID-19 so we can better understand how to help protect healthcare personnel?

If you decide to answer the survey, it should take about 30 - 45 minutes. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Information that you provide to me will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name will not be shared. We will not share any individual-level information with the health facility where you work. This information will be used to inform the public health response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

Do you wish to participate?

___Yes; GO TO Q5. ___No; GO TO Q4.1.

Q4.1 Your participation in this project is very important. May I schedule a time to talk that would be better for you?

___Yes; RECORD DAY/TIME ON CALL LOG. Thank you very much for your time. =STOP=

___No; Sorry to have disturbed you. Good-bye. =STOP=

Q5 Thank you for agreeing to participate. If you have a calendar or planner, it may be helpful to get it to help you remember certain events. Do you need a few minutes to get your calendar?

___Yes; Okay, why don't you go get your calendar now, and when you return to the phone we can begin. [ONCE HCW CASE RETURNS TO PHONE, GO TO CRF]

___No; Okay, let's get started. [GO TO CRF]

PROXY INTERVIEW SCRIPT FOR HCW CASES:

Q6 IF YOU HAVE NOT INTRODUCED YOURSELF YET: Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project to understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well vaccine to prevent COVID-19 is working among healthcare workers.

[HCW CASE] may be eligible to be included in this project. Once again, I am sorry to hear that [HCW CASE] is [DECEASED/NOT ABLE TO BE INTERVIEWED]. It is very important that we get information from as many people as possible, and you may be able to participate on [HCW CASE'S] behalf. Your participation is voluntary and involves completing a phone interview. The interview should take about 15 minutes. It will include

questions about [HCW CASE'S] home, health, and vaccinations. Are you the person that can best answer questions about [HCW CASE]? Your responses will be kept confidential. We will ask for your permission to contact [HCW CASE'S] medical provider(s) to obtain information about the vaccinations [HCW CASE] has received and their health status.

Information that you provide to me will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name and [HCW's] will not be shared. We will not share any individual-level information with the healthcare facility where [HCW] works. This information will be used to inform the response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you or HCW.

Do you wish to participate?

___ YES; PROCEED TO PROXY INTERVIEW

___NO; GO TO Q6.1

Q6.1 Is there someone else who can better answer questions about [HCW CASE'S] home, health and vaccinations?

___YES; RECORD INFORMATION IN CALL LOG

___ NO; Thank you very much for your time. =STOP=

Section C: HCW Controls

BEFORE CALLING: Complete the information on the call log sheet. List the district of residence, national ID number (if known), HCW name, and telephone number(s).

NOTE: HCW controls may be selected multiple times for inclusion in the project, based on multiple negative SARS-CoV-2 tests. Project staff should review the initial interview form to determine whether the control had symptoms at that time. When contacting the HCW control to re-interview them, project staff should first talk with the HCW control to determine when the previous illness resolved before proceeding with the full interview. If the illness did not resolve at least 4 weeks prior to the re-interview, the HCW control is not eligible for re-inclusion.

Q1E TO THE PERSON WHO ANSWERS THE PHONE, IF ADULT; OTHERWISE, ASK TO SPEAK TO AN ADULT: Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project about COVID-19. May I please speak to [HCW]?

___YES: PERSON WHO ANSWERED IS HCW; GO TO Q4E

___ YES: PERSON WHO ANSWERED IS HCW AND WAS PREVIOUSLY ENROLLED; GO TO Q5E

___YES: COMING TO THE PHONE; GO TO Q3E.

___NO: PERSON IS NOT AVAILABLE NOW; GO TO Q1E.1.

___ NO: PERSON IS DECEASED: I'm sorry. I was not aware of your loss. I would like to offer my condolences to you and your family. We are still able to include [HCW] in the project using an interview from you or others who know about him/her, if you would like – Is this a good time to talk or should I call back another time? IF A GOOD TIME TO TALK, GO TO Q6; IF NOT, RECORD CALL-BACK DAY/TIME ON PHONE LOG.

___NO: PERSON IS INCAPACITATED; I'm sorry to hear that. GO TO Q1E.2

___NO: REACHED WRONG NUMBER; ASK IF YOU HAVE DIALED THE NUMBER NOTED ON **CALL LOG**.

Sorry, I must have the wrong number. Good-bye. =STOP=

___DOES NOT SPEAK ENGLISH; RECORD LANGUAGE IN COMMENT SECTION OF **CALL LOG**. We will try to call back with someone who speaks [preferred language].

