INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASES

A multi-center clinical research network in Indonesia

History of INA-RESPOND

On March 29, 2010 the Indonesian Minister of Research and Technology, Mr. Suharna Surapranata, and the US Ambassador for Indonesia, Mr. Cameron Hume, signed the Science and Technology agreement between the two countries which among others roll-out the idea to establish a clinical research network. INA-RESPOND was conceived during the tenure of the late Health Minister, Dr. Endang R. Sedyaningsih.

The collaboration was discussed between the delegation led by Minister Endang and NIAID Director Dr. Anthony Fauci in April 2010, which resulted in the establishment of implementing partnership between *Badan Litbangkes* of the Ministry of Health of Indonesia (National Institute of Health Research and Development) and the United States National Institute of Health / National Institute of Allergy and Infectious Diseases (NIH-NIAID).

Vision

To become the premier research network in the region providing evidence to inform policy making, minimize the impact of infectious diseases and improve human well-being.

Mission

To improve the health of the people of Indonesia and benefit the international community by conducting high-quality infectious disease research through a collaborative, sustainable and well-recognized research network.

Values "BRIGHT"

- Beneficial and Responsive to the research needs of Indonesia and the international community
- Innovative in designing, implementing, and integrating research in a healthcare setting
- Goal-Oriented to achieve the mission of the network
- High-Quality in conducting scientifically sound and ethical research
- Trust and Teamwork with respect, transparency, communication, collaboration, and shared responsibility

Goals

We will strive to create standard protocol operating procedures, implement studies, and develop site staff to publish and present findings to ultimately affect treatment, diagnosis guidelines, and policy

Goal 1

Generate knowledge, disseminate results, and promote utilization of research findings

Goal 2

Build INA-RESPOND as a sustainable clinical research network capable of conducting excellent clinical research

We will strive to train site staff to increase competencies and conduct quality research in an effort to establish clinical research units and obtain new funding sources

We will strive to streamline operations to maintain a functional specimen repository and data management center

Goal 3

Develop, implement, and maintain internal management and operations practices

INA-RESPOND Partners

1. National Institute of Health Research and Development (NIHRD) (Badan Litbangkes, Indonesia)
2. Universitas Airlangga / RSUD Dr. Soetomo, Surabaya
3. Universitas Diponegoro / RSUP Dr. Kariadi, Semarang
4. Universitas Gadjah Mada / RSUP Dr. Sardjito, Yogyakarta
5. Universitas Hasanuddin / RSUP Dr. Wahidin Sudirohusodo, Makassar
6. Universitas Indonesia / RSUPN Dr. Cipto Mangunkusumo, Jakarta
7. Universitas Padjadjaran / RSUP Dr. Hasan Sadikin, Bandung
8. Universitas Udayana / RSUP Sanglah, Denpasar
9. RSUP Persahabatan, Jakarta
10. RS Penyakit Infeksi Sulianti Saroso, Jakarta
11. Eijkman Institute for Molecular Biology, Jakarta
12. United States National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIH-NIAID)
13. United States Centers for Disease Control and Prevention (CDC)

Network Policies

In all the activities of INA-RESPOND study, from data and specimen collection, data entry, specimen storage and shipment, laboratory testing, data analysis and presentation, and submission of the abstracts and manuscripts, INA-RESPOND researchers will adhere to the three important issues which are listed in Science and Technology agreement between the Indonesia and US governments as well as in the INA-RESPOND implementation arrangement between the two countries.

Intellectual Protection of Property (IPR)

These will be guided by the Intellectual Protection of Property (IPR) terms as provided under Article X in the S and T agreement between the two countries, Protection of Intellectual Property, as follow:

1. Provisions for the protection and distribution of intellectual property created or furnished in the course of cooperative activities under this Agreement are set forth in Annex I, which shall form an integral part of this Agreement.
2. Scientific and technological information of a non-proprietary nature resulting from cooperation under this Agreement (other than information which is not disclosed for commercial or industrial reasons) shall be made available, unless otherwise agreed, to the world scientific community through customary channels and in accordance with normal procedures of the participating agencies and entities.

And under Paragraphs III.A and III.B(1), (2)(a), (2)(b), (2)(c) of Annex I, Intellectual Protection Rights, of the Science and Technology agreement between the Government of the Republic of Indonesia and the Government of the United States of America.

Material Transfer Agreement (MTA)

All research activities using material and or data originating from Indonesia shall to the fullestt extent possible be conducted in Indonesia. Any transfer of such materials and data, when really needed and on the agreement of the participants, shall be carried out in accordance with the laws, regulations and policies of the Parties, as provided in Article VIII of the Science and Technology Agreement and a Material Transfer Agreement concluded between Parties.

Genetic Resources and Traditional Knowledge (GRTK)

The collection, conservation and exchange of genetic resources and associated traditional knowledge under this protocol shall be subject to Article VI of the Science and Technology Agreement and shall be based on the following considerations:

1. Obtaining informed consent from the appropriate authority/institutional review board prior to accessing genetic resources collected during the conduct of this protocol under the control of such authority.
2. Equitably sharing the benefits arising from the use of traditional knowledge and genetic resources.

Strategic Map

The strategy map serves as a communication tool for all levels of INA-RESPOND staff. This tool effectively summarizes the strategic plan in a quick easy-to-read format.

The mission of the INA-RESPOND is improve the health of the people of Indonesia and to benefit the international community by conducting high-quality infectious disease research through a collaborative, sustainable, and well-recognized research network

Goal 1: Generate knowledge, disseminate results, and promote utilization of research findings	**Goal 2:** Build INA-RESPOND as a sustainable clinical research network capable of conducting excellent clinical research	**Goal 3:** Develop, implement, and maintain internal management and operations practices

Values : Beneficial and Responsive | Innovative | Goal oriented | High Quality | Trust & Teamwork

Stakeholder Benefit	**OBJ.1.1:** Develop, implement, and complete the studies	**OBJ.1.2:** Presentation of research finding in scientific forum	**OBJ.1.3:** Presentation of research finding for the user (policy maker and clinician)
Sustainability		**OBJ.2.3:** Secure additional partners and funding sources for INA-RESPOND	
Training	**OBJ.2.2:** Develop and promote training and experience opportunities for INA-RESPOND researchers and staff		
Operations	**OBJ.2.1:** Develop clinical research unit in each of the 9 sites at the hospitals	**OBJ.3.2:** Monitor, track and report progress against Network strategy	**OBJ.3.1:** Establish an efficient and effective system of technical and administrative management to support research activities

Balanced Score Card Methodology

Contact Us at INA-RESPOND Secretariat

Pusat Teknologi Terapan Kesehatan dan Epidemiologi Klinik,
Badan Penelitian dan Pengembangan Kesehatan - Kementerian Kesehatan Republik Indonesia
Gedung 4 (Laboratorium Terpadu), Lantai 5
Jl. Percetakan Negara No. 29 Jakarta, 10560 Phone: +62 21 4287 9189 Website: www.ina-respond.net

Partners

Jointly Funded by
National Institute of Health Research and Development
National Institute of Allergy and Infectious Diseases

FROM IDEAS TO POLICIES:
The Process of INA-RESPOND Study

INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

What is the process to develop a high quality and beneficial Protocol ?

