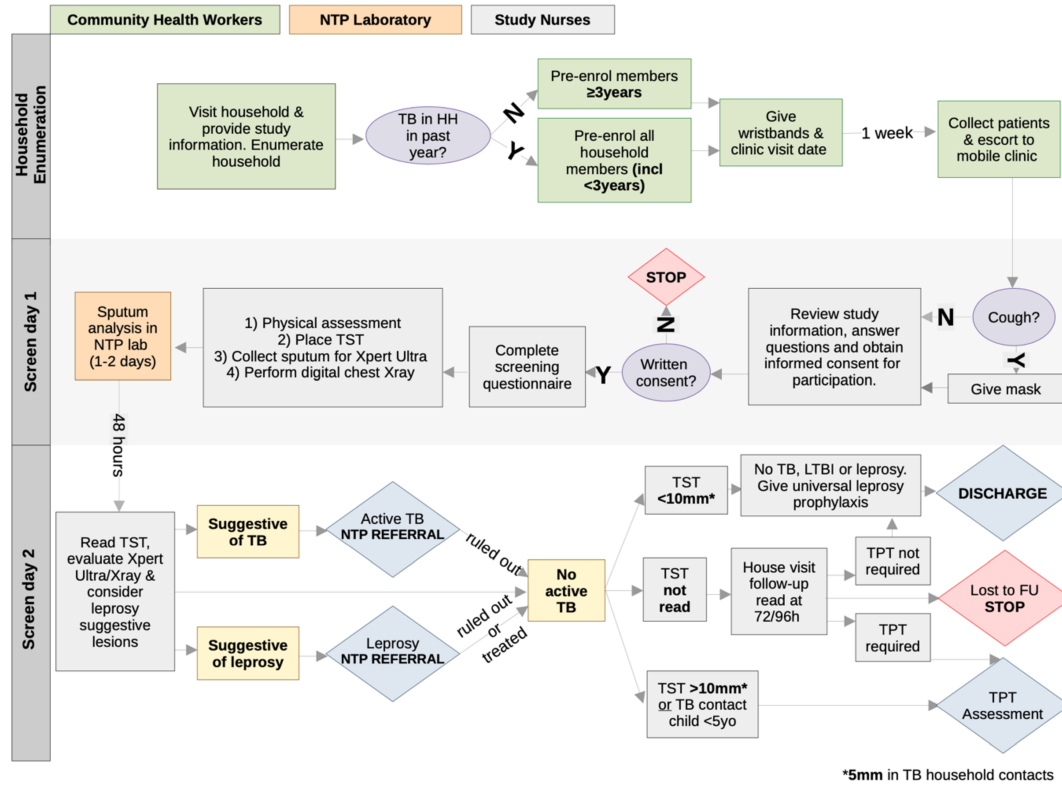


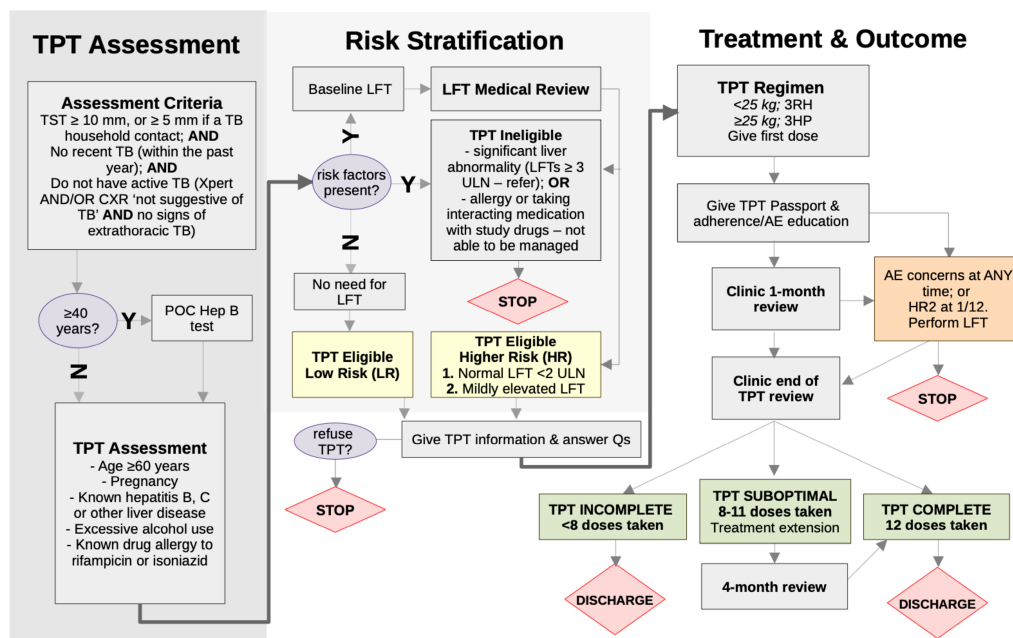
Supplementary Material

Figure S1. PEARL TB and leprosy screening algorithm



FU – follow-up; HH - household; LTBI - latent TB infection; N - no; NTP - National TB Program; TB - tuberculosis; TPT - TB Preventive Treatment; TST - Tuberculin Skin Test; Y - yes

Figure S2. TB preventive Therapy (TPT) algorithm



3HP - 3-months weekly rifapentine and isoniazid; 3RH - 3-months daily rifampicin and isoniazid; AE - adverse event; CXR - chest X-ray; FU - follow-up; HR2 - higher risk group 2; LFT - liver function test; LTBI - latent TB infection; NTP - National TB Program; POC - point-of-care; TB - Tuberculosis; TPT - TB Preventive Treatment; TST - Tuberculin Skin Test; ULN - upper limit of normal



S3. Participant Information Form

PEARL PARTICIPANT INFORMATION

Finding and preventing TB and leprosy in Tarawa

Dear participant,

We would like to invite you (and your child if relevant) to be evaluated for TB and leprosy, with treatment to be provided as appropriate. This document provides information about the intervention, but we will also explain things in person.

Please read this Participant Information sheet carefully and ask questions about anything that you don't understand or want to know more about. You may refuse participation and this will not be held against you or affect any future access to healthcare.

What is this intervention about?

TB is a disease caused by germs that are coughed into the air by someone who is ill with TB. Most people who are infected with the TB germ do not become ill and do not even know that they are infected, this is referred to as latent or 'sleeping' TB. **Sometimes sleeping TB can wake up and make you ill, which may also spread the germ to others.** This intervention aims to eliminate TB from Tarawa by identifying and treating all people with TB and those with sleeping TB who may become ill in future. At the same time we are also trying to eliminate leprosy, by treating people with leprosy and preventing leprosy in others.

Who is doing this?

The study is carried out by researchers at the University of Sydney, Australia, in close collaboration with the Kiribati Ministry of Health and Medical Services (MHMS). The study is funded by the Australian Medical Research Future Fund and fully supported by the Kiribati government.

What will happen?

This study involves screening for TB (both 'sleeping TB' and TB disease) and leprosy. Screening will include looking at your skin, doing a TB skin test, having a chest X-ray and providing a sputum sample. People who are ill with TB or leprosy will be referred to the TB and Leprosy Programme for appropriate treatment. People with 'sleeping TB' will be offered TB preventive treatment (TPT) and those without any illness or TB infection will be offered leprosy prophylaxis.

People diagnosed with sleeping TB (this is common and is expected in 20-30% of people) will be offered treatment for sleeping TB. Treatment is for three months and is usually safe, but we will have to perform a few checks. A study nurse will ask some personal questions, including questions about previous and current illnesses, medications used, drinking of alcohol or kava, and questions about pregnancy if you are a woman. People between 40-59 years of age will be given a finger prick to test for hepatitis B infection. Those with hepatitis B infection or any other risk factors for TB treatment will need to have a small amount of blood drawn to make sure their liver function stays healthy during the time that they are treated for sleeping TB.

How much of my time will it take?

We will try to waste as little of your time as possible. To complete the TB and leprosy screening will require you (and your whole household) to be seen on two separate days. This is to complete all the necessary documentation and tests. It is expected that this will take about 2-3 hours of your time on each of these days. Those diagnosed with sleeping TB will need to take tablets once a week for 12 weeks (or daily for 3 months in children). Tablets will be given out at the mobile health clinic and are free of charge.



Who can take part?

Every person older than 3 years of age living in Tarawa and Betio islet is invited to take part. People younger than 3 years of age who live in a house that shares a kitchen with someone who has had TB or leprosy in the past 12 months are also invited to take part.

Do I have to be in the study? Can I withdraw from the study once I've started?

Taking part in this study is strongly recommended to help us get rid of TB and leprosy across Tarawa. However, participation is completely voluntary and you do not have to take part. Your decision will not affect your current or future relationship with the researchers, or the Kiribati Ministry of Health and Medical Services (MHMS).

If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by visiting the study clinic and speaking with a study nurse or doctor who will ask you some questions and give you advice on how to stay healthy from TB in the future.

If you decide to withdraw from the study, we will not collect any further information from you. Information that we have already collected will be kept in our study records and may be included in the study results.

Are there any costs or risks?

All tests and treatment are provided free of charge and study clinics will be conveniently situated to be easily accessible.

If treatment for 'sleeping TB' is provided it is normal to feel a bit tired and to have bright orange urine while you are taking the tablets. Rarely people may develop more serious symptoms that mainly affects the liver, which is why we do the additional testing described above. We will explain all of this to you in detail before providing you with any treatment.

What are the benefits?

There are major benefits to yourself and the wider community

- You (and your child) will get treatment for TB or leprosy – if required
- You (and your child) will get treatment for sleeping TB (TPT) – if required
- You (and your child) will get treatment to help keep leprosy away
- You will help to eliminate TB and leprosy from Tarawa
- You will help other Pacific Island nations to learn from Tarawa

Is my data safe?

Medical information will be kept in private MHMS medical records or with the PEARL team. Data collected during the intervention will only be shared with the Kiribati MHMS as relevant and will otherwise be kept confidential. The information may be included in reports and publications, but your name and personal information will never be shared.

Where can I get further information about the intervention?

Further information about the study can be found on our website www.thepearlstudy.org or by speaking to any of the study personnel.

Will I be informed about the results?



The results of the study will be reported to the MHMS and shared with the residents of Tarawa by radio announcement and other means, it will also be accessible on the website www.thepearlstudy.org.

What if I have a complaint or any concerns about the study?

This research has been reviewed and approved by an independent group of people called a Human Research Ethics Committee (HREC) at the University of Sydney and the Kiribati Ministry of Health and Medical Services.

If you are concerned about the way this study is being conducted please inform the study team; we want to learn and hear how we can improve things. If you wish to make a complaint to someone independent then please contact any of the people listed below.

Terotia Tabwaka Kelese, Human Resource Officer, Republic of Kiribati
Email: ttabwaka@gmail.com

or

The Manager, Ethics Administration, University of Sydney:
Telephone: +61 2 8627 8176
Email: human.ethics@sydney.edu.au
Fax: +61 2 8627 8177 (Facsimile)

WE THANK YOU FOR YOUR TIME AND COOPERATION.


The PEARL Research Team with the support of the Kiribati National TB and Leprosy Control Programmes

On behalf of the Kiribati Ministry of Health and Medical Services

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Eretii Timeon
Director of Public Health

S4. 3HP TB Preventive Treatment (TPT) Passport

3HP



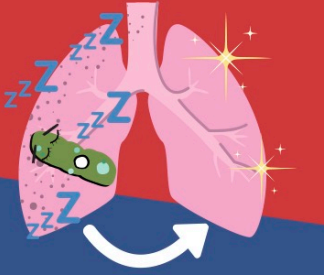
TPT Passport

Name: _____

Start date: ____/____/____

Dose: 3 tablets 2 tablets

Schedule: *Take once per week on the same day*




Record ID

12 doses to treat sleeping TB

Take your tablets **with water** - never with alcohol

Take your tablets on the **same day every week**



Sunday Monday **Tuesday** Wednesday Thursday Friday Saturday

week 1

week 2

week 3

week 4

4-week visit: ____/____/____

week 5

week 6

week 7

week 8

8-week visit: ____/____/____

Treatment Completion Date: _____

Missed a day? Take your tablets as soon as you remember

Store your tablets **out of the sun** and out of reach from children

Sunday Monday **Tuesday** Wednesday Thursday Friday Saturday

week 9

week 10

week 11

week 12

12-week visit: ____/____/____

week 13

week 14

week 15

week 16

16-week visit: ____/____/____

PEARL staff sign: _____

Stamp

Things to look out for

NORMAL AND HARMLESS
Bright orange urine, sweat or tears

GET HELP IF THIS DOES NOT GO AWAY
headache or sore throat
dizzy or light-headed

STOP MEDICINE AND GET HELP
yellowing eyes or skin
nausea, vomiting, stomach pain
unusual tiredness
loss of appetite

How to get help

Contact a CHOW in your community
Call the PEARL helpline - XXX XXX XXX
Visit a screening clinic to see a nurse
If very unwell - go to the hospital

S5. 3RH TB Preventive Treatment (TPT) Passport

3RH

TPT Passport

Name: _____

Start date: ____/____/____

Dose: 3 tablets 2 tablets

Take once per day every day

3 months to treat sleeping TB

Mix tablets **with water** – check they drink every drop!

Give tablets **every day** for 3 months

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
week 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 4	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4-week visit: ____/____/____							
week 5	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 6	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 7	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 8	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8-week visit: ____/____/____							

Missed a day? Keep giving tablets **every day** until finished

Store tablets **out of the sun** and out of reach from children

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
week 9	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 10	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 11	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 12	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12-week visit: ____/____/____							
week 13	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 14	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
week 16	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16-week visit: ____/____/____							

Things to look out for in kids

NORMAL AND HARMLESS

Bright orange urine, sweat, tears or nappies

GET HELP IF THIS DOES NOT GO AWAY

nausea, vomiting, stomach pain unusual tiredness loss of appetite

STOP MEDICINE AND GET HELP

yellowing eyes or skin face or body rash

How to get help

Contact a CHOW in your community
Call the PEARL helpline - XXX XXX XXX
Visit a screening clinic to see a nurse
If very unwell - go to the hospital

Estimated alpha for effect on TB and leprosy case notifications

For study outcomes measures relating to the case notification rate (CNR) before and after the intervention, the sample size is the entire population of South Tarawa and the outcome is measured programmatically through routine service delivery. The population of South Tarawa is estimated to be 65,566 in 2021 and 71,091 in 2025 (Kiribati NSO, SPC SDD). TB CNR was 0.42% for South Tarawa in 2020 (Kiribati NTP, unpublished, November 2021) and 0.16% for leprosy (Pacific Leprosy Foundation, unpublished, November 2021). Population wide active case finding and prevention interventions for TB have achieved a reduction in case notification rate of approximately 50% in Vietnam and the Republic of the Marshall Islands (Marks et al, NEJM, 2019; RMI MoHHS and USCDC, unpublished, 2021). In Indonesia, impact on case notifications was also approximately 50% among participants in a population wide screening and prevention project (Tiwari et al, BMC ID, 2018). Using a two-tailed z-test to approximate Poisson regression in a large sample and with power of 0.8, the estimated alpha for an anticipated reduction in CNR by 50% is <0.001 for TB and leprosy. The estimated alpha is plotted for a range of effect sizes in Figures S1 and S2, which demonstrates adequacy of the sample/population size. Although the study is sufficiently powered to demonstrate a major short-term reduction in CNR, we will interpret the results with due consideration for the overall goals of achieving a durable public health impact and with careful consideration of the limitations in attribution inherent in a quasi-experimental analysis.

Figure S6. Estimated alpha as a function of post-intervention TB case notification rates (expressed as a proportion of the population), with pre-intervention population of 65,566 and post-intervention population of 71,091; baseline case notification rate of 0.42% (420/100,000 population) and power of 0.8.

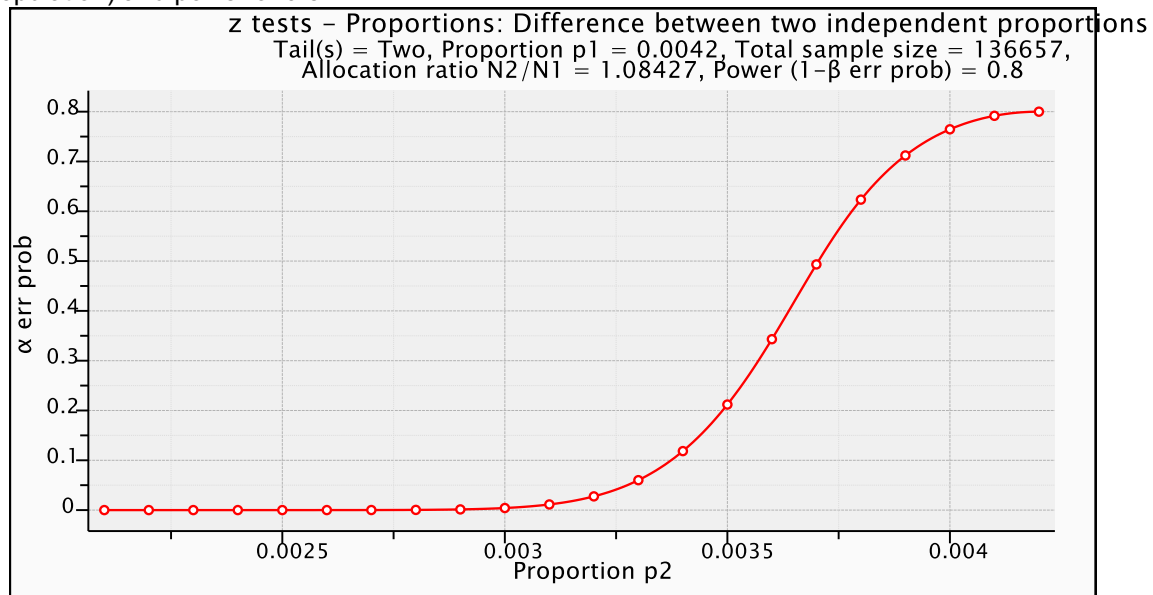
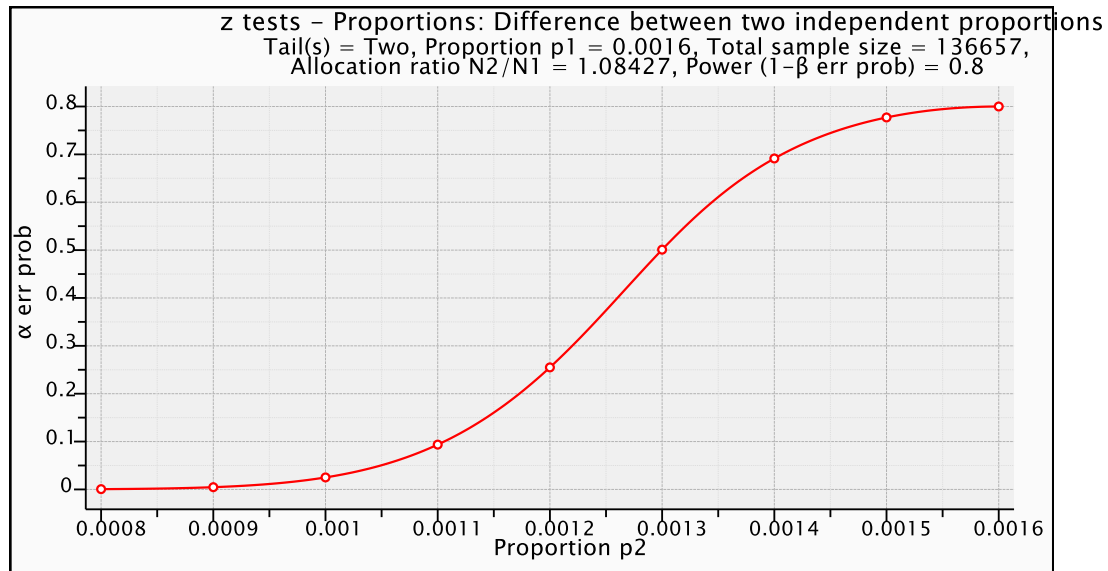



Figure S7. Estimated alpha as a function of post-intervention TB case notification rates (expressed as a proportion of the population), with pre-intervention population of 65,566 and post-intervention population of 71,091; baseline case notification rate of 0.16% (160/100,000 population) and power of 0.8.



S8. Informed Consent Form

INFORMED CONSENT PROCESS FORM

Date of informed consent
/Date of informed consent  Today D-M-Y
** must provide value*

Does the participant have capacity to consent?
** must provide value*

Yes
 No - young person < 18 years of age
 No - disability
 No - other reason

[reset](#)

Name of Consenting Guardian
** must provide value*

Relationship of consenting guardian
** must provide value*

parent
 spouse
 grandparent
 aunt/uncle
 sibling
 other relative
 non-relative guardian

[reset](#)

Does the participant assent to participate in the study?
** must provide value*

Yes
 No

[reset](#)

Does the participant/primary caregiver agree to participate in study?
** must provide value*

Yes
 No

[reset](#)

Can participant/caregiver read Kiribati?
** must provide value*

Yes
 No

[reset](#)

Can participant/caregiver read English?
** must provide value*

Yes
 No

[reset](#)

Participant information given and all participant questions answered?
** must provide value*

Yes
 No

[reset](#)

Participant is aware that this is a public health intervention endorsed and supported by the Kiribati Ministry of Health and Medical Services? [reset](#)

*** must provide value**

Yes

No


Participant is aware that screen may involve providing sputum or blood samples? [reset](#)

*** must provide value**

1. Yes/ Yes

0. No/ No


Date & Time Participant/caregiver signed [reset](#)

Written Consent Form  D-M-Y H:M

*** must provide value**

Sign

*** must provide value**

 [Add signature](#)

Other comments