Q1E.1 When would be a good time to reach him/her or is there another phone number to reach him/her? RECORD PERSON'S NAME TO ASK FOR, AND DAY/TIME TO CALL AND ALTERNATIVE NUMBER ON CALL LOG. Thank you very much for your time. Good-bye. =STOP=

Q1E.2 Can I call back in 7 days to see if [HCW] will get better and be able to talk?

___YES; RECORD ON **CALL LOG** TO CALL AGAIN IN **7 DAYS**. Thank you very much for your time. I wish [HCW] a quick recovery. GO TO Q1 WHEN CALL IN 7 DAYS; IF [HCW] IS STILL INCAPACITATED ON DAY 7 AFTER INITIAL CALL, GO TO Q1E.2 (IF HCW IS STILL INCAPACITATED AFTER 5 ATTEMPTS, GO TO Q6)

___NO; Thank you very much for your time. I wish [HCW] a quick recovery. [RECORD DAY/ TIME ON **CALL LOG**]. =STOP=

Q2E May I speak with him/her?

___YES; COMING TO THE PHONE; GO TO Q3E.

___NO; BUT NOT HOME; GO TO Q2E.1.

Q2E.1 Is there another phone number at which I could reach him/her?

___YES; RECORD ALTERNATE PHONE NUMBER ON **CALL LOG**. Thank you very much for your time. =STOP=

___NO; When would be a good time to call back to reach him/her? [RECORD DAY/ TIME ON **CALL LOG**]. Thank you very much for your time. =STOP=

Q3E Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project on COVID-19. Are you [HCW]?

___YES; GO TO Q4E.

___NO; GO TO Q2E.

Q4E I am helping to investigate the outbreak of coronavirus infection (known as COVID-19) in Zambia. Public health officials are trying to better understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well the COVID-19 vaccine is working in healthcare workers to prevent illness. You have been identified as a healthcare worker who was tested for COVID-19. Would you be willing to answer some questions to help us describe the types of exposures that healthcare workers have had to COVID-19 and if you have received the COVID-19 vaccine so we can better understand how we can help protect healthcare workers?

If you decide to answer the survey, it should take about 30 – 45 minutes. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Information that you provide to me will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name will not be shared. We will not share any individual-level information with the healthcare facility where you work. This information will be used to inform the response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

Do you wish to participate?

___YES; GO TO Q4E.2 ___NO; GO TO Q4E.1

Q4E.1 Your participation in this project is very important. May I schedule a time to talk that would be better for you?

___YES; RECORD DAY/TIME ON CALL LOG. Thank you very much for your time. =STOP=

___NO; Sorry to have disturbed you. Good-bye. =STOP=

Q4E.2 If you have a calendar or planner, it may be helpful to get it to help you remember certain events. Do you need a few minutes to get your calendar?

___YES; Okay, why don't you go get your calendar now, and when you return to the phone we can begin. [ONCE HCW RETURNS TO PHONE, GO TO CRF]

___NO; Okay, let's get started. [GO TO CRF]

Q5E I am helping to investigate the outbreak of coronavirus infection (known as COVID-19) in Zambia. Public health officials are trying to better understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well the COVID-19 vaccine is working in healthcare workers to prevent illness. You have been identified as a healthcare worker who was tested for COVID-19. I see that you were previously enrolled and may be eligible to be enrolled again. May I ask you one question to see if you are eligible?

___YES; GO TO Q5E.1

___NO; Thank you for your time. Good-bye. =STOP=

Interviewer Instruction: *Calculating the date 4 weeks prior to subsequent negative: e.g. if the initial negative test was on March 30, 2021 and subsequent negative was May 3 then the date 4 weeks prior is April 26, 2021. Thus, to be eligible, any symptoms associated with the previous negative test should have resolved prior to April 26.*

Q5E.1 Per our records, we last interviewed you on [XX DATE]. Did you/have you had any symptoms associated with the prior illness after [MM, DD, YYYY – This is the Date 4 weeks prior to the subsequent negative test date]?

___YES; SORRY, YOU ARE NOT ELIGIBLE TO PARTICIPATE AT THIS TIME. THANK YOU =STOP=

___NO; GO TO Q5E.2

Q5E.2 You are eligible to participate. Would you be willing to answer some questions about whether you have received the COVID-19 vaccine and other health related questions so we can better understand how we can help protect healthcare workers? The survey takes 30-45 minutes. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Information that you provide to me will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name will not be shared. We will not share any individual-level information with the healthcare facility where you work. This information will be used to inform the response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

Do you wish to participate?

