INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

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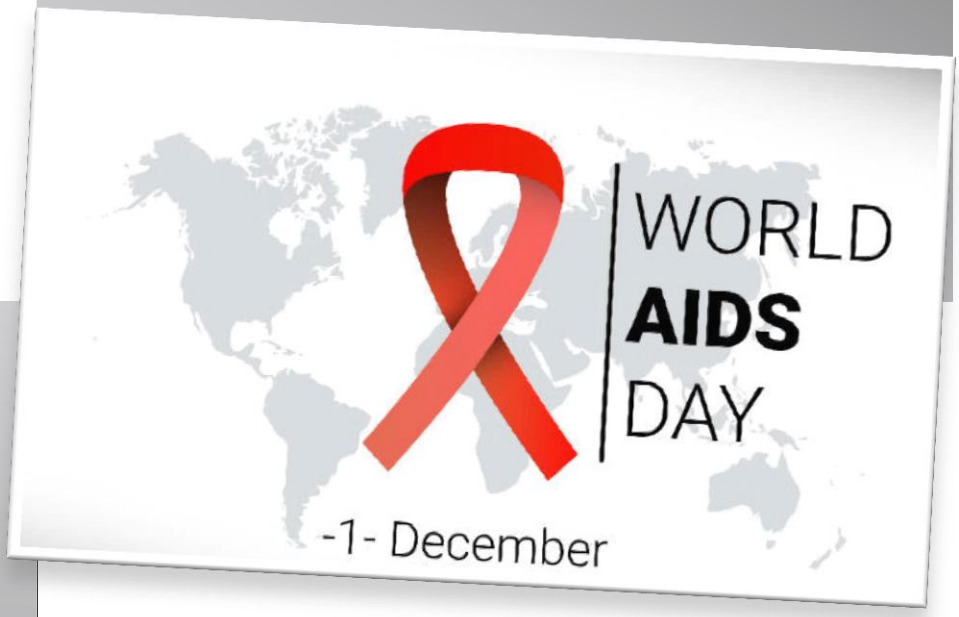
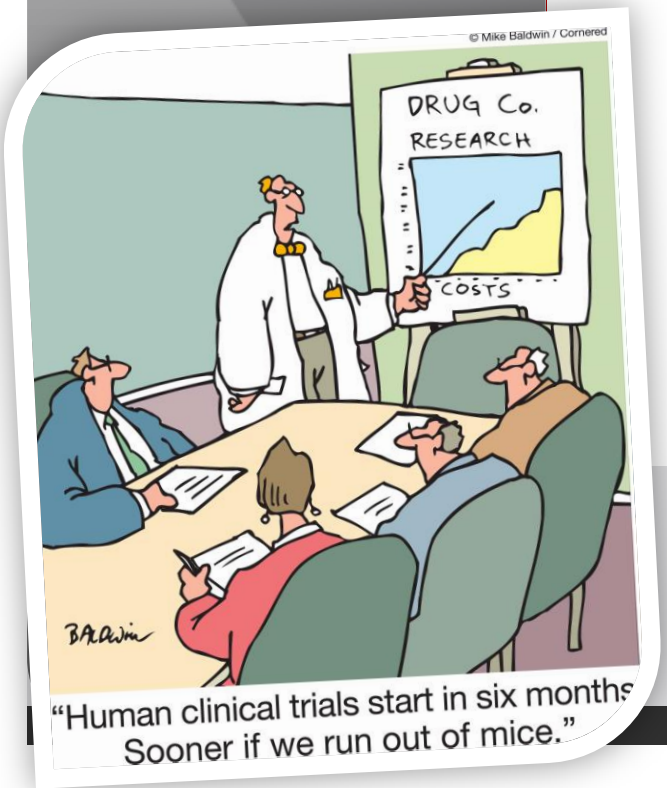
Newsletter December 2017



In This Issue



World AIDS Day: The Right to Health

World AIDS day which takes place on December 1 is an opportunity for people to fight against HIV, show support for people living with HIV (PLHIV), and commemorate those who have died from AIDS-related illness. Founded in 1988, this year marks the 30th anniversary of World AIDS day. It is the first ever global health day, and this year's theme is "Right to Health".

Based on a survey done by World Health Organization (WHO) in 2016, there are approximately 36.7 million people living with HIV. This year's theme reminds us of the need for those 36.7 million people and those who are vulnerable and affected by the epidemic. To reach the goal of universal health coverage, and under the slogan "Everybody Counts", WHO will advocate for access to safe, effective, and affordable medicines, including diagnostics and health care services. So, what has Indonesia done to commemorate the day and fight against HIV? Most importantly, have we shown our support for those who are at risk or living with HIV around us? Find out here!

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Clinical Trials: The Fairest of Them All

In the last decade, more and more clinical trials are conducted. However, not all people understand what these trials are and their benefits. Let's learn a bit more about them in this edition!

Save The Date

Important Events & Meetings

7	Dec	Schistosomiasis Meeting @NIHRD, Jakarta
12	Dec	TRIPOD Laboratory Meeting
22-27	Jan	HIV Investigator Meeting

Announcement

December is here! That means Christmas is approaching. It's the season of joy, peace, love, and happiness. It's the time where we can spend the days with our loved ones doing things that we love; whether going on a long vacation or just staying at home. So, have you decided on how you're going to spend this Holiday season?

Wishing you all a Merry Christmas 2017 and a Happy New Year 2018. May this Christmas be bright and cheerful, and may the New Year begin on a prosperous note. Happy Holidays!

December Birthday

5 Dec	Dr. Dona Arlinda	NIHRD
6 Dec	Dr. Bachti Alisjahbana	INA101 PI Site 510
6 Dec	dr. M. Karyana, M. Kes	Head of SC
8 Dec	Dr. Banteng Hanang Wibisono	INA102 PI Site 560
16 Dec	dr. Delima	NIHRD
22 Dec	dr. Umi Haryanti	Lab Technician Site 570
23 Dec	dr. Desvita Sari	INA102 Co-PI Site 560
24 Dec	Dr. Ketut Jaya Ningrat	INA102 RA Site 520
28 Dec	Prof. Dr. Ketut Tuti Merati, SpPD, KPTI	SC Member at Site 520
29 Dec	Prof. DR. dr. Ida Parwati	INA101 Co-PI Site 510

INA-RESPOND
Study Updates

By:
dr. Anandika Pawitri

TRIPOD (INA102) Updates

Screening and Enrollment

By the end of November 2017, from a total of 906 patients screened, 137 subjects had been enrolled. The top recruiter is still site 570 – RSUD dr Soetomo with 41 subjects, but site 580 – RSUP dr Sardjito is just 2 subjects behind with 39 subjects. On November 20, site 590 – RSUP Persahabatan, Jakarta joined the TRIPOD team to screen patients. That they managed to fulfill the weekly enrollment target is fantastic news! Site teams must still enroll 1,220 subjects and will stop enrolling patients 2 years after the activation of the first site, which will be at the end of January 2019. On that note, let's put all our hearts into this study, and keep enrolling!

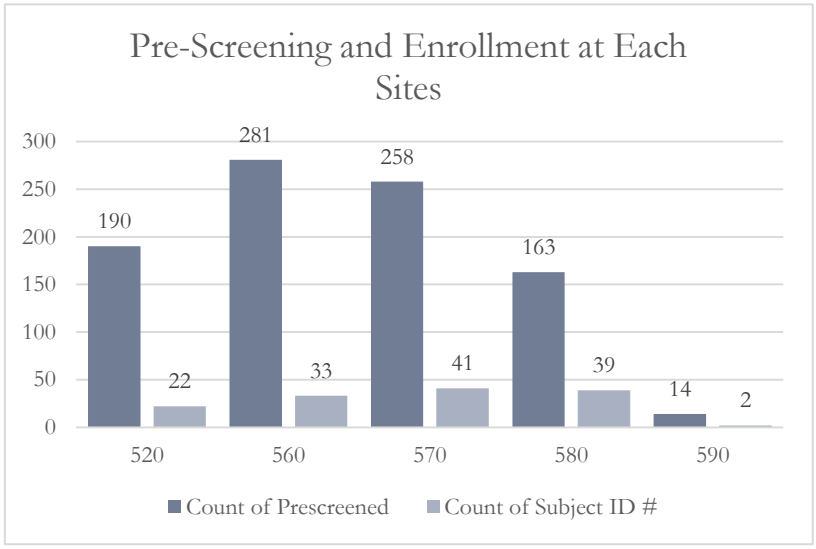
Screening Failure Reasons

The screening failure reason table shows us a glimpse of why the patients at our sites could not join the study. The biggest reason for screening failure was patient's treatment history. Patients who took TB treatment within 2 months before coming to the hospital were so many that we had to amend the protocol to adjust the situation. You can see the other reasons from the table above.

Site Assessment Visit (RSUP H. Adam Malik)

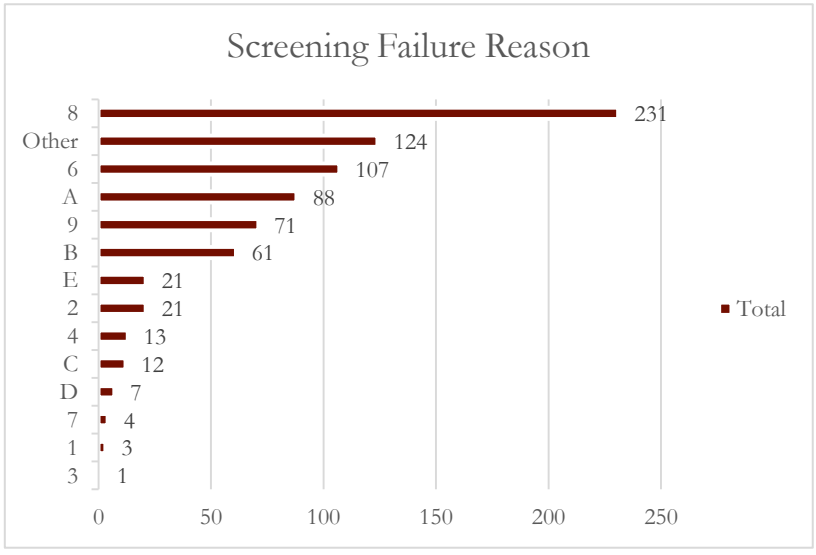
On November 15 – 16, the Secretariat visited a new site for TRIPOD study, RSUP H. Adam Malik, Medan (site 600). We were well-received by eager hospital staffs that cannot wait to start the study. During the meeting, the Secretariat team introduced INA-RESPOND and explained about the TRIPOD protocol as well as the study's requirements. Afterwards, the staff showed us the hospital facilities so we know what is still needed for the study. In general, the hospital mostly has what the study requires and is ready to meet the study needs.

On December 5 – 6, Site Preparation Visit (SPV) was done. Site Initiation Visit (SIV) will be conducted after the team agrees on the time. Hopefully, the site can join us to start enrolling subjects by the end of the year.



*Site Number code:

520 – RSUP Sanglah, Denpasar
560 – RSUP dr Kariadi, Semarang
570 – RSUD dr Soetomo, Surabaya
580 – RSUP dr Sardjito, Yogyakarta



1 : Patients suspected of having pulmonary TB
2 : Cough ≥ 2 weeks
3 : At least one other TB clinical symptom
4 : Suggestive TB x-ray
5 : Age ≥ 18 years old
6 : Willing to be treated or evaluated at study site
7 : Willing to have specimens stored for use in future studies
8 : Having TB treatment within 2 months
9 : Having TB treatment for 7 days within 1 month

A : Liver disease
B : Chronic kidney disease
C : Pregnancy
D : Severe psychiatric illness
E : Serious Condition/ Poor Condition

"Human clinical trials start in six months. Sooner if we run out of mice."

Comic Corner

Clinical Trials: The Fairest of Them All

By:
dr. Aly Diana

Yes, clinical trials have been famous since a long time ago, and the trend will continue. On that note, let's briefly discuss what critical trials are, the phases, the main purposes, and the challenges to keep things straight beyond the conflict of interests.

Clinical trials are "research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans". Clinical trials should produce the best data available for health care decision-making. However, clinical trials also have the potential to pose unknown risks to their participants, and biased knowledge extracted from flawed clinical trials may lead to the inadvertent harm of patients. Although conducting well-designed clinical trials may appear straightforward, it really depends on its rigorous methodology and has to follow key ethical principles. In short, conducting clinical trials and evaluating results from other clinical trials are not a simple task.

The studies should follow strict scientific standards to protect patients and help produce reliable study results. Clinical trials are one of the final stages of a long and careful research process. The process often begins in a laboratory where scientists first develop and test new ideas. If an approach seems promising, the next step may involve animal testing. This shows how the approach affects a living body and whether it's harmful. However, an approach that works well in the laboratory or animals doesn't always work well in people. Therefore, research in humans is needed. The processes in the laboratory and non-human subjects are called preclinical studies.

So, clinical trials always involve human as subjects, and they are divided into 4 phases: 1. **Phase I** is done to test a new biomedical intervention for the first time in a small group of people (20-80 people) to evaluate safety (to determine a safe dosage range and identify side effects); 2. **Phase II** is done to study an intervention in a larger group of people (several hundreds) to determine efficacy (that is, whether it works as intended) and to further evaluate its safety; 3. **Phase III** is done to study the efficacy of an intervention in large groups of trial participants (from several hundreds to several thousands) by comparing the intervention to other standard or experimental interventions (or to non-interventional standard care). Phase III is also used to monitor adverse effects and to collect information that will allow the intervention to be used safely; and 4. **Phase IV** is done after an intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use over longer periods of time. They may also be used to investigate the potential use of the intervention in a different condition, or in combination with other therapies.

A clinical trial may find that a new strategy, treatment, or device improves patient outcomes; offers no benefit; or causes unexpected harm. Although we know that all of these results are important because they advance medical knowledge and help improve patient care, nobody starts clinical trials and expects to obtain negative results, given the times and resources needed. Another issue is that almost all clinical trials need huge amount of funding and usually, the funding comes from the company that will produce the medical strategies (device, drugs…) which make conflict of interests difficult to avoid. Some of clinical trials report positive statistically significant effects, although the researchers are aware that the effect has no clinical values.

Closing remarks: The fairest clinical trials are emphasizing safety first and benefits, for the sake of the patients (not for the supporting company or the researchers). Again, a rigorous methodology, which follows key ethical principles, is critical for clinical trials.

ASTMH 66th Annual Meeting

By:
dr. Dona Arlinda
Ms. Nawang Wulan Sari

The American Society of Tropical Medicine and Hygiene (ASTMH) 66th Annual Meeting was held on November 5-9, 2017 at Baltimore Convention Center, Baltimore, Maryland, USA. The ASTMH is a non-profit organization of scientists, clinicians, students, and program professionals whose longstanding mission is to promote global health through the prevention and control of infectious and other diseases. The annual meeting was attended by 4,400 delegates from 100 countries. They include researchers, professors, government and public health officials, military personnel, travel clinic physicians, practicing physicians in tropical medicine, students, and all health care providers working in the fields of tropical medicine, hygiene, and global health. INA-RESPOND's representatives attending the meeting were dr. Bachti Alisjahbana, PhD, Sp.PD-KPTI; Prof. dr. Pratiwi Sudarmono Ph.D, Sp.MK; dr. Dona Arlinda; and Ms. Wahyu Nawang Wulan.

Numerous subjects representing interests in tropical disease research were presented in the scientific sessions, symposiums, plenary sessions, poster sessions, as well as late breakers. The subject categories include clinical tropical medicine, diarrhea and bacterial illness, ectoparasite-borne diseases, entomology, filariasis, global health, HIV and tropical coinfections, integrated control measures for neglected tropical diseases (NTDs), intestinal and tissue helminths, cestodes, kinetoplastida, malaria, molecular parasitology, one health: interface of human health/animal disease, opportunistic and anaerobic protozoa, pneumonia, respiratory infections and tuberculosis, schistosomiasis-helminths, virology, water, sanitation, hygiene, and environmental health. In addition, the meeting organization also included pre-meeting courses in parasitology, arbovirology, and global health; and awards session, namely the Young Investigator and Clinical Research Awards.

INA-RESPOND presented 6 abstracts at the 66th ASTMH Annual Meeting to showcase its achievements. Five abstracts were presented during the poster sessions, and the other one was an oral presentation during the HIV and Tropical Co-Infections symposium session. The posters were (1) Rickettsial Infection: An Unexpected Cause of Fever in Patient Hospitalized with Acute Febrile Illness in Indonesia, (2) The Dynamics of Dengue Virus Infection in Indonesia: Observations from a National, Multicenter Study of Acute Febrile Illness Among Hospitalized Patients, (3) The Etiologies of Fever Requiring Hospitalization in Indonesia, (4) Clinical, Serological, and Molecular Diagnosis of Typhoid Fever, A Significant Cause of Acute Febrile Illness among Hospitalized Patients in Indonesia from 2013 – 2016, (5) Building the Infectious Disease Diagnostic Capacity of a Developing Nation: Experience from the Indonesia Research Partnership on Infectious Diseases (INA-RESPOND). The talk, Unfavorable Tuberculosis Outcome Associated with HIV, Drug Resistance, and Previous Treatment in Indonesia, was presented by dr. Dona Arlinda. The abstracts, presented in both poster and symposium sessions, drew attention from fellow attendees who visited the poster booth/talk session and gave comments or asked questions.

An interesting talk about the use of Wolbachia to control Aedes aegypti transmitted viruses was delivered by Dr. Scott O'Neill from Monash University, Australia. Wolbachia can be found in over 60% of all insects worldwide and is able to disrupt pathogens' replication in their hosts. Due to cytoplasmic incompatibility, when an infected male mosquito mates with an uninfected female, no eggs are viable. However, when an infected male mates with an infected female or an infected female mates with an uninfected male, all resulting eggs are also infected; and Wolbachia spread through the population. In Indonesia, the

effectiveness of Wolbachia is being tested in Yogyakarta. We look forward to the results of this exciting intervention study.

Aside from all the "common" science events, there were also scientific works presented in a more "modern" way. The Project Zero (Huffington Post) is 360-degree virtual reality (VR) films about the untold stories of the victims and health workers battling elephantiasis, river blindness, and sleeping sickness in the most remote and underdeveloped regions of the world. Under the Net (United Nations Foundation) there is another VR story of refugees in Nyarugusu Camp, Tanzania, who struggle to survive without protection from mosquitoes that carry malaria. The films were created to raise awareness around neglected tropical diseases and increase efforts to fight them.

All in all, attending the ASTMH annual meeting is a valuable experience as we could meet experts in tropical disease research and get updates on the latest achievements in the field. The experience have broadened our knowledge and raised our inspiration in infectious disease research, which would hopefully be valuable for INA-RESPOND's activities. We are thankful for the sponsorship to attend the meeting and present the abstracts.

NIAID Grantsmanship Workshop & Meet the Experts Session for International Scientists

This two-day workshop was held on November 2-3, 2017 at NIAID Office in Rockville, Maryland, USA. Prof. dr. Pratiwi Sudarmono Ph.D, Sp.MK, dr. Dona Arlinda, and dr. M. Karyana attended this workshop on behalf of INA-RESPOND. It was a workshop to provide overview on how to develop and apply for successful NIH extramural grant application. Although the application submission process and registration requirements for NIH extramural grant application are quite strenuous, the take home message of the workshop was researchers need to layer their funding sources to ensure the continuity of the study, and the NIH extramural grant application is a great alternative for research funding source. Having multiple funding sources would allow researchers to have better success in their research career.

NIAID/DCR Symposium: International and Domestic Collaborations for Clinical Research

This half-day symposium was held on November 3, 2017 at NIAID Office in Rockville, Maryland, USA. The Chair of INA-RESPOND, dr. M. Karyana, gave his talk on the establishment and achievements of INA-RESPOND. There were also other representatives from the University Clinical Research Center (UCRC), Mali; the Mexican Emerging Infectious Disease Clinical Research Network, Mexico (La Red); Partnership for Research on Ebola Virus in Liberia (PREVAIL); and Infectious Disease Clinical Research Program (IDCRP), U.S. Department of Defense. These were the international and domestic collaborations under NIAID Special Projects.

30th World AIDS Day – The Right to Health

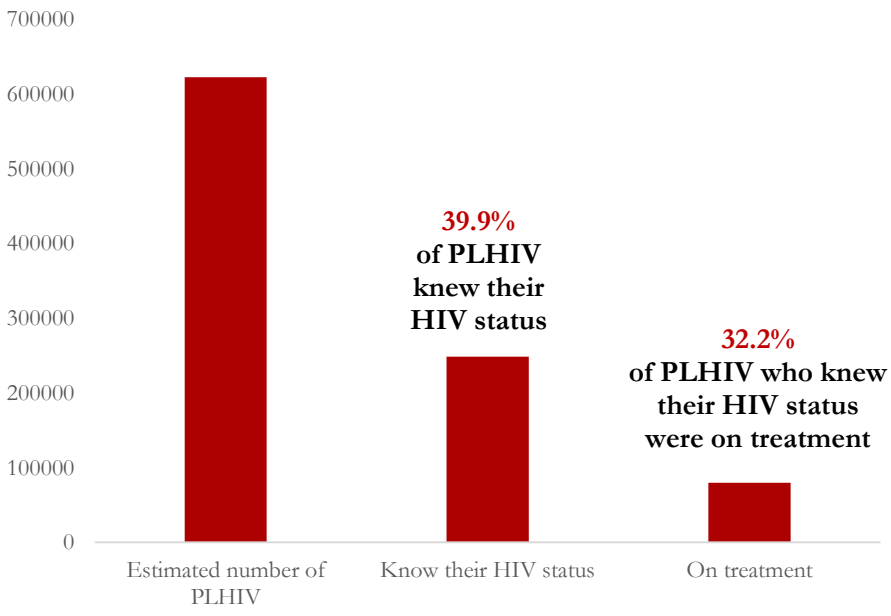
By:
dr. Dona Arlinda

December 1, 2017 marked the 30th anniversary of World AIDS Day. As the most extensively studied virus, the modalities to fight the disease continue to advance, e.g. the development of basic sciences to identify new targets for intervention, new tools for diagnosis and prevention, and new drugs for less toxic, low dose and low-cost treatment. The combination of these modalities was said to be able to turn the trajectory of HIV epidemic. Scientists are now convinced that we can end not only AIDS but also HIV epidemic.

The 2017 UNIADS Global AIDS Update reported progress towards the 90-90-90 targets. This target, when fully achieved, translates into 73% of all people living with HIV being virally suppressed. In 2016, seven countries had achieved this, i.e. Botswana, Cambodia, Denmark, Iceland, Singapore, Sweden, and the United Kingdom. Globally, there are 36.7 million [30.8 million–42.9 million] people living with HIV (PLHIV) in 2016 and more than two thirds of them knew their HIV status. Among those who knew their HIV status, 77% [57–89%] were accessing antiretroviral therapy (ART), and 82% [60–89%] of people on treatment had suppressed viral loads. Although the global data showed narrowing gaps across the cascade, when combined, they translate to 44% [32–53%] of all people living with HIV being virally suppressed, which is still much lower than the 73% target.

The National HIV Program reported that by the end of March 2017, there were estimated 622,435 people living with HIV. Among those people living with HIV, 248,250 (39.9%) knew their HIV status and 79,833 (32.2%) of people who knew their HIV status were on treatment (Fig. 1). Viral suppression data, the best indicator to evaluate response to ART, was not available as this test was not routinely done.

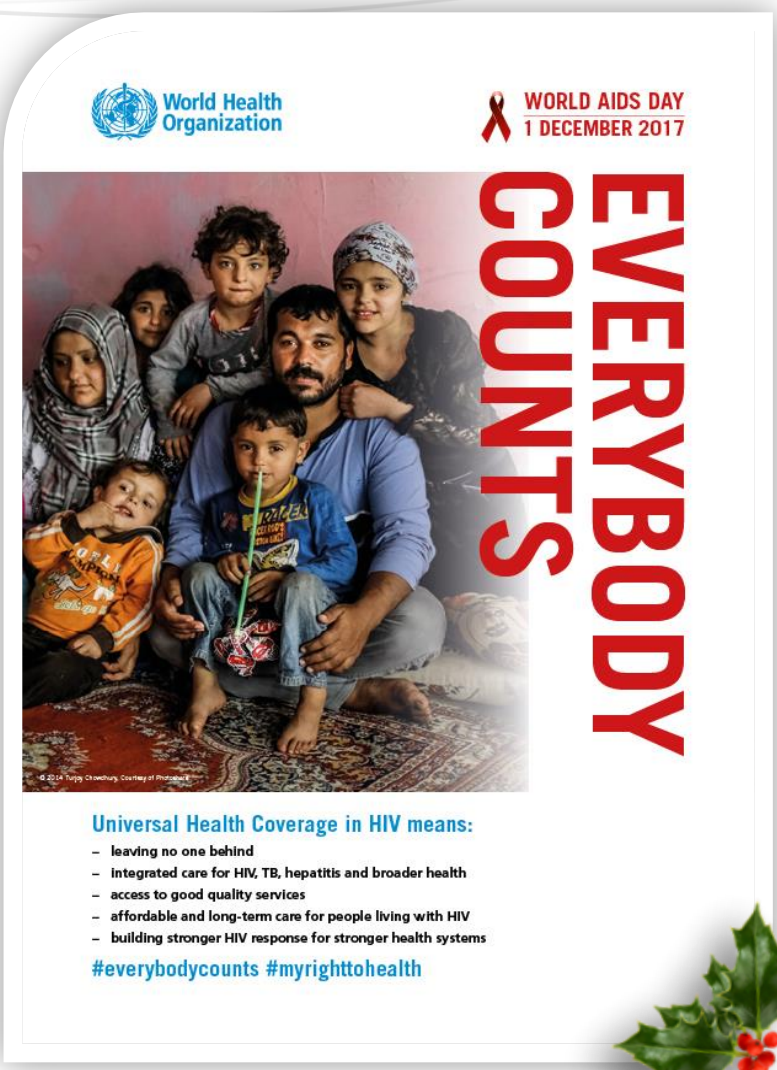
This year's theme of UNAIDS World AIDS Day, "Right to Health", reminds people that everyone has the right to quality health services and medicines. Reflecting on the theme, HIV care in Indonesia is slowly growing to reach out PLHIV and those at risk, as well as addressing challenges and barriers to care. Medical expenses for HIV care and related opportunistic infections, as well as laboratory examination for CD4 and viral load have been covered by BPJS, the national health insurance. Test and treat all policy (ART regardless CD4 to all) is expected to replace the current policy of strategic use of antiretroviral (SUFA). Antiretroviral medicines were being provided by the National HIV Control Program and delivered through 842 Care, Support and Treat (CST) services spread across Indonesia's 34 provinces. Viral load



National ART Cascade reported until March 2017 (MoHRI, 2017)

testing, which was rarely available, is projected to expand through the integration of Xpert MTB/Rif and HIV-1 Viral load to address the lack of data in viral suppression. The current guideline (under development) will also emphasize the importance of viral load testing over CD4, and recommend the test at month 6 and 12 after ART initiation, and then annually.

The NIHRD, through INA-RESPOND, is working together with the National HIV Program for the INA-PROACTIVE study. By recruiting new sites for INA-PROACTIVE, we would like to expand the INA-RESPOND network, build, and strengthen the infrastructure for future clinical research. Our expected contribution is a national-level and standardized data that describes the HIV care and management in Indonesia, which provide evidence-based policy and clinical recommendations for the improvement of HIV Program towards the triple zero goal (zero new HIV infection, zero AIDS-related death, and zero discrimination) by 2030.



INA-RESPOND Newsletter

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