Author:	Nicole Shamier, Chief Economist
In consultation with:	Kamar Tanyan, Chief Medical Officer; Jack Howkins, Biomedical Scientist; John Woollacott, Pharmacist.
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Evidence considering COVID-19 vaccinations

This paper is the second in a series. The first is 'evidence considering quarantining and test arrangements'.

This paper does not make recommendations for policy. It provides evidence available and positives and negatives of options. Risk appetite will dictate policy options and recommendations.

This paper is concerned with the use of vaccination to mitigate the arrival and spread of COVID-19 in St Helena.

For other components of the risk picture, St Helena Government's (SHG) COVID-19 Strategy should be referred to. This Strategy is concerned with risk reduction should the virus present itself in St Helena; therefore risk of transmission in the community, risk of infection, risk of death and increased complications amongst those who survive the pandemic.

a. Immunisation Prioritisation

The following case studies provide a blue print which could be useful for St Helena Government when setting its Vaccine/Immunisation Strategy.

Case Study: New Zealand Government (NZG)

The NZG have secured access to the following vaccines (as of December 2020 time of writing):

- Pfizer and BioNTech
  The first COVID-19 vaccine purchase agreement was for 1.5 million COVID-19 vaccines from Pfizer and BioNTech. This is enough vaccines for 750,000 people. Each person will need two doses of this vaccination, about a month apart.
- Janssen Pharmaceutica
  An in-principle agreement has been signed with Janssen Pharmaceutica to purchase up to 5 million COVID-19 vaccines. The Janssen vaccine is likely to be a single-dose.
- Novavax
  In December 2020, the Government signed an agreement with Novavax to purchase 10.72 milion doses of a COVID-19 vaccine. This vaccine requires two doses and will therefore be enough for 5.36 million people. New Zealand is not likely to receive this vaccine until later in 2021.
- AstraZeneca
  A fourth Advance Purchase Agreement was signed in December 2020 with AstraZeneca. This vaccine also requires two vaccines and the Government has purchased 7.6 million doses which is enough for 3.8 million people

NZG have a Vaccine Strategy in place. In brief, this states that:

- NZG expect vaccines to be delivered to the first group of people in the second quarter of 2021.
- Any vaccines NZG distribute will be approved by Medsafe so it meets strict health and safety requirements.
- COVID-19 vaccines will be free of charge.
- They will not be mandatory for the New Zealand public.
- There will be a sequenced rollout plan so that the appropriate vaccines are made available to people at the right time.
- NZG are planning for an extra 2,000-3,000 full time (or equivalent) vaccinators who will be trained and available when needed throughout New Zealand. The workforce will continue to scale up during 2021 in line with vaccine delivery schedules.
- NZG are developing a National Immunisation Solution (NIS). NIS will enable any health worker to record vaccinations anywhere, anytime. The public will be able to digitally access their own immunisation records.

The table below summarises New Zealand Government's COVID-19 Sequencing Framework[1] for vaccine distribution.

	Scenario one: Low/no community transmission	Scenario two: Clusters and controlled outbreaks	Scenario three: Widespread community transmission
Aim	*Prevent transmission*	*Reduce transmission and protect people in close contact*	*Protect those most vulnerable to prevent illness and mortality*
Group one First group of people to receive the vaccine in each scenario	• Border and managed isolation & quarantine workforce • Health workforce at highest risk of exposure to COVID-19 • Household contacts of the above two groups	• Border and managed isolation & quarantine workforce • Health workforce at highest risk of exposure to COVID-19 • Population affected by the outbreak	• Older people (aged care residents, Māori and Pacific people, then others aged over 65 years) • People under 65 with underlying conditions • People living in long-term residential care settings
Group two Second group of people to receive the vaccine in each scenario	• High risk frontline health workforce • High risk frontline public sector and emergency services	• High risk frontline health workforce • High risk frontline public sector and emergency services	• High risk frontline health workforce • High risk frontline public sector and emergency services • Remaining frontline health workforce

[1] https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-vaccine-planning

	Scenario one: Low/no community transmission	Scenario two: Clusters and controlled outbreaks	Scenario three: Widespread community transmission
Group three Third group of people to receive the vaccine in each scenario	• People in the community, including older people and those with underlying conditions • At risk health and social services workforce	• People in the community, including older people and those with underlying conditions • At risk health and social services workforce	• Remaining health and public sector workforce • Other population groups

Case Study: Australia (Australian Government, AG)

The Australian Government has agreements for the supply of COVID-19 vaccines, if they are proved to be safe and effective, (as of December 2020 time of writing), with:

- University of Oxford/AstraZeneca
- Novavax
- Pfizer/BioNTech
- COVAX Facility

AG's advice from the Australian Technical Advisory Group on Immunisation (ATAGI)[2] outlines the following:

'An Australian COVID-19 vaccination program should seek to achieve the following aims, noting they are interrelated:

- Reduce COVID-19 related harm by preventing serious illness and death, and where possible, disease transmission
- Ensure equity of vaccine access and uptake, especially for groups likely to experience a disproportionate burden of disease
- Promote public and health professional trust in the utility of COVID-19 vaccines and their implementation to the Australian community
- Ensure COVID-19 Vaccines are listed within the national immunisation program
- Maintain functioning of health care and other essential services to preserve health, social and economic security'

'The overarching goal and specific aims of the COVID-19 vaccination program are guided by key ethical principles, as outlined in the WHO SAGE Values Framework[3]. These include but are not limited to well-being, respect, equity, reciprocity and legitimacy'.

Possible priority population groups are advised in Australia as follows

1. Those who have an increased risk, of developing severe disease or dying from COVID-19
    a. Older people
    b. People with pre-existing underlying select medical conditions
    c. Aboriginal and Torres Strait Islander people

[2] https://www.health.gov.au/resources/publications/australias-covid-19-vaccine-and-treatment-strategy
[3]WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination, 14 September 2020 (link here)

2. Those who are at increased risk of exposure and hence of being infected with and transmitting SARS-CoV-2 to others at risk of severe disease or are in a setting with high transmission potential
    a. Health and aged care workers
    b. Other care workers
    c. People in other settings where the risk of virus transmission is increased
3. Those working in services critical to societal functioning
    a. Select essential services personnel
    b. Other key occupations required for societal functioning

Case Study: England, UK (HMG)

The 'Joint Committee on Vaccination and Immunisation' developed a paper in December 2020, entitled 'advice on priority groups for COVID-19 vaccination'[4]. The paper stated that the Pfizer-BioNTech vaccine appeared to be safe and well-tolerated, and there were no clinically concerning safety observations. The data indicate high efficacy in all age groups (16 years and over), including encouraging results in older adults. The Committee advised that this vaccine be used in the first phase of the programme, according to the priority order set out below.

JCVI advises that the first priorities for the COVID-19 vaccination programme should be the prevention of mortality and the maintenance of the health and social care systems. As the risk of mortality from COVID-19 increases with age, prioritisation is primarily based on age.

Note that this is similar to New Zealand's "Scenario 3" approach whereby the vaccination is being used where there is widespread community transmission. In St Helena, the Island has not presented a "Scenario 3" so this should be kept in mind when applying this particular case study.

1	Residents in a care home for older adults and their carers
2	All those 80 years of age and over Frontline health and social care workers
3	All those 75 years of age and over
4	All those 70 years of age and over Clinically extremely vulnerable individuals
5	All those 65 years of age and over
6	All individuals aged 16 years to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality
7	All those 60 years of age and over
8	All those 55 years of age and over
9	All those 50 years of age and over

It is estimated by JCVI that taken together, these groups represent around 99% of preventable mortality from COVID-19.

This prioritisation list was based upon a consideration of population groups and evidence relating to their risk. This is as follows.

Population group	**Scientific evidence**	**Ethics**	**Deliverability and implementation**
Older age groups	Highest absolute risk of morbidity and mortality	Maximises benefit and reduces health inequalities	Age is almost universally recorded on NHS records, so easy to identify individuals; flexible delivery model to reduce inequalities in vaccine uptake
People with high-risk clinical conditions	Elevated relative risk; comorbidities increase with age; mediated/driven by other factors	Maximises benefit and reduces health inequalities	High risk clinical conditions are well recorded on NHS records, so individuals are easy to identify; flexible delivery model to reduce inequalities in uptake

4 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940936/Priority_groups_for_coronavirus__COVID-19__vaccination_-_advice_from_the_JCVI__2_December_2020.pdf

Population group	Scientific evidence	Ethics	Deliverability and implementation
Health and social care workers	Elevated relative risk – mediated/driven by other factors not just occupation; vaccination of staff protects vulnerable patients	Contributes to individual benefit and population benefits: protect patients and ensure NHS and adult social care resilience	Health and social care workers can be identified through occupational health structures; established delivery model in occupational settings
Men	Elevated relative risk – mediated/driven by other factors, not just biological or genetic	Some benefit achieved by vaccinating older age groups and those with high risk clinical conditions	Sex is almost universally recorded on NHS records, so men would be easy to identify
Black, Asian and Minority Ethnic groups	Elevated relative risk – mediated/driven by other factors, not just biological or genetic	Risks further increasing stigma. Some benefit achieved by vaccinating health and social care workers	Ethnicity recording on NHS electronic systems is poor quality, so individuals would be difficult to identify; communications strategy and flexible delivery model to reduce inequalities in vaccine uptake

b. Herd Immunity

Herd immunity describes the phenomenon that at-risk individuals are protected from infection because they are surrounded by immune individuals. The spread of the virus is thus minimised[5].