___YES; PROCEED TO CONSENT/INTERVIEW

___YES, BUT NOW IS NOT A GOOD TIME –RECORD CALL BACK INFORMATION ON CALL LOG. =STOP=

___NO; Thank you very much for your time. =STOP=

PROXY INTERVIEW SCRIPT FOR HCW CONTROLS:

Q6 IF YOU HAVE NOT INTRODUCED YOURSELF YET: Hello, my name is _____. I'm calling from the Ministry of Health/Zambia National Public Health Institute. We are conducting a public health project to understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well vaccine to prevent COVID-19 is working among healthcare workers.

[HCW] may be eligible to be included in this project. Once again, I am sorry to hear that [HCW] is [DECEASED/NOT ABLE TO BE INTERVIEWED]. It is very important that we get information from as many people as possible, and you may be able to participate on [HCW's] behalf. Your participation is voluntary and

involves completing a phone interview. The interview should take about 10-15 minutes. It will include questions about [HCW's] home, health, and vaccinations. Are you the person that can best answer questions about [HCW]? Your responses will be kept confidential. We will ask for your permission to contact [HCW's] medical provider(s) to obtain information about the vaccinations [HCW's] has received and their health status.

Information that you provide to me will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name and [HCW's] will not be shared. We will not share any individual-level information with the healthcare facility where [HCW] works. This information will be used to inform the response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you or HCW.

Do you wish to participate?

___ YES; PROCEED TO PROXY INTERVIEW

___NO; GO TO Q6.1

Q6.1 Is there someone else who can better answer questions about [HCW's] home, health and vaccinations?

___YES; RECORD INFORMATION IN CALL LOG ___ NO; Thank you very much for your time. =STOP=

Appendix 5: Sample introductory EMAIL TEXT

Section A: HCW COVID-19 Cases

Dear [Name of HCW Case],

We are emailing you to ask for your help with the public health response to the pandemic of novel coronavirus infections, known as COVID-19, in Zambia. The Provincial Health Office and the healthcare facility where you work have agreed to participate in an effort led by the Ministry of Health/Zambia National Public Health Institute. Public health officials are collecting information from healthcare workers who tested positive for COVID-19 to better understand how well the vaccine to prevent COVID-19 is working among healthcare workers. The Ministry of Health/Zambia National Public Health Institute is notified of all persons in Zambia that have a positive test for COVID-19. You have been identified as a healthcare worker who tested positive for the coronavirus that causes COVID-19.

If you are willing to help, we would like to ask you to complete a survey. The survey contains questions about your health, your activities as a healthcare worker, and exposures to COVID-19 in the community and in the workplace. We will also ask you questions about vaccinations you received, including new vaccines against COVID-19. If you decide to answer the survey, it should take about 30 - 45 minutes. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Information that you provide will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name and contact information will not be shared. We will not share any individual-level information with the healthcare facility where you work. This information will be used to inform the public health response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

If you have questions or concerns about the survey, please contact: Dr. Oliver Mweso at +260 966493016 or oli.mweso86@gmail.com

If you agree to participate, please click here to access the survey:

If you do not wish to participate, please click here:

If we do not receive a reply from you within three business days of this message, we may reach out to you again by email or by telephone.

Thank you for all that you do as a healthcare worker.

Sincerely yours,

Dr. Oliver Mweso
Ministry of Health
Zambia National Public Health Institute

SECTION B: HCW Controls

Dear [Name of HCW Control],

We are emailing you to ask for your help with the public health response to the pandemic of novel coronavirus infections, known as COVID-19, in Zambia. The Provincial Health Office and the healthcare facility where you work have agreed to participate in an effort led by the Ministry of Health/Zambia National Public Health Institute. Public health officials are collecting information from healthcare workers who tested for COVID-19 to better understand how well the vaccine to prevent COVID-19 is working among healthcare workers. You have been identified as a healthcare worker who has been tested for the coronavirus that causes COVID-19.

If you are willing to help, we would like to ask you to complete a survey. The survey contains questions about your health, your activities as a healthcare worker, and exposures to COVID-19 in the community and in the workplace. We will also ask you questions about vaccinations you received, including new vaccines against COVID-19. If you decide to answer the survey, it should take about 30 -45 minutes. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will also ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Information that you provide will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name and contact information will not be shared. We will not share any individual-level information with the healthcare facility where you work. This information will be used to inform the public health response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

If you have questions or concerns about the survey, please contact: Dr. Oliver Mweso at 260 966493016 or oli.mweso86@gmail.com

If you agree to participate, please click here to access the survey:

If you do not wish to participate, please click here:

If we do not receive a reply from you within three business days of this message, we may reach out to you again by email or by telephone.