IDEAS from Indonesian Researchers

NSC Reviews and Approves
- GB endorses NSC's decisions
- Investigator selection

Protocol Development
Study Protocol, Manual Of Procedures, Informed Consent Form, Case Report Form, Database are prepared by a Protocol Core Team, Protocol PI, Co-PI and Investigators.

Protocol Submission
Submitted to :
- SCIENTIFIC COMMITEE
- The EC and BPOM

ETHICAL CLEARANCE AND APPROVAL

What preparation activities are conducted before the approved protocol is applied at site ?

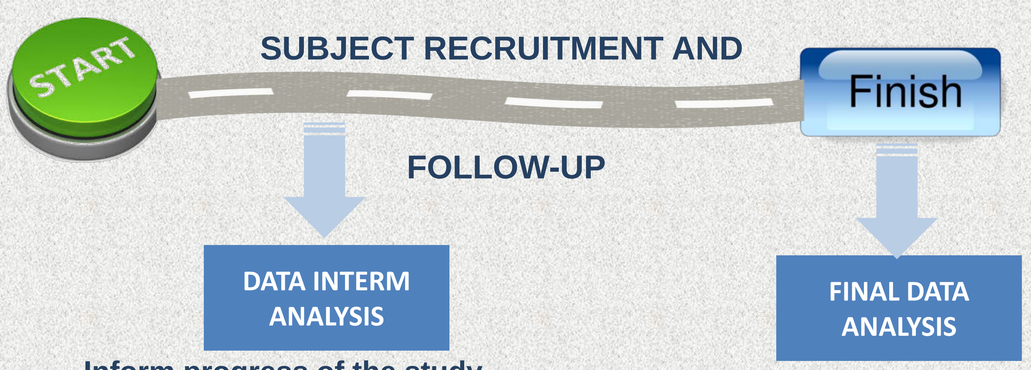
APPROVED PROTOCOL
To ensure site team members across sites have common understanding.

INVESTIGATOR MEETING
Site Preparation Visit - To prepare the site team, necessary documents, supplies, and equipment.
Site Initiation Visit - To ensure the readiness of the sites.

SITE VISITS
SPV
SIV

SITE ACTIVATION
Site can be activated after obtaining approval from Protocol PIs, NIH & NIHRD, and NSC Chair.

The real journey begins. How does a research produce something?



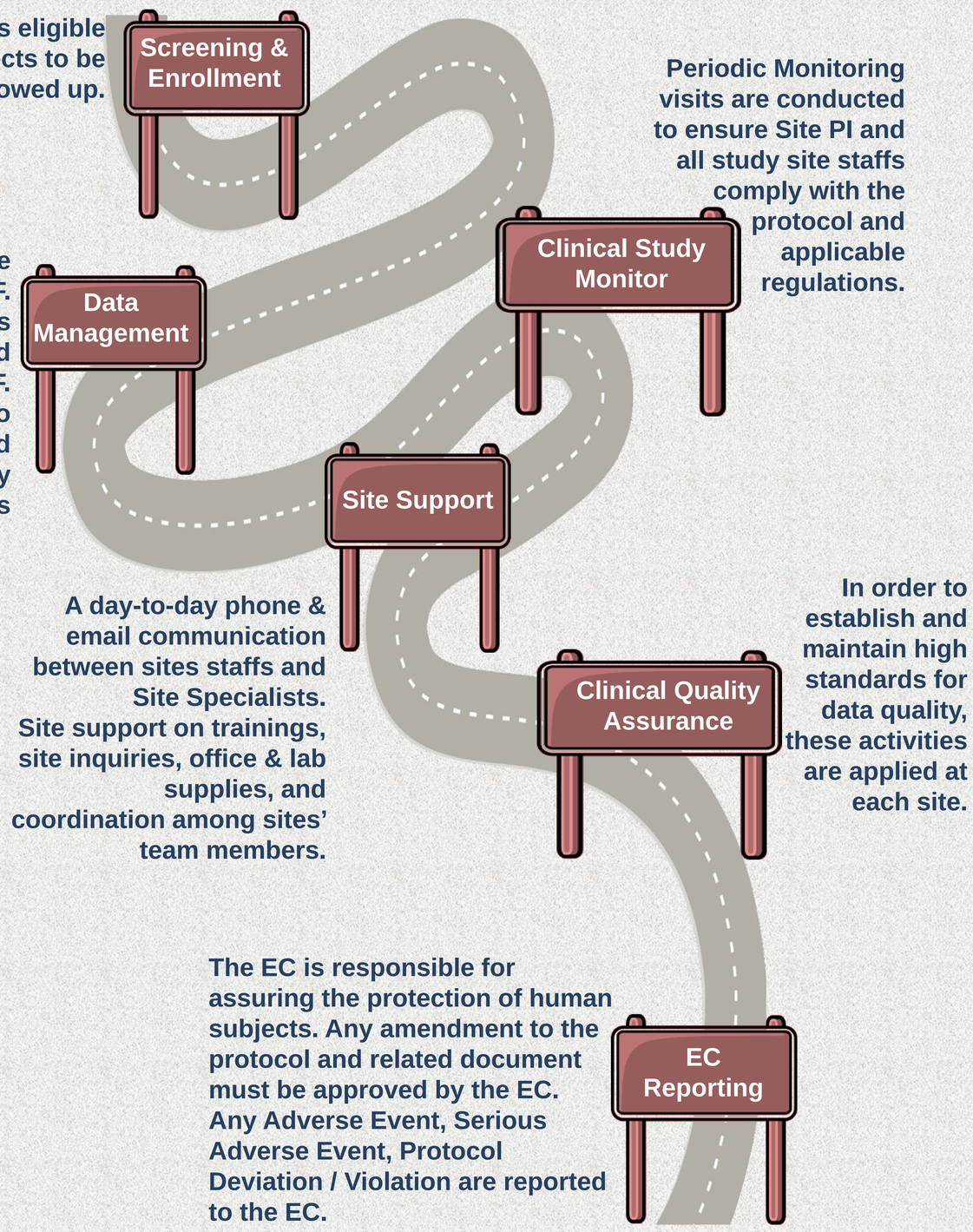
- Inform progress of the study.
- Discuss and recommend if any alteration is needed.
- Gather information for preliminary publication.

PUBLICATION
Secretariat processes the publication (submission, review, revision, re-submission)

MANUSCRIPT PUBLISHED
- NSC reviews and approves
- GB endorses

INPUTS FOR PUBLIC HEALTH POLICIES & IDEAS FOR FUTURE STUDIES

What is going on behind the scene?



RA identifies eligible subjects to be enrolled and followed up.

Periodic Monitoring visits are conducted to ensure Site PI and all study site staffs comply with the protocol and applicable regulations.

RAs complete SDW and CRF. DM checks completeness and accuracy of CRF. DM enters data to database and resolves any discrepencies

A day-to-day phone & email communication between sites staffs and Site Specialists. Site support on trainings, site inquiries, office & lab supplies, and coordination among sites' team members.

In order to establish and maintain high standards for data quality, these activities are applied at each site.

The EC is responsible for assuring the protection of human subjects. Any amendment to the protocol and related document must be approved by the EC. Any Adverse Event, Serious Adverse Event, Protocol Deviation / Violation are reported to the EC.

GLOSSARY
- CRF : Case Report Form
- DM : Data Manager
- EC : Ethical Committee
- GB : Governing Board
- NSC : Network Steering Committee
- PI : Principal Investigator
- RA : Research Assistant
- SDW : Source Document Worksheet
- SPV : Site Preparation Visit
- SIV : Site Initiation Visit

Partners

Jointly Funded by
National Institute of Health Research and Development
NIH National Institute of Allergy and Infectious Diseases

The Etiology of Acute Febrile Illness Requiring Hospitalization (INA101)

AFIRE Study Team

INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

Background

- Febrile illness is found approximately 20-25% of hospitalizations in Indonesia and presents a major cause of morbidity and mortality.
- In developing countries, a clinical presentation with fever is usually linked to an infectious etiology.
- Clinical diagnoses only → inappropriate clinical management
- Large-scale studies to identify causes of febrile illnesses in Indonesia have not been conducted.
- Most studies were designed to identify for specific agents and did not collect clinical data, outcomes and etiologies to measure disease burden systematically.

Primary Objectives

- To identify the etiology of acute febrile illness cases and evaluate clinical manifestations and outcomes.

Secondary Objectives

- To provide clinical data.
- To enhance research capacity and networking for infectious diseases in Indonesia.
- To establish a repository of biological specimens for future study

Study Method

Study location and Activation status

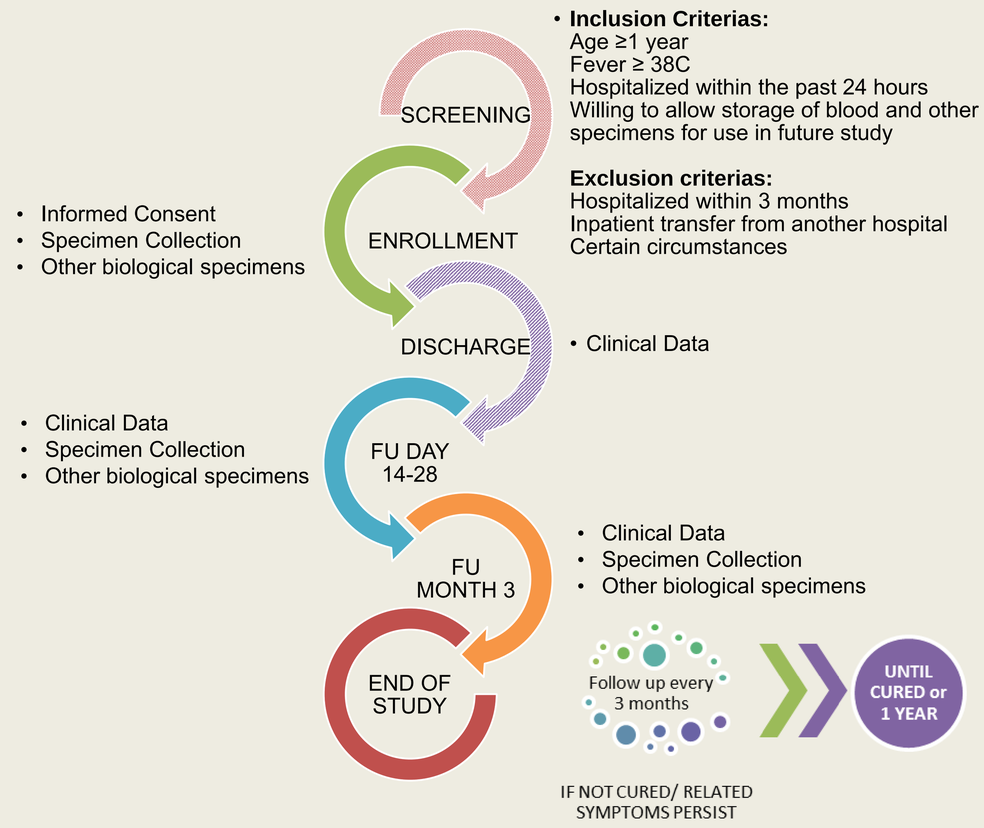
- Site 510: RSUP Dr Hasan Sadikin, Bandung
- Site 520: RSUP Sanglah, Denpasar
- Site 530: RSUPN Dr Cipto Mangunkusumo, Jakarta (will start in Nov 2014)
- Site 540: RSPI Prof Dr Sulianti Saroso, Jakarta (will start in Nov 2014)
- Site 550: RSUP Dr Wahidin Sudirohusodo, Makassar
- Site 560: RSUP Dr Kariadi, Semarang
- Site 570: RSUD Dr Soetomo, Surabaya
- Site 580: RSUP Dr Sardjito, Yogyakarta

	Site 520 Denpasar	Site 560 Semarang	Site 580 Yogyakarta	Site 510 Bandung	Site 550 Makassar	Site 570 Surabaya
Activation status	Jul 15	Aug 12	Aug 14	Sept 04	Oct 04	Dec 27
Actual FPFV* date	Jul 18	Aug 19	Aug 26	Sept 04	Oct 16	Jan 3, 2014

Study Population

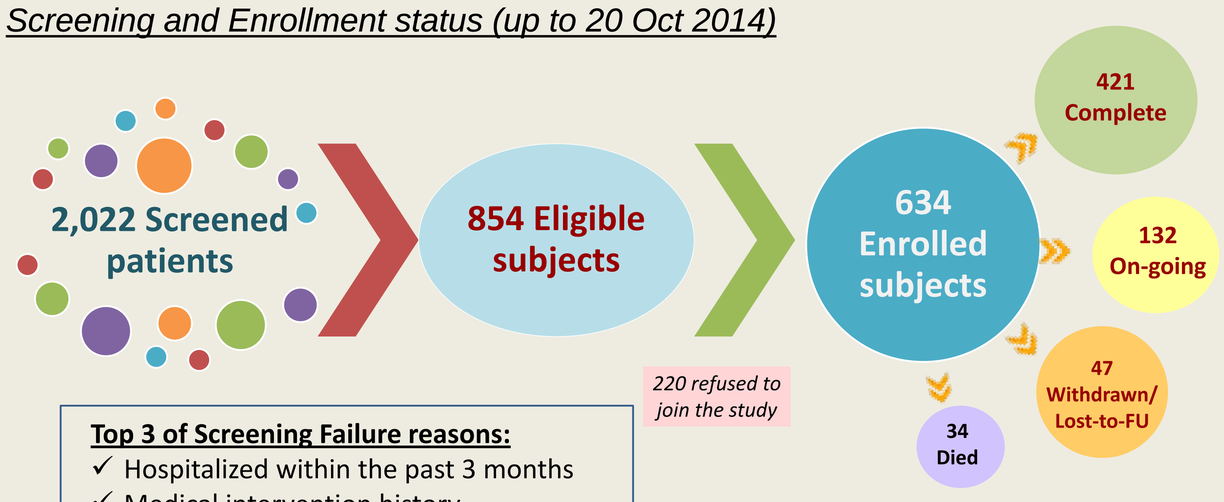
1,600 subjects; Approximately 100 adults and 100 children per site.

Study Plan

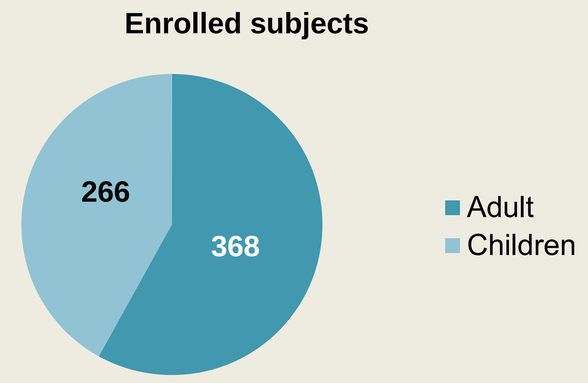


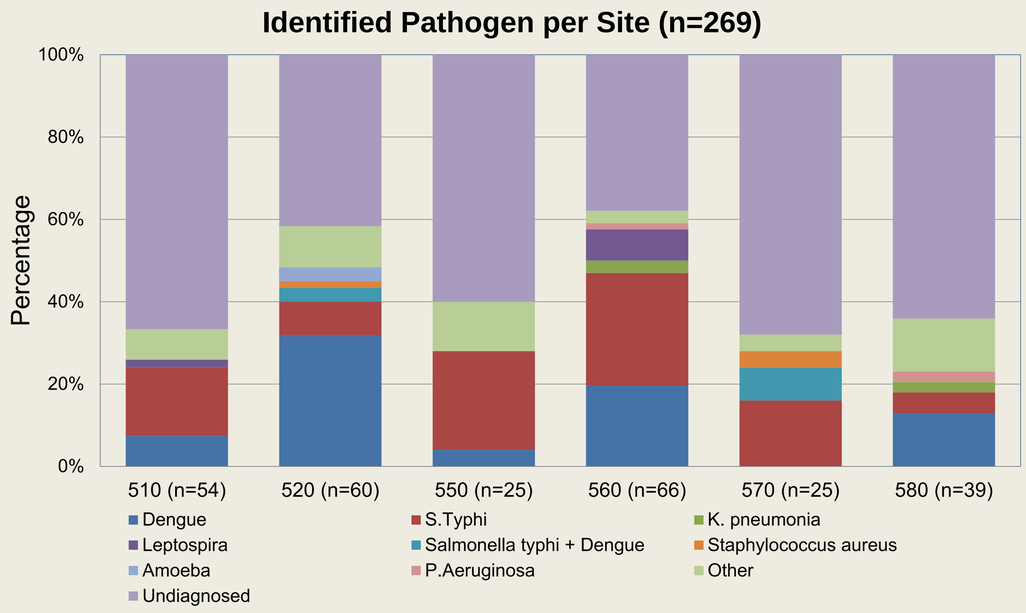
Preliminary Results

Screening and Enrollment status (up to 20 Oct 2014)



Top 3 of Screening Failure reasons:
- ✓ Hospitalized within the past 3 months
- ✓ Medical intervention history
- ✓ Medical disorder or other circumstance





The preliminary analysis shows:

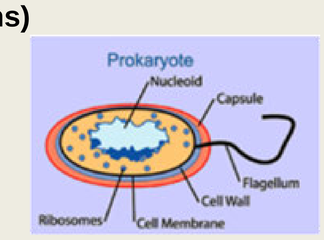
- 46.8% (n=269) etiologies of fever were confirmed, among which 30.2% (n=126) was confirmed by culture
- The most common identified pathogens are:
  - ✓ Dengue (site 520, 580)
  - ✓ S. typhi (site 510,550,560, 570)
- **53.2%** (n=269) etiologies of fever were not confirmed based on diagnostic testing (Standard of Care) at the hospital.

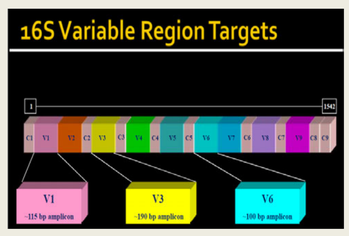
It shows that the diagnostic testing (SoC) for infectious disease at the hospital needs to be reviewed and improved, to increase the detection of etiological causes of fever.

FUTURE PLAN:

Identifying etiologies in unconfirmed cases

- **PCR RNA 16s (acute specimens)**





- **Virus Panel (PCR, Serology)**

RNA viruses:
- ✓ Flaviviridae
- ✓ Alphaviridae
- ✓ Bunyaviridae

DNA viruses
- ✓ Herpesviridae
- ✓ Paramyxoviridae
- ✓ Enteroviridae

Partners

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National Institute of Health Research and Development
National Institute of Allergy and Infectious Diseases

Tuberculosis Research of INA-RESPOND on Drug-resistant (INA-102)

TRIPOD STUDY TEAM

Background

- To provide valid data which are beneficial for the government to better prepare a national program in controlling this disease, it is important to closely observe a large number of various TB patients from many centers prospectively
- This study is INA-RESPOND's first study of TB, which may be followed by other studies focused on questions specific to improving diagnosis and treatment of TB in Indonesia

Objectives

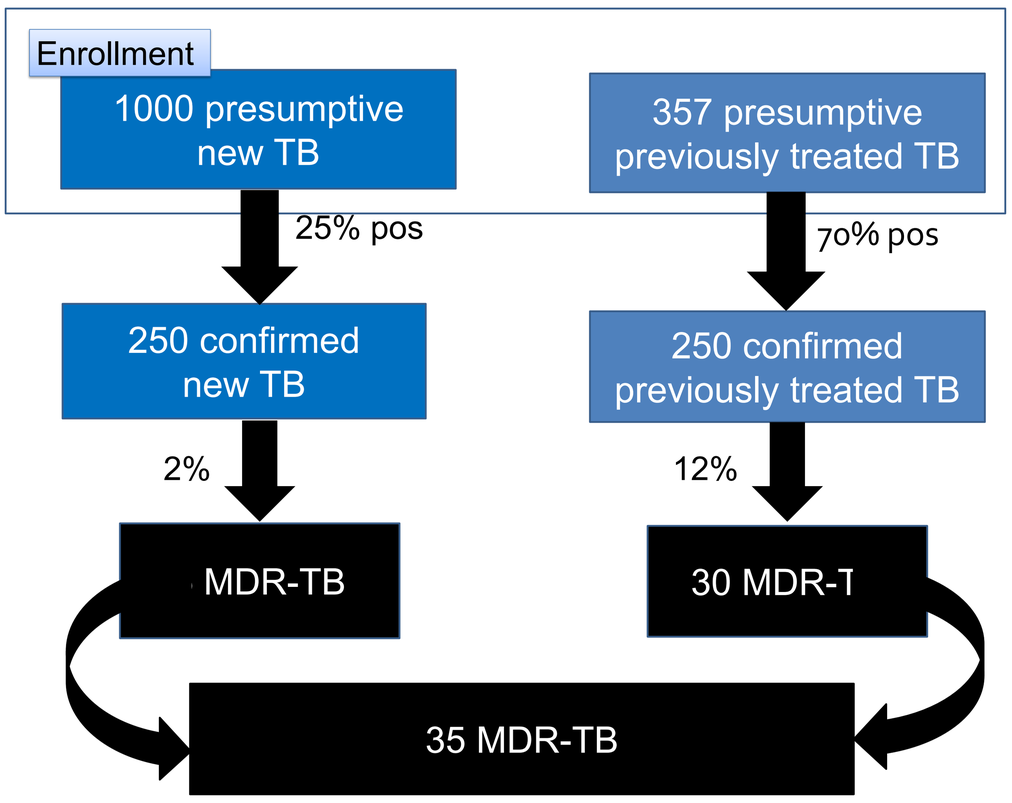
Primary Objectives

- To estimate the proportion of MDR TB of new and previously treated cases

Secondary Objectives

- To estimate the proportion of cured, completed, failed, died, and lost to follow up as treatment outcomes in drug susceptible & drug resistant cases
- To evaluate the association of treatment success with the following: demographic, TB contact history, smoking habit, treatment seeking, comorbidities (HIV, DM), primary drug resistance, symptoms, lung cavity, nutrition status, treatment regimens, compliance, number of bacteria, TB strains (Beijing)
- Comparison of clinically defined TB vs laboratory confirmed TB for accuracy of diagnosis.
- Comparison between AFB and Xpert as TB diagnostic tests vs culture result.
- Estimation of Rif susceptibility result sens and spec in Xpert vs Rif susceptibility result in DST.

Sample Size Estimation

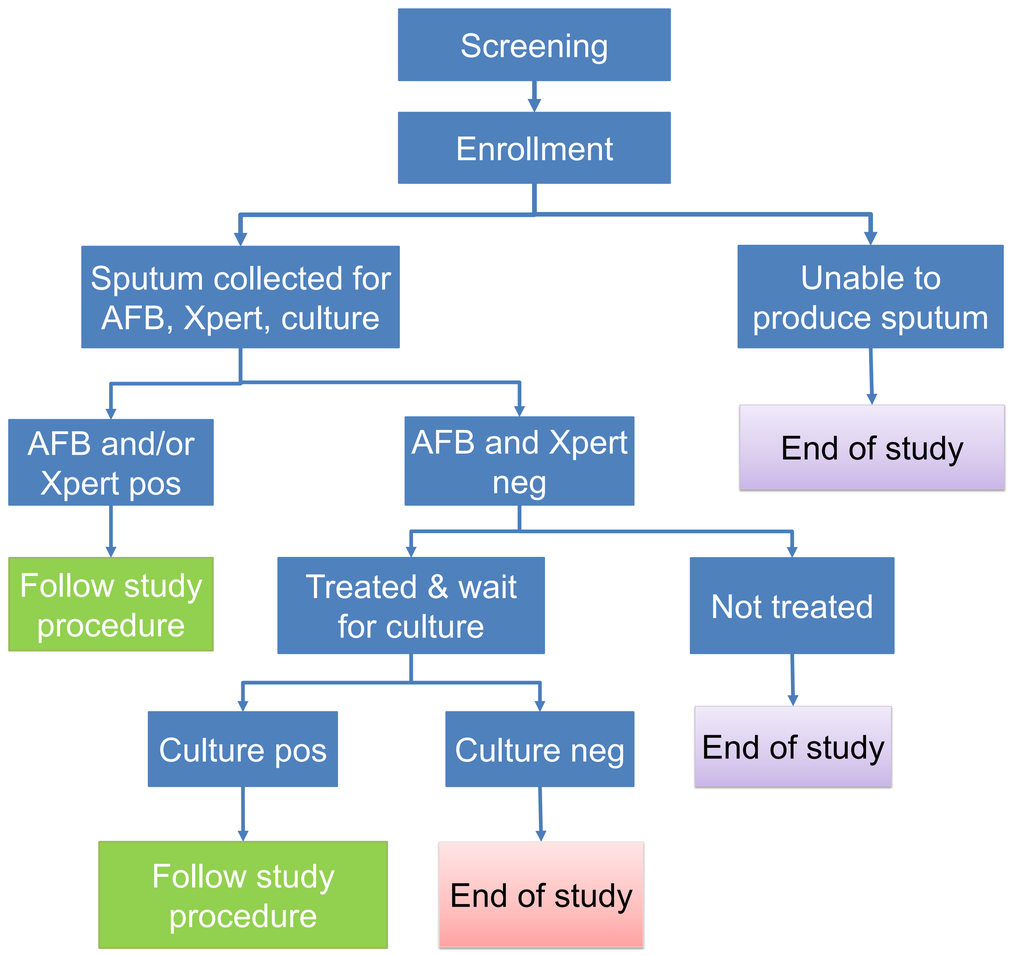


Eligibility Criteria

Patients (with or without TB treatment history) who meet the following criteria:

- Patients suspected of having pulmonary TB
- Cough ≥ 2 weeks
- At least 1 other TB clinical symptoms Suggestive pulmonary TB chest X-ray results
- Denies having TB treatment in the last 2 months
- Age ≥18 years old
- Willing to be treated/evaluated at study site
- Willing to have specimens stored
- No liver or chronic kidney disease or pregnancy or severe psychiatric illness that might interfere with study compliance

Study Procedures



Study Hospitals

1. RSUP Persahabatan/FK UI (Jakarta)
2. RSUD Dr Soetomo/FK UA (Surabaya)
3. RSUP Dr Hasan Sadikin/FK Unpad (Bandung)
4. RSUP Dr Kariadi/FK Undip (Semarang)
5. RSUP Sanglah/FK Udayana (Bali)
6. RSUP Sulianti Saroso (Jakarta)
7. RSUP Dr Sardjito/FK UGM (Yogyakarta)

Partners

Jointly Funded by
National Institute of Health Research and Development
NIH National Institute of Allergy and Infectious Diseases

An Observational Study of the Causes, Management, and Outcomes of Community-acquired Sepsis and Severe Sepsis in Southeast Asia

Sepsis Study Team

Background

- Bacterial and viral infectious diseases are still the leading cause of death in Southeast Asia
- Sepsis is defined as the body's response to infectious diseases, including bacterial and viral causes.
- Patients with severe infectious diseases may not present with fever, and infectious causes may be overlooked by physicians.
- On the other hand, it is common for patients who are diagnosed with sepsis on admission to later have a confirmed non-infectious diagnosis.

Objectives

Primary objective

To determine the causes of community-acquired sepsis and severe sepsis in adult and pediatric subjects across Southeast Asia.

Secondary objective

- To define the current acute management (within the first 48 hours after admission) of subjects presenting with community-acquired sepsis and severe sepsis. This will provide the basis for designing practical interventions to reduce the mortality of subjects with sepsis and severe sepsis in the future.
- To define the clinical outcomes of community-acquired sepsis and severe sepsis in Southeast Asia.

Study Design

Sample size

- 2,250 patients with sepsis or severe sepsis patients
- Each country (Thailand, Vietnam, and Indonesia) will enroll 750 subjects. 3 participating sites in Indonesia are RSUPN dr Cipto Mangunkusumo, RSUP dr Wahidin Sudirohusodo, and RSUP dr Sardjito.
- Indonesia will recruit 375 adults and 375 children

Accrual Period

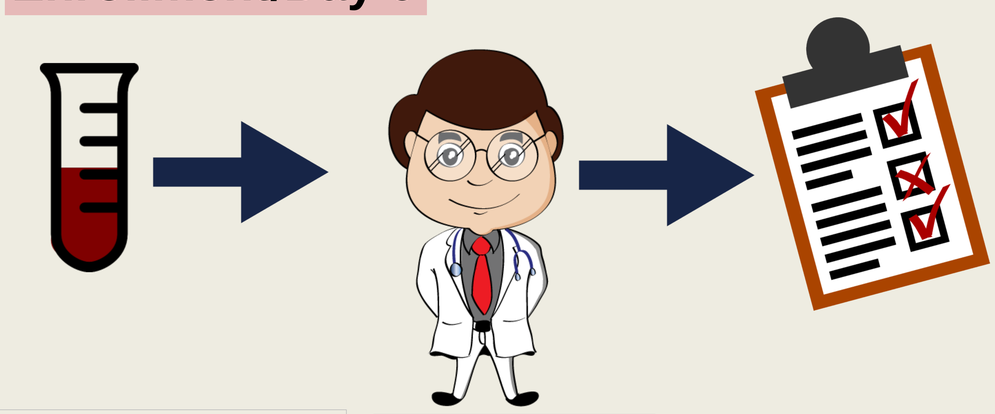
Up to 2 years

Laboratory Testing

Disease	Test	Specimen
Tests to be performed in Blood Culture Negative cases [estimated to be 90% of subjects]		
Common bacterial infection	PCR 16s	Blood
Tests to be performed on patients with CNS symptoms where CSF is available [estimated to be 10% of subjects]		
Bacterial and fungal infection	Culture	CSF
M tuberculosis	AFB Slides	
Neisseria meningitis Streptococcus pneumonia	PCR 4-plex	CSF
Herpes simplex virus Varicella Zoster virus	PCR 2-plex	CSF
Dengue virus	PCR	CSF
Japanese Encephalitis virus	IgM ELISA	CSF
Tests to be performed on subjects with respiratory symptoms [estimated to be 10% of subjects]		
M tuberculosis	AFB Slides	Respiratory specimen
14 respiratory virus (including influenza)	PCR 14-plex	Nasal swab + Pharyngeal swab
Mycoplasma pneumoniae	PCR 5-plex	Nasal swab + Pharyngeal swab
Tests to be performed on subjects with diarrheal symptoms [estimated to be 20% of subjects]		
General bacterial infection	Stool culture	Stool
Rotavirus	ELISA or PCR	Stool
Tests to be performed in cases where the cause of sepsis/severe sepsis is unknown [estimated to be 80% of subjects]		
Leptospirosis	PCR & MAT	Blood
Scrub Thypus	PCR & IFA	Blood
Murine Thypus	PCR & IFA	Blood
Hanta virus	PCR	Blood
Spotted fever group	PCR	Blood

Study Flow

Enrollment/Day 0



Blood Sample Collection for:
- Research tests
- Rapid Diagnostic tests
- EDTA for DNA (Optional for adults only)
- CSF, respiratory specimen, urine, stool (if available)

Monitor if AE/SAE/UP
Occurred within 48 hours

Review Medical Records:
- Medical History
- Basic Physical Exam
- Vital Signs
- Any Investigations
- Treatments received from the primary hospital (if available) to the time of admission to the ER to the time of enrollment

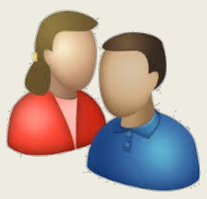
1st Follow-up (Day 14-20)

Blood collection for research specific tests:
Adult and Children ≥ 7 years old: 10 mL (8-12 mL)
Children ≥ 3 and < 7 years old: 5 mL (4-6 mL)
Children ≥ 30 days and < 3 years old: 3 mL (2-4 mL)

Complete subject follow-up visit log and complete CRF

Follow-up if AE/SAE/UP occurred within 48 hours

2nd Follow-up/End of Study (Day 28-35)



Visit at ward, phone interview or home visit
- Survival Questionnaire
- Clinical Outcome

CRF Completion:
FINAL

Partners

Jointly Funded by
National Institute of Health Research and Development
National Institute of Allergy and Infectious Diseases

Data Safety Monitoring Board (DSMB) for Clinical Trial

INA-RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

What is a Data Safety Monitoring Board?

DSMB is a group of individuals with pertinent scientific expertise that:

- Reviews, on a regular basis, the accumulated research data from an ongoing clinical trial;
- Advises the sponsor and/or researcher regarding the continuing safety of trial subjects and those yet to be recruited into the research trial
- Advises as to the continuing validity and scientific merit of the trial

Purposes of a DSMB

DSMBs are considered to have "stewardship" of a trial.
The board has responsibilities to both subjects (in terms of safety) and the sponsor (in terms of trial credibility)

❖ Specific purpose of a DSMB includes:
- ➢ Protecting participant safety
- ➢ Ensuring the credibility and integrity of the trial for future subjects
- ➢ Ensuring the timely conclusion of a trial so its results can be disseminated
- ➢ Identify protocol violations that suggest clarification or changes to protocol are needed
- ➢ Identify unexpectedly high dropout rates that threaten the trial's ability to produce credible results
- ➢ Ensure the validity of study results

DSMB Roles & Responsibilities

- Conducting an advisory review of the draft study protocol and study procedures
- Providing suggestions, where feasible for potential solutions to identified problems
- Performing ongoing interim reviews of safety and efficacy data
- May also be requested by the sponsor to conduct emergency reviews of data to assess safety-related issues
- Other : Making recommendation; Maintain meeting record

DSMB Member's Qualifications

- Prior experience.
- Knowledge and understanding of clinical trial.
- Willingness and ability to commit to attending meetings and preparatory review of material.
- Demographic diversity or international representation.
- Should not be affiliated with sponsor, investigators, or study staff.
- Should also not have vested conflicts of interest.
- From multiple disciplines represented:
  - ✓ Trial-specific medical/clinical expertise (e.g., physicians)
  - ✓ Biostatisticians
  - ✓ Ad hoc experts (e.g., bioethicists, scientists, epidemiologists), as needed
  - ✓ Patient representatives, when appropriate

What Kind of Studies Need DSMB?

- Randomized
- Are expected to provide answers concerning a medical intervention's efficacy and safety
- Address critical health outcomes (e.g., life-threatening events)
- May involve high levels of toxicity
- Evaluate an endpoint where the inferiority of one treatment arm has both safety and efficacy implications
- Might require early stoppage for ethical reasons if the primary question has been answered (even if secondary ones have not)

DSMB Activities

- Protocol Review.
- Charter Review.
- Orientation Meeting.
- Regular Meetings : Open Session, Closed Session & Closed. Executive Session.
- Provide reports: interim review report, Verbal Report, Summary Report:, Closed Session Report, Immediate Action Report.
- Making recommendation based on reports.

ReDEFINe (Rifampicin DosE FINding Study): The First Study Monitored by INA-RESPOND DSMB

High-dose Rifampicin for the Treatment of Tuberculous Meningitis: a dose-finding study

Rovina Ruslami, Ahmad Rizal Ganiem, Faculty of Medicine UNPAD / RSUP Hasan Sadikin - Bandung
A Peer Health Granted Study,
Sponsored by Padjadjaran University in Collaboration with the United States Agency for International Development (USAID) and Radboud University,
ClinicalTrial.gov Identifier: NCT no:02169882

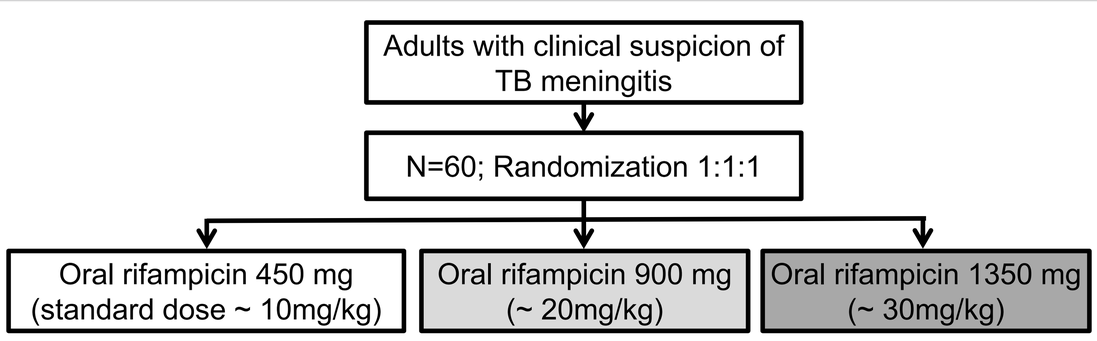
Background & Rationale

- ❖ Meningitis is the most severe manifestation of TB
- ❖ Difficult to diagnose, high mortality.
- ❖ Current treatment regimens: not evidence-based, Follow Pulmonary TB treatment.
- ❖ Rifampicin (RIF) is keystone drug for TBM but its penetration to the Brain Blood Barrier (BBB) is limited
- ❖ Previous study using RIF 600 mg intravenous (iv) found that required RIF concentration in Cerebro Spinal Fluid (CSF) was safer and provided better outcome than the 450 mg p.o
- ❖ However, RIF iv. is invasive, impractical, expensive, and not widely available
- ❖ Alternatively, since the RIF is a friendly and well-tolerated drug, the ReDEFINe study will use higher oral doses

Study Objectives

- ❖ **Primary Objective :**
  To generate PK data of higher dose of RIF in TBM patients.
- ❖ **Secondary Objective:**
  - Safety and tolerability
  - Efficacy, clinical & neurological response
  - Gene-expert for TBM
  - Bio repository of blood, CSF for future research

Schematic Study Design



A Prospective Study , single-center, **double-blinded**, 1:1:1, **randomized**, **placebo** controlled trial Phase IIIb clinical trial (dose-finding study).
Estimation subjects enrolled 60 subjects.

INA-RESPOND Roles In ReDEFINe Study

- ❖ DSMB and Monitoring supported by INA-RESPOND.
- ❖ DSMB Activities scheduled for orientation meeting in November 2014.
- ❖ Purpose of Monitoring:
  - ➢ Protecting human subjects.
  - ➢ Maintaining the integrity of study data.
  - ➢ Compliance with regulations and Good Clinical Practice (GCP).
- ❖ Visit Types of Monitoring:
  - ✓ Study Initiation Visit (SIV).
  - ✓ Routine Site Monitoring Visit (MV).
  - ✓ Study Close Out Visit (COV).

Partners

Radboud University Nijmegen

Jointly Funded by
National Institute of Health Research and Development
National Institute of Allergy and Infectious Diseases

NEXT STUDY:

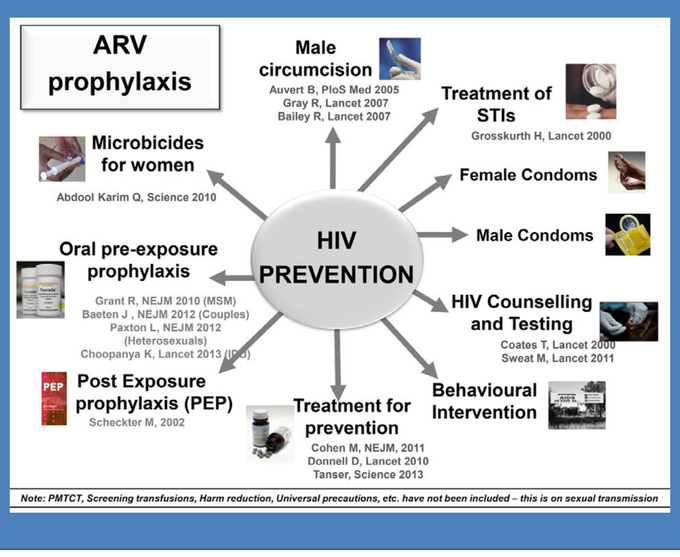
Test and Treat for HIV Prevention in Communities (T R O P I C)

A Cluster Randomized Community Trial

INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

Background

- Globally 1.5m deaths, 35m living with HIV, 2.1m new infections in 2013
  - In Indonesia: 590,000 living with HIV, 58,000 new infections in 2012
- Impressive progress in HIV prevention, but
- To stop HIV/AIDS epidemics, a comprehensive HIV prevention that combines time-tested prevention modalities (behavioral intervention, condoms, circumcision, etc), ARV-based prophylaxis and VACCINE is a must, because of:
  - Programmatic barriers (inadequate fund and/or human resources)
  - Limited uptake, underused and non adherence
  - Stigma, discrimination and violence
  - Risk-taking behavior, complacency
- Among the HIV prevention methods, the most compelling is the effectiveness of Universal testing and early treatment
  - Cohen (2011) : immediate treatment reduced HIV transmission to sexual partner by 96%
  - Rodger (2014): Risk of HIV transmission through condom-less sex is exceedingly rare when the partner has an undetectable viral load at ART
- Why do we need this study then? UNKNOWN:
  - Universal Test and Treat (UTT) intervention can be delivered with high uptake and acceptability
  - Population level impact of intervention package
  - EVIDENCE to support whether UTT will prevent HIV transmission in various settings in Indonesia



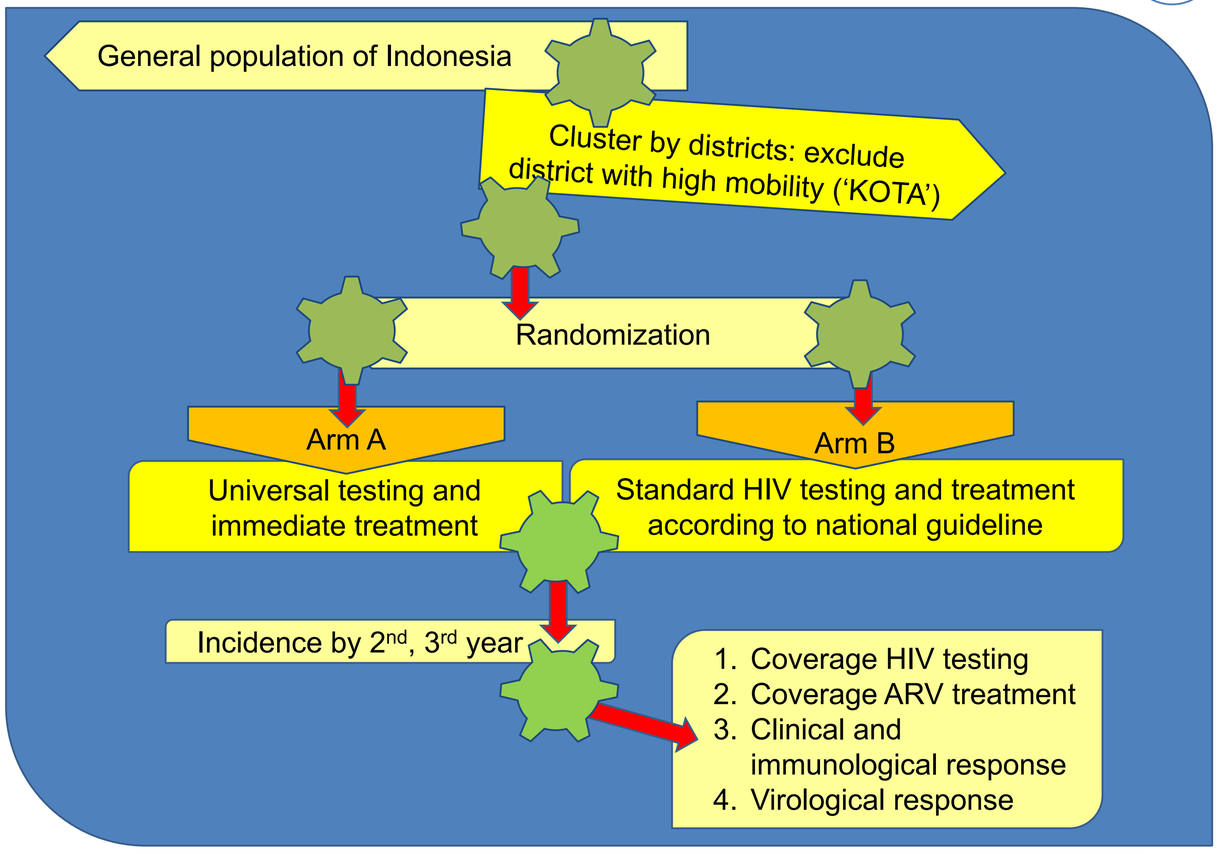
Primary Objective

To measure the impact of universal testing and immediate treatment on preventing HIV transmission in Indonesia, indicated by reduction of HIV incidence in general population.

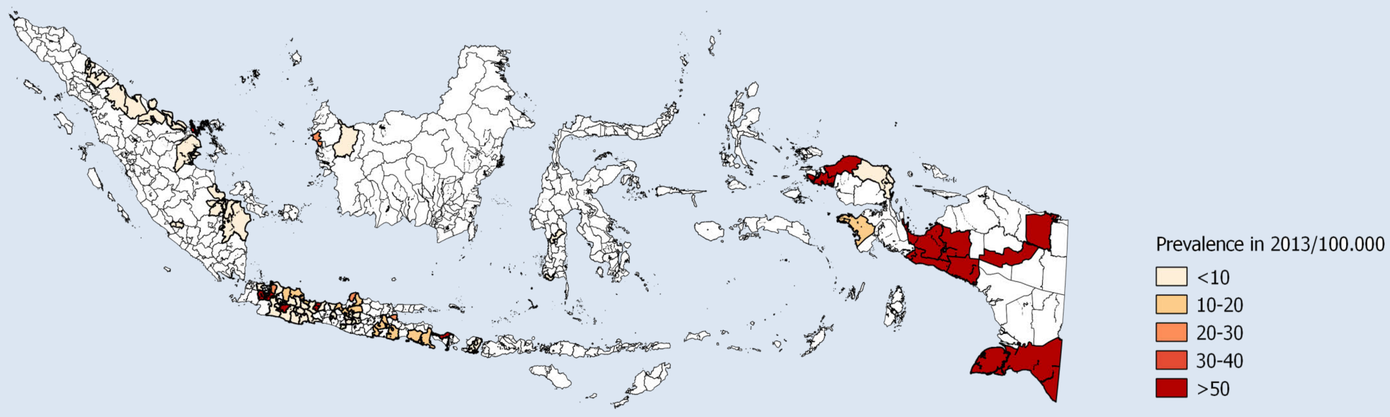
Secondary Objectives

To measure: coverage of universal HIV testing, coverage of immediate HIV treatment, clinical response to HIV treatment, immunological response to HIV treatment, virological response, including resistance to HIV treatment

Study Design



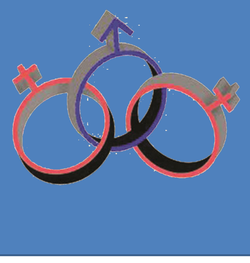
Sites will be randomly selected from 76 high-prevalence districts (colored) and low-prevalence districts (white)



Other Prospective Studies on HIV/AIDS

According to the National Strategies and Plans to control HIV and AIDS, Indonesia needs to conduct several studies, including:

1 Epidemiology and behavior study



The objective of this study is to determine the epidemiology of HIV/AIDS in Indonesia, such as the prevalence, incidence and distribution of HIV/AIDS in Indonesia, the behavior of the population, and factors that influence them. The results will provide data and facts that are important to prepare policies to control the disease.

2 Operational research

The objectives are to obtain reliable data and evidence that are useful to prepare a better HIV/AIDS control program, for example how to increase the adherence.

3 Capacity building for the researchers and institutions, strengthening research network

INA-RESPOND in collaboration with US-NIAID has built research capacities in 7 medical schools and their corresponding hospitals so that it will be ready to conduct any epidemiological, operational or clinical HIV Study. Collaborations with industries to support these studies are also welcome.

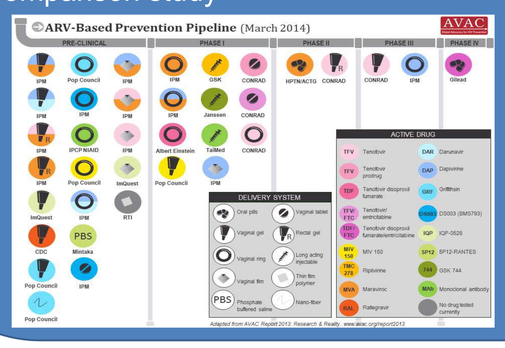
4 Drug management, e.g. the efficacy and safety of a new medication, treatment strategy, drug resistance, and other topics.

One of drug management studies that is needed by clinicians is dose reduction of Efavirez which is associated with worse neuro-cognitive functions

Lower dose of Efavirenz a non-nucleoside reverse-transcriptase inhibitor (NNRTI)
- A study (Puls, 2014) the efficacy is comparable, but less adverse events then 600mg

Can it be reduced further to 200mg?
- Phase II, dose finding comparison of 200, 400, 600mg suggested comparable viral load suppression rate (Horn & Clayden)

dose finding comparison study for other ARV regimen comparison study



ARV drugs also play an important role in HIV prevention. The diagram on the left side shows the progress of ARV as prevention in the world. To determine the most suitable method for Indonesia, we need to also participate in these studies.

Partners

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