INA RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

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Newsletter

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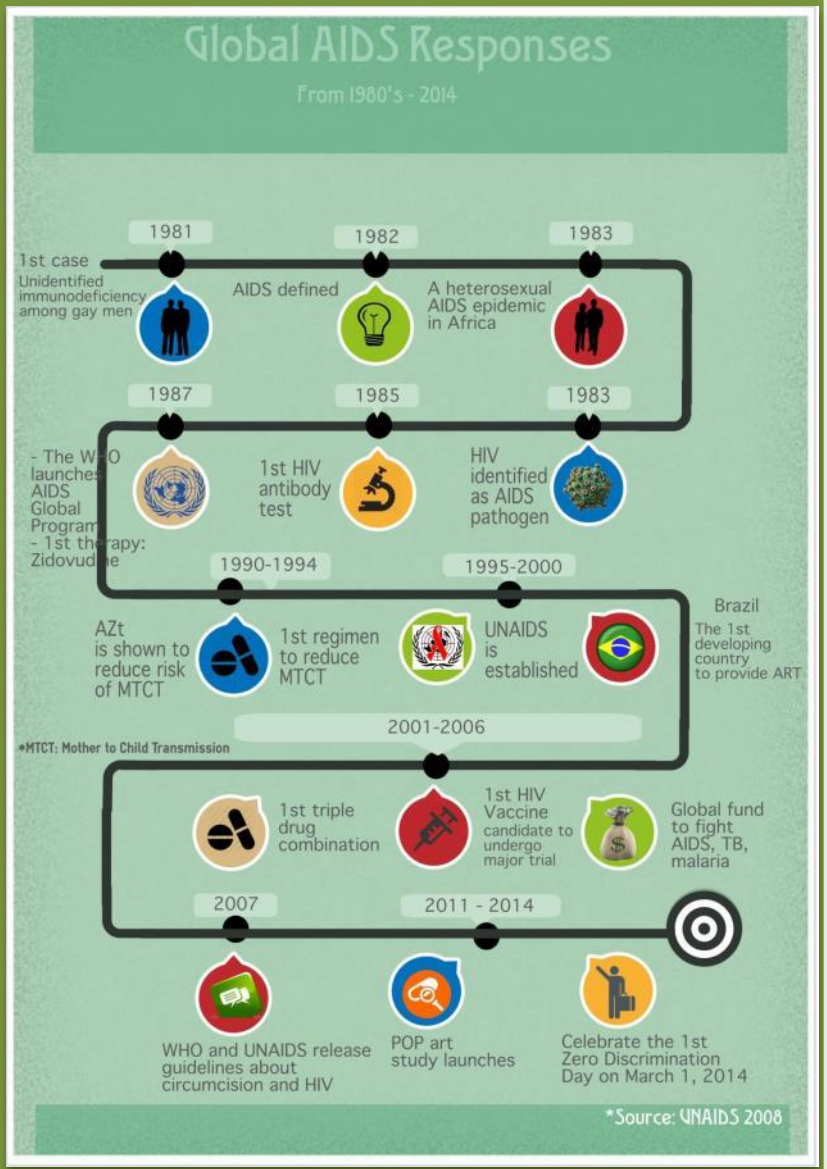
I remember a quote from an old storybook I read, The Little Prince: "It is the time you have wasted for your rose that makes your rose so important." — Antoine de Saint-Exupéry, The Little Prince. Just like the quote says, this newsletter is important as it is a part of us all especially since we have put lots of our efforts and time into it this whole year and given our contribution to its success. This month's edition features valuable information on HIV/AIDS, which our network is preparing to conduct in the future. Have fun reading it as we had our fun preparing it. –DH–

Kill or Save?