Whilst Herd Immunity is not necessarily reached in a safe manner by allowing the virus to spread, if COVID-19 caused deaths of even 1%, it can be reached safety by suitable vaccination implementation.

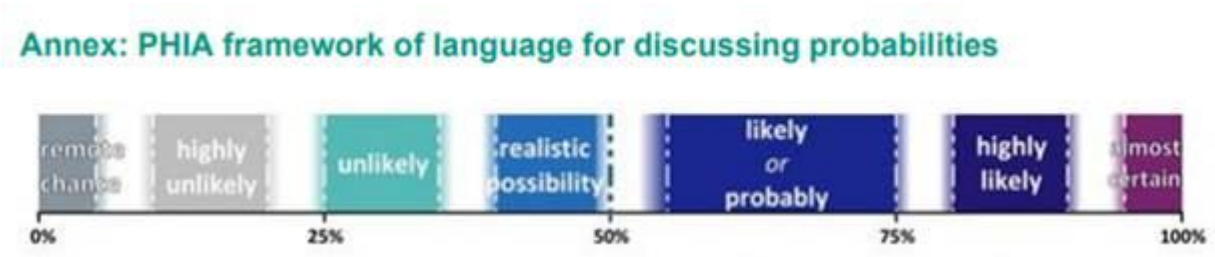
It is estimated through modelling[6] that the Herd Immunity Threshold for COVID-19, i.e. the point at which the proportion of susceptible individuals in a population falls below the threshold needed for transmission, is when the immunity in the population exceeds 67%. Elsewhere in the literature, experts such as the UK's Chief Medical Advisor have estimated 60% threshold[7].

What would this mean for St Helena? This would require around 3,000 of the 4,500 population to acquire vaccination. According to St Helena Census data[8], this would be the equivalent of vaccinating everyone over 30 years old. In comparison, ages 40-60 make up around a quarter of the population and over 60s make up another quarter of the population.

c. Vaccination options

Vaccinations are being developed and more is known about them as clinical trials provide results, and implementation of vaccine programmes progress.

Since the previous evidence paper was developed, PHIA have provided a useful language framework in order to communicate risk. This is below[9]:



[5] https://www.sciencemediacentre.org/expert-comments-about-herd-immunity/
[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7236739/
[7] https://www.sciencefocus.com/news/coronavirus-can-herd-immunity-protect-us-from-covid-19/
[8] Based on 2016 data. Census shall be repeated February 2021.
[9] Consensus Statement, December 2020, https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/945801/S0940_201202_SPI-M-O_Consensus_Statement_FINAL_UPDATEDv2_for_release.pdf

The AstraZeneca, Pfizer and BioNTech, Moderna, based on clinical trials, are almost certainly effective.

This evidence is sources from the WHO, the European Medicines Agency, the UK Government and the CDC.

A full list of clinical trial research can be found at https://www.clinicaltrials.gov/ct2/results?cond=COVID-19

1. **AstraZeneca**

This vaccine is called 'AZD1222'.

AstraZeneca COVID-19 vaccine is a viral vector vaccine which uses a weakened adenovirus as a carrier to deliver the SARS-CoV-2 antigen. The adenovirus has been modified so that it cannot replicate (grow and multiply by making copies of itself) in human cells and therefore cause any disease.

The genes that encode for the spike protein on the SARS-CoV-2 virus have been inserted into the adenovirus's genetic code to make the vaccine. When the vaccine is injected, it enters the host's cells which then manufacture the spike protein. This then stimulates the immune system which reacts by producing antibodies and memory cells to the SARS-CoV-2 virus without causing disease.

The vaccine can be stored and transported at normal refrigerated temps of +2ºC to +8ºC (36 degrees to 46 degrees Fahrenheit) for six months[10]. After first opening the vial, it should be used within 6 hours when stored at room temperature (up to 30ºC) or within 48 hours when stored in a refrigerator (2 to 8ºC). After this time, the vial must be discarded. The total cumulative storage time must not exceed 48 hours.

This vaccine provides the easiest to transport option for St Helena, largely because of the temperature requirements.

Headline data from vaccine trials undertaken indicate high vaccine efficacy, with no serious safety events related to the vaccine. Based on data taken from 11,636 volunteers across the United Kingdom and Brazil, a peer reviewed study shows **overall vaccine efficacy of 70.4%** from a pooled analysis of two-dose regimen at least one month apart; the standard dose/standard dose sub-groups showing 62.1% efficacy, and with the low dose/standard dose sub-group demonstrating 90% efficacy. No hospitalisations or severe disease were observed in the vaccinated groups[11].

An independent Date Safety Monitoring Board determined that the analysis met its primary endpoint showing protection from COVID-19 occurring 14 days or more after receiving two doses of the vaccine[12].

Trials of the AstraZeneca COVID-19 vaccine showed that it produced neutralising antibodies in Rhesus macaques as well as a reducing the amount of detectable virus in the lower respiratory tract following challenge with SARS-CoV-2. In human trials, the vaccine was compared with a placebo vaccine in healthy adults aged between 18-55 years. Preliminary findings show that neutralising antibodies were induced after the first vaccination and that levels of these increased after a second dose. Specific T cell responses were also induced after a single immunisation and were maintained after the second dose. Data showed that spike antibody responses and neutralising antibody 28 days after the second dose were similar across the three age cohorts (18–55 years, 56– 69 years, and ≥70 years). More than 99% of the participants had neutralising antibody responses two weeks after the booster dose. Peak T-cell responses were seen 14 days after the first dose and were broadly equivalent in the three age groups[13].

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10 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/943663/Greenbook_chapter_14a_v3.pdf

11 https://www.ox.ac.uk/news/2020-12-08-first-peer-reviewed-results-phase-3-human-trials-oxford-coronavirus-vaccine

12 https://www.astrazeneca.com/media-centre/press-releases/2020/astrazenecas-covid-19-vaccine-authorised-in-uk.html

13 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/943589/COVID-19_vaccination_programme_guidance_for_healthcare_workers_December_2020_V2.1.pdf

A further clinical trial to assess the safety, efficacy, and immunogenicity of AZD1222 for the prevention of COVID-19 will be undertaken on 40,000 participants over a one year period. This is currently in recruitment phase.

If the second dose of the AstraZeneca COVID-19 vaccine is given at less than the recommended 28 day interval, but at least 21 days after the first dose, it does not need to be repeated. If the second dose is given less than 21 days after the first, it should be discounted and another dose (a third dose) should be given at least 28 days after the dose given too early.

2. **Pfizer and BioNTech**

This is called the COVID-19 mRNA Vaccine 'BNT162b2' concentrate for solution for injection.

Instructions provided by the UK Government[14] in its use are provided below. This summary should not be used in place of official guidance.

This is a multidose vial and must be diluted before use. 1 vial (0.45 mL) contains 5 doses of 30 micrograms of BNT162b2 RNA (embedded in lipid nanoparticles), and is for injection- administered intramuscularly after dilution as a series of two doses (0.3 mL each) 21 days apart- for individuals 16 years of age or older. Individuals may not be protected until at least 7 days after their second dose of the vaccine.

Frozen vials should be transferred to 2 °C to 8 °C to thaw. Alternatively, frozen vials may also be thawed and kept at temperatures up to 25 °C for a maximum of two hours in preparation for dilution for use.When removed from the freezer, the undiluted vaccine has a maximum shelf life of up to 5 days (120 hours) at 2 °C to 8 °C, and and additional 2 hours at temperatures up to 25 °C in preparation for dilution. The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques. After dilution, the vaccine should not be transported by motor vehicle away from the site of dilution.

The Pfizer-BioNTech vaccine is a lipid nanoparticle–formulated mRNA vaccine. The mRNA encodes the SARS-CoV-2 full length spike protein. The mRNA in the vaccine is translated and transcribed by the body to produce the spike protein. The protein then acts as an intracellular antigen to stimulate the immune response. The mRNA in the vaccine is normally degraded within a few days and cannot incorporate into the host genome. Data from the Pfizer-BioNTech vaccine trials undertaken in over 40,000 individuals indicate high vaccine efficacy, with no serious safety concerns observed.

The efficacy of COVID-19 mRNA Vaccine BNT162b2 was evaluated in participants 16 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa and South America. Study 1 enrolled 60 participants, 18 through 55 years of age. Study 2 is a multicentre, placebo-controlled efficacy study in participants 12 years of age and older.

There were 8 confirmed COVID-19 cases identified in the COVID-19 mRNA Vaccine group and 162 cases in the placebo group, respectively. In this analysis, compared to placebo, **efficacy of COVID-19 mRNA Vaccine BNT162b2 is 95%** (95% credible interval of 90.3% to 97.6%). In participants 65 years of age and older and 75 years of age and older without evidence of prior infections with SARS-CoV-2, efficacy of COVID-19 mRNA Vaccine BNT162b2 was 94.7% (two-sided 95% confidence interval of 66.7% to 99.9%) and 100% (two-sided 95% confidence interval of -13.1% to 100.0%) respectively.In a separate analysis, compared to placebo, efficacy of COVID-19 mRNA Vaccine from first COVID-19 occurrence from 7 days after Dose 2 in participants with or without evidence of prior infection with SARS-CoV-2 was 94.6% (95% credible interval of 89.9% to 97.3%).

3. **Moderna**

This is called the 'mRNA-1273' vaccine. It is authorised in the US for use.

[14] https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizerbiontech-covid-19-vaccine

The vaccine requires 2 shots, one month (28 days) apart. The shots are applied in the muscle of the upper arm. This vaccine does not need to be mixed with a diluent before administration. The vaccine arrives frozen between -25°C and -15°C (-13°F and 5°F) and must be stored in a freezer or refrigerator. Vaccine may be stored in a freezer between -25°C and -15°C (-13°F and 5°F). Vaccine vials may be stored in the refrigerator between 2°C and 8°C (36°F and 46°F) for up to 30 days before vials are punctured.

The vaccine was found to be safe and highly effective in a randomized controlled clinical trial that included 30,351 participants randomized 1:1 to receive either vaccine or placebo.

Based on evidence from clinical trials, **the Moderna vaccine was 94.1% effective** at preventing laboratory-confirmed COVID-19 illness in people who received two doses who had no evidence of being previously infected. The vaccine appeared to have high effectiveness in clinical trials (efficacy) among people of diverse age, sex, race, and ethnicity categories and among persons with underlying medical conditions.

The clinical trial for the Moderna COVID-19 vaccine demonstrated very high efficacy of the 2-dose regimen against symptomatic, laboratory-confirmed COVID-19.1,2 The overall efficacy* was 94.1% (95% Confidence Interval [CI]: 89.3%, 96.8%). Consistent high efficacy (≥86%) was observed across age, sex, race, ethnicity, and among those at risk for severe COVID-19.

4. **Janssen Pharmaceutica**

The vaccine is called 'Ad26.COV2.S' produced by Johnson & Johnson's (J&J) pharmaceutical division, Janssen Pharmaceutical.

This is undergoing clinical trials and reviews. Early studies suggest that the vaccine triggers the production of antibodies and immune cells that target the SARS-CoV-2 coronavirus.

The vaccine contains genetic instructions for a protein known as spike (S) protein which is present on the surface of SARS-CoV-2 coronavirus. When a person is given the vaccine, their cells will read the genetic instructions and produce the spike protein. The person's immune system will then treat this protein as foreign and produce natural defences — antibodies and T cells — against it. If later on, the vaccinated person comes into contact with SARS-CoV-2, the immune system will recognise the virus and be prepared to attack it. The antibodies and immune cells can work together to kill the virus, prevent its entry into the body's cells and destroy cells that are infected, thus helping to protect against COVID-19.[15]

5. **Novavax**

This vaccine is called 'NVX-CoV2373'.

Novavax's vaccine comprises a recombinant nanoparticle technology containing an engineered COVID-19 spike protein and the saponin-based adjuvant Matrix-M designed to enhance the immune response and stimulate high levels of neutralising antibodies. When coronavirus invades the body, the immune system fights back in multiple ways including by producing antibodies to neutralise the virus. These antibodies bind to the spike protein on the surface of the coronavirus and prevent them from entering the cells. For immuno-supressed people who cannot mount an immune response, injections of neutralising antibodies could be used to provide several months of protection[16].

6. **Others**

[15] https://www.ema.europa.eu/en/news/ema-starts-rolling-review-janssens-covid-19-vaccine-ad26cov2s
[16] https://www.gov.uk/government/news/uk-government-secures-new-covid-19-vaccines-and-backs-global-clinical-trial

Other vaccines[17] which are undergoing trials include:

- Valneva
- GSK/Sanofi
- Sputnik V
- CanSino Biologics
- EpiVacCorona

[17] https://www.pharmaceutical-journal.com/news-and-analysis/features/ten-things-pharmacists-should-know-about-covid-19-vaccines/20208429.article?firstPass=false