Thank you for all that you do as a healthcare worker.

Sincerely yours,

Dr. Oliver Mweso
Ministry of Health
Zambia National Public Health Institute

Appendix 6: Medical Record Review form (see attachment)

Appendix 7: Vaccine Registry/Pharmacy Record Review form (see attachment)

Appendix 8: Informed Consent From

The Zambia Ministry of Health/Zambia National Public Health Institute is investigating the outbreak of coronavirus infection (known as COVID-19 or SARS-CoV-2) in Zambia. The Ministry of Health/Zambia National Public Health Institute is notified whenever a person is tested for COVID-19.

Purpose of the study

You have been identified as a healthcare worker who tested for the coronavirus that causes COVID-19. We would like to ask you some questions to help us describe the types of exposures that healthcare workers have had to COVID-19, and ask about if you have received the new vaccine to prevent COVID-19 so we can better understand how to help protect healthcare personnel. We would like to invite you to be this study. This study is trying to better understand how we can prevent the virus that causes COVID-19 from spreading, including in healthcare facilities. We are also trying to learn how well vaccine to prevent COVID-19 is working among healthcare workers. Participation in this study is voluntary; you don't have to take part if you don't want to.

What is involved in the study

If you decide to take part in the study, we will administer a survey. The survey should take about 30 - 45 minutes. We will ask you questions, and your answers will be kept between us. The questions will be about your age, your health, your workplace. You are free to skip questions that you deem personal or otherwise without penalty. You can stop at any time, and you do not have to answer any question if you do not want to. Your responses will be kept confidential. We will ask for your permission to contact your medical provider(s) to obtain information about the vaccinations you have received and your health status.

Benefits and risks of participation

Your taking part in this study could help us learn more about COVID-19 in Zambia. It can help us learn about how COVID-19 prevention programs are working in the country. There is no incentive to participate in this study.

Potential risks involved with taking part in the study are small. The main risk is that there is a chance that someone could find out you participated in the study, as with all studies. We are doing everything possible to ensure confidentiality and minimize this risk. The information you will give is collected on a tablet. The information is stored securely and can only be accessed by selected study staff. Information that you provide to us will be shared with the Ministry of Health/Zambia National Public Health Institute, but your name will not be shared. We will not share any individual-level information with the health facility where you work. This information will be used to inform the public health response to COVID-19 and may be reported in publications or presentations, but we will not include information in a way that would identify you.

Additional testing of the coronavirus genes

Additionally, an important part of this project involves testing the genetic code of the coronavirus when it is detected in a specimen. This will help us identify instances where changes may have allowed it to escape a person's immune system. If you were positive for coronavirus, we would like to test your specimen to understand the coronavirus' genetic code. This sort of testing is routinely done for selected instances in Zambia. Doing as part of this study will potentially enable Zambia to find variants that could affect the vaccine program. We will not be testing your cells (genetic material) as part of this test. If you do not agree to have the coronavirus in your specimen tested you can still take part in the study without penalty.

Storage of specimens for other potential studies

Furthermore, we would also like to ask you to allow us to keep your nasal specimen that was tested for coronavirus for other tests that will be of public health benefit in Zambia. These tests may be related to diseases caused by viruses or other health issues important to people living in Zambia. We would like your permission to keep your specimen for up to 10 years. The sample will not have your name on it, so we will not be able to tell you the results of these other tests. If you do not agree to storage of your nasal samples, you can still take part in the study and your specimen will be destroyed per standard practices at the laboratory.

Rights of participants

Participation in this study is voluntary. You have the right not to participate at all or to leave the study at any time. Deciding not to participate or choosing to leave the study will not result in any penalty or loss of benefits to which you are entitled, and it will not harm your relationship with your employer.

Study contact

If you would like to have more information about the study, you may contact:

Dr. Oliver Mweso

Ministry of Health | Zambia National Public Health Institute

260 966493016 | oli.mweso86@gmail.com

Do you understand the purpose of the study?

☐ Yes

☐ No

Do you wish to participate in the study?

☐ Yes

☐ No

Is it ok for use to contact medical providers to review your medical records?

☐ Yes

☐ No

Do you agree to have your leftover specimen tested for the genetic code of the coronavirus?

☐ Yes

☐ No

Do you agree to have your leftover specimen stored for other testing that will be of public health benefit in Zambia?

☐ Yes

☐ No

Name of person obtaining consent

_____