In a 'Questions and Answers' panel during the International AIDS Conference, the audience applauded the Indonesia Minister of Health, Dr Nafsiah Mboi, SpA, MPH when she shared her experience in fighting against the challenges she faced when she introduced the Harmful Reduction Policy to control HIV/AIDS among drug users. We can kill them by letting them die from overdose, from AIDS itself, or from hepatitis C, or we can save them by introducing this policy. In other occasion, despite a huge and sometimes offensive resistance, she emphasized the need for controlling HIV/AIDS comprehensively, including from the upstream, i.e. by introducing condoms for high risk groups.

After 34 years since the first epidemic in 1981, despite a lot of progress that the world has achieved, 3 key challenges remain: dysfunctional health system that fails to convert efficacious treatment and prevention interventions fully for maximum effectiveness, most new HIV infections still occur in key affected populations, and stigma, discrimination, and legislative hurdles are still the major obstacle to prevention and care.

Considering the seriousness of this disease, National Institute Health and Research Development, Ministry of Health, places HIV/AIDS as one of Indonesia's top research priorities. Since one of the principles of INA-RESPOND is to respond to the research need for the benefit of Indonesia people,

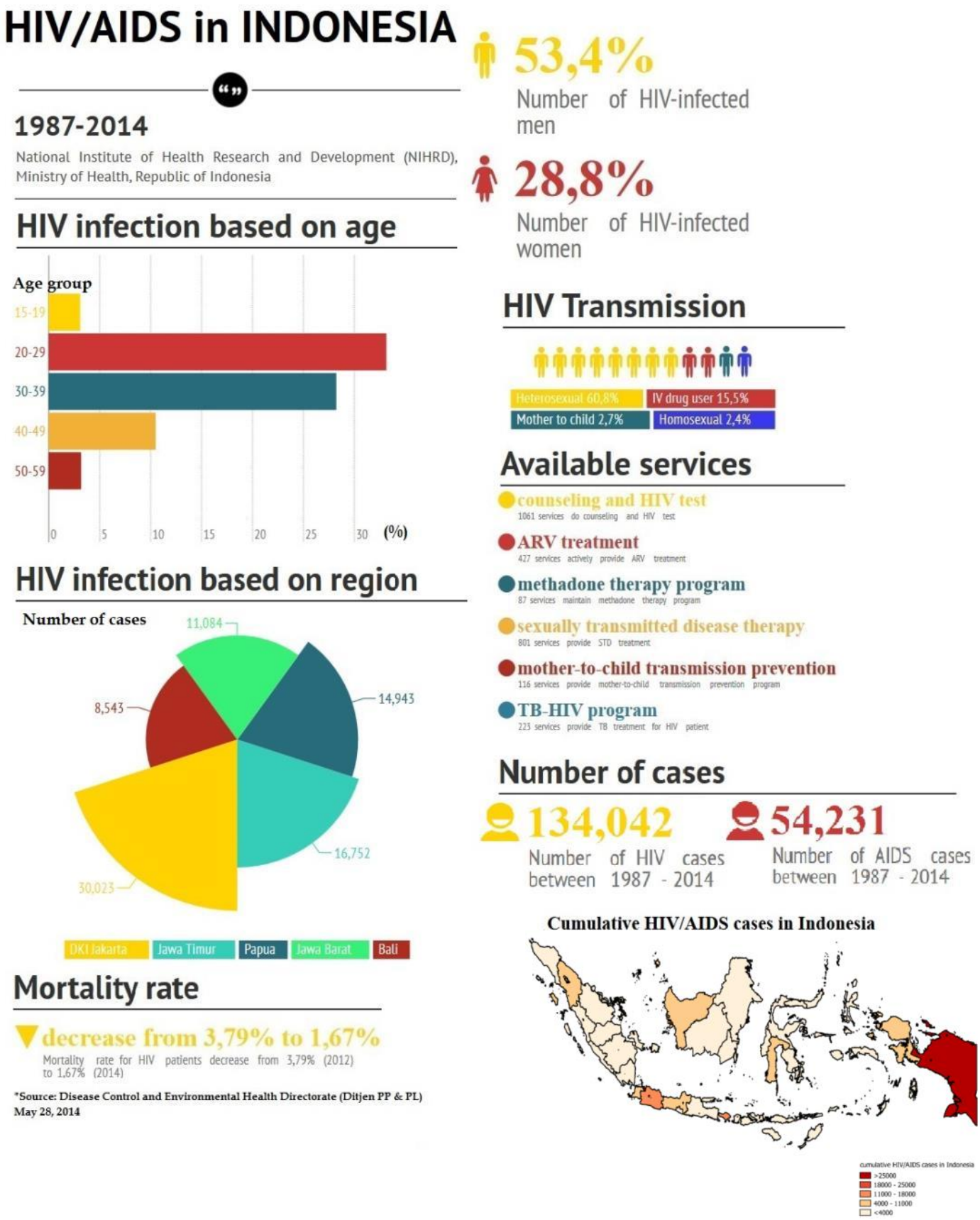


INA-RESPOND is preparing for its new studies in this field.

In this newsletter edition, we would like to specially present a more in-depth discussion on HIV/AIDS, starting with the current situation in Indonesia, the draft concepts of our study, and updates on HIV/AIDS taken from different perspectives. As our pages are limited, please visit http://www.aids2014.org/ for more detailed updates. –HK–

HIV/AIDS in INDONESIA: in numbers

Since it was first found, it only took 6 years for the HIV/AIDS to enter Indonesia. Since then, the number of cases has increase every year, from 5 AIDS in 1987 to 6,266 in 2013 and from 859 HIV cases in 1987 - 2005 to 29,037 in 2013. Other important statistics are listed below.



INDONESIA PASTI BISA

What is the title of the future INA-RESPOND HIV/AIDS study?

It is *INDONESIA PASTI BISA* which stands for **Indonesia P**revention of HIV/**AI**D**S T**ransmi**s**sion **b**y **I**ncrea**s**ing Testing and Prompt Tre**a**tment

Population

As this study will be conducted in many districts, a very large population will be involved as tens of thousands subjects will be enrolled (more than 10,000 samples). Consequently, we need a lot of support from the Indonesia Ministry of Health, other related Ministries as well as provincial and district governments.

Study Background

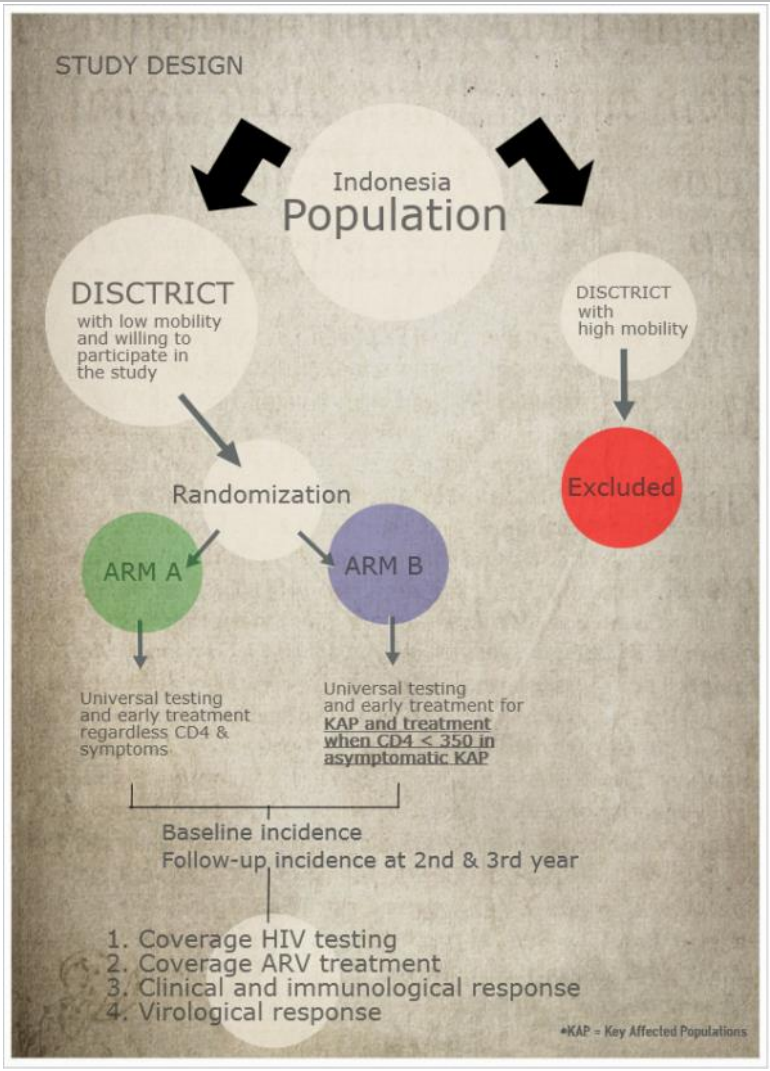
a) HIV growth in Indonesia is expanding most rapidly among the Southeast Asia countries with HIV prevalence of 7.12 in 2008 to 22 per 100,000 in 2013. This number is still lower than the estimated because the number of people tested is low (215,787 in 2012).

b) Continuum of Care (*Layanan Komprehensif Berkesinambungan / LKB*) has been established to face the challenges such as the unsatisfying overall cascade of treatment despite the introduction of free anti-retroviral therapy (ART) in 2004, the low number of people who have access to care and still on treatment, the unsatisfying HIV control program in Indonesia for key affected population (KAP), uneven distribution and integration of programs, and low retention rate of the clients even in areas with high burden of disease.

c) Indonesia's policy delivers ART treatment regardless of CD4 or symptoms in KAP, but it still uses the threshold of CD4 <350 cells/ml for asymptomatic non KAP populations.

d) Early ART has been proven to significantly reduce the transmission to sexual partners by 96%

e) A study in large communities in areas with LKB is needed to prove the benefit of universal testing and early ART regardless of CD4 threshold before nationally implemented



Research Question

Can universal testing and early treatment prevent HIV transmission in Indonesia?

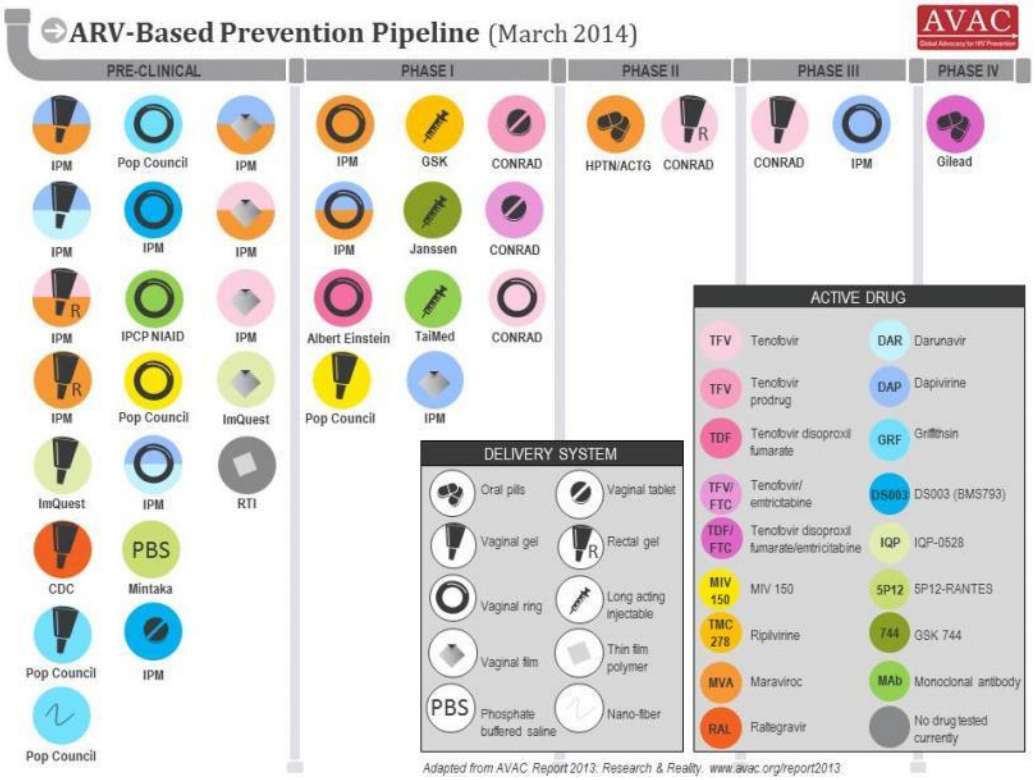
What are the objectives of this study?

PRIMARY: To study the benefit of universal testing and early HIV test regardless of CD4 examination or symptoms in reducing HIV incidence in a large population.

SECONDARY: To measure the coverage of universal testing, immediate HIV treatment, and clinical, immunological and virological responses of HIV treatment.

Priorities for New Technologies

The choices for HIV prevention we have now are increasing, including the ARV-based. To improve the effectiveness of ARV, new technology is applied, including research on alternative delivery systems (pill, vaginal, rectal, and injectable) and the controlled release (on demand, sustained release, or long acting).



Above is the list of products that are on several phases of clinical trial. The color (s) in every circle represents the active ARV drug(s). The icon indicates the delivery system and the names under the circles are the names of the companies or organizations conducting the research.

CURING AIDS

Why is it so difficult to cure HIV/AIDS?

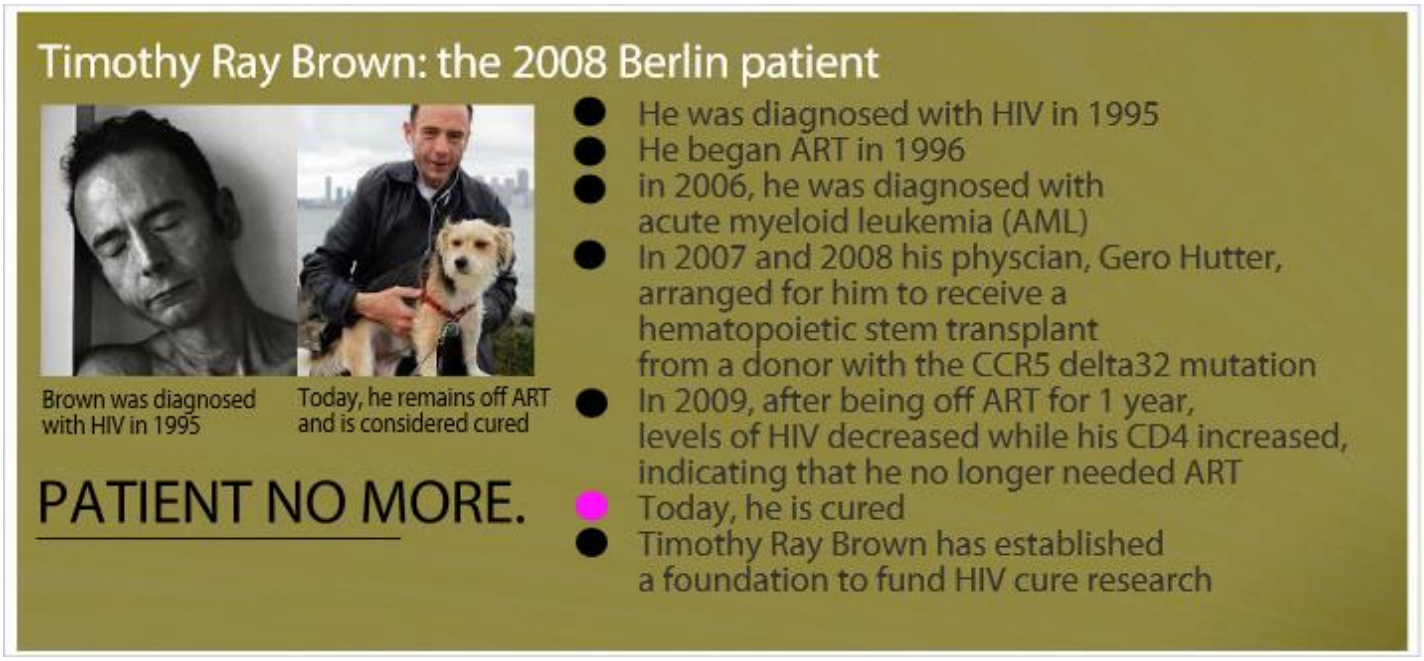
Curing Acquired Immune Deficiency Syndrome (AIDS) is defined as clearing the body of Human Immunodeficiency Virus (HIV), the virus that causes AIDS. The virus replicates by inserting its genetic code into human cells, a type known as CD4 cells. Usually the infected cells produce numerous HIV particles and die soon eventually. Antiretroviral Therapies (ART) reduces the amount of HIV in a patient's body by impeding this replication process. These therapies can reduce a patient's viral load to an undetectable level.

Unfortunately, not all infected cells behave the same way. There are so called "resting" or "hiding" cells which the ART can never remove. Chun et al reports that AIDS virus hides out in significant reservoirs, particularly in the gut lining. Current therapies cannot remove HIV's genetic material from these cells. Even if someone takes antiretroviral drugs for many years they will still have some HIV hiding in various parts of his/her body.

Hoping out loud: HIV cure

A cure for HIV/AIDS must either remove every single infected cell (known as eradication) **or** control HIV effectively by keeping the virus dormant *after* the discontinuation or treatment (known as functional cure). Until now, potential benefits for 'functional cure' gives us a more promising result. There have been sets of HIV cure case: Berlin Patient, Boston Patients, and Mississippi Child.

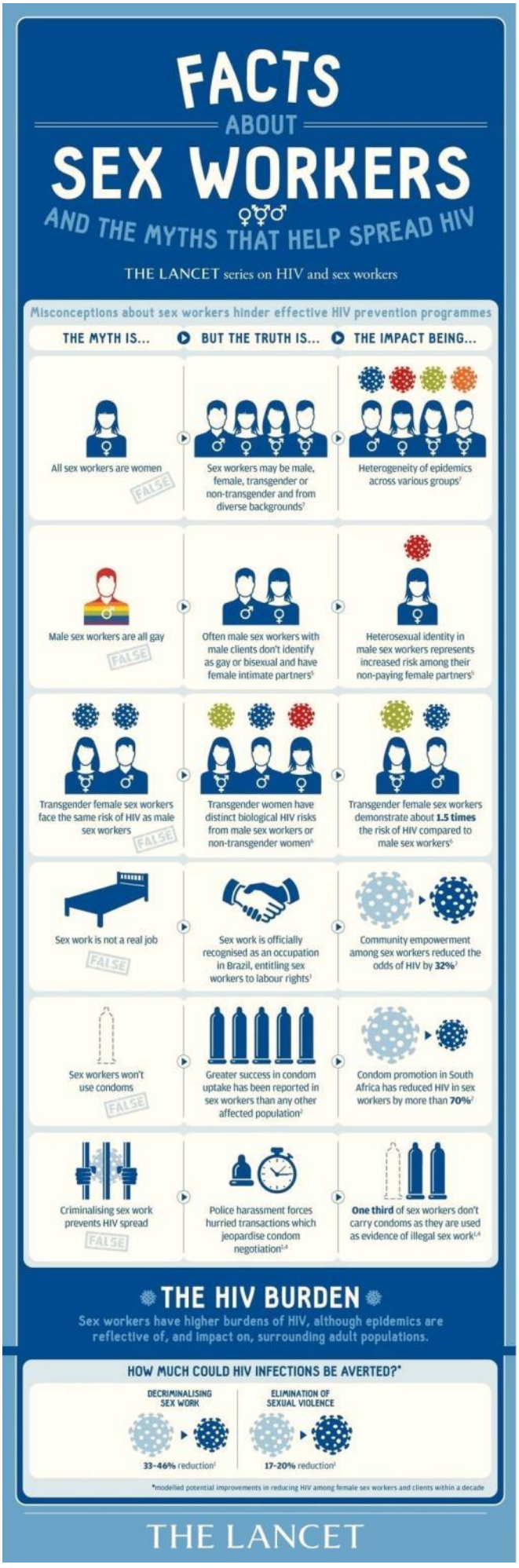
Encouraging story: The man who once had HIV and now does not



CCR5-DELTA 32 MUTATION: A VERY BENEFICIAL FLAW

The doctors and researchers who manage the Berlin patient believe that Cysteine-cysteine chemokine receptor 5 (CCR5) mutations is the answer to HIV curing in this case. Up to 20% of ethic western Europeans carry this mutation, which is rare or absent in other ethnic groups. This mutation can be advantageous to those individuals who carry it. The virus HIV normally enters a cell via its CCR5 receptors, especially in the initial stage of a person becoming infected. But in people with receptors crippled by the *CCR5-delta32* mutation, entry of HIV by this means is blocked, providing immunity to AIDS for homozygous carriers and greatly slowing progress of the disease in heterozygous carriers. *(Source: Hutter G NEJM 2009. Aidsmap, 2012. Kawamura, et al. 2003. Zagury, et al, 1998. Liu et al, 1996)*

–AP–



Discrimination is NOT a Cure

AIDS-related stigma and discrimination refers to prejudice, negative attitudes, abuse and mistreatment directed at people living with HIV and AIDS (*Orang Dengan HIV/AIDS - ODHA*). The consequences of stigma and discrimination are wide-ranging: being despised by family, friends and the wider community, poor treatment in healthcare and education settings, an erosion of rights, psychological damage, and a negative effect on the success of HIV testing and treatment.

Stigma does not only make people living with HIV/AIDS difficult dealing with their condition but also interferes with attempts to fight the HIV and AIDS epidemic as a whole. On a national level, the discrimination restrains government from taking fast, effective action against the epidemic, whilst on a personal level it can make individuals reluctant to access HIV testing, treatment and care.

Sex workers

Decriminalization of sex worker could have the greatest effect on the course of HIV epidemics across all settings studied. Within a criminalized environment, sexual violence is prevalent and has a negative effect on condom use. It forces sex workers to work in unsafe environments that promote high-risk behavior.

Male-to-male sex

Globally, 81 countries criminalize same-sex sexual activities. These countries release an anti-homosexuality law that discriminates this particular group to gain access of health care service. Moreover, these people mostly stay hidden for fear of the discriminating actions towards them and safety of their life.

What is your call to action towards *ODHA*?

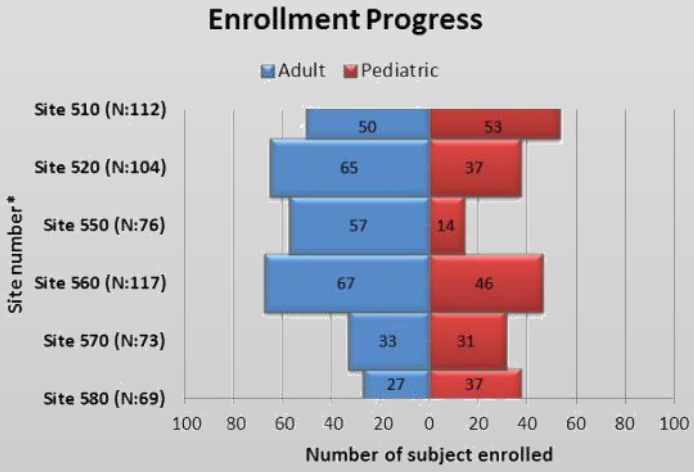
AFIRE STUDY

The Etiology of Acute Febrile Illness Requiring Hospitalization (AFIRE)

For further information on this study please go to:
http://www.ina-respond.net/afire-study/

Up to August 17, 1,747 patients had been screened from 6 active sites and 551 subjects had been enrolled (315 adults and 236 children).

Enrollment progress up to August 17 can be seen in the graphic below:



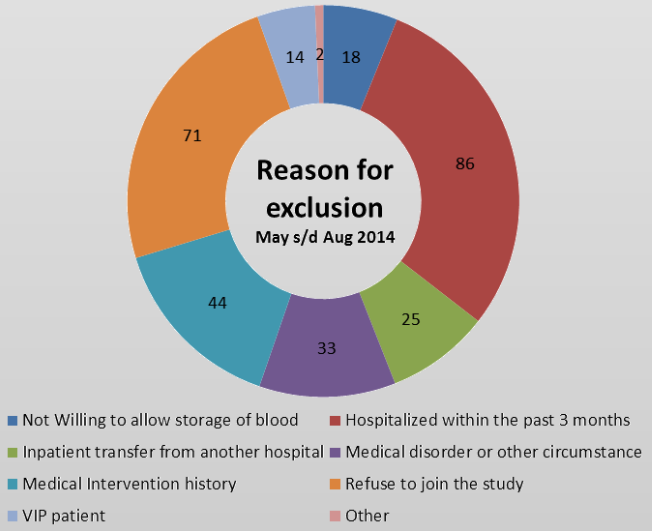
*510 – RSUP dr Hasan Sadikin, Bandung
520 – RSUP Sanglah, Denpasar
550 – RSUP dr Wahidin, Makassar
560 – RSUP dr Kariadi, Semarang
570 – RSUD dr Soetomo, Surabaya
580 – RSUP dr Sardjito, Yogyakarta

Detailed screening and enrollment progress is available in portal folder: Studies\INA101\Screening progress.pdf or go to the following link: https://ina-respond.s-3.com/EdmFile/getfile/797233

Reasons for Exclusion

A total number of 432 patients were screened from May to August 2014. Out of this number, 68% patients could not be enrolled into the study. The 3 most common reasons for this are history of hospitalization in the past 3 months, refusal to give consent, and medical intervention history.

Detailed reason for exclusion can be seen in the chart below:



Document Update!

Final CRF SAE/UP version 3.0 dated 02JUN2014 and SAE/UP Form Completion guideline version 3.0 dated 02JUN2014 are available on Portal at https://ina-respond.s-3.com/edm/index/794898. Please review and take heed of the information in the documents. Do not hesitate to contact Site Support if you have any questions.

-UN-

TRIPOD STUDY

JAKARTA – We are all excited to learn that the TRIPOD protocol has been approved by NIHRD scientific committee, and all necessary documents have also been submitted to NIHRD ethical committee. The INA-RESPOND Secretariat, PI, and Investigator team from NIHRD and NIAID are now focusing their minds on revising the Informed Consent Form (ICF) and Case Report Form (CRF).

With all the ongoing excitement, the Secretariat decides to hold a meeting in September to discuss the Manual of Procedures (MOP) with the study PI, Co-PI, and Laboratory Specialist where not only laboratory-related sections are going to be discussed but also other sections of the MOP such as safety, screening and enrollment as well as data management.

Meanwhile, all INA-RESPOND sites are busy assembling their TRIPOD teams. These teams will attend the Investigator Meeting in early October 2014 and will fully participate from the start of the study in the last week of November 2014.

-NHS-

- Sept 3 – 13 : ICAAC Conference @ Washington, D.C
- Sept 10 – 11 : SEAICRN Executive Committee Face-to-Face Meeting @ Hanoi

SEPSIS STUDY

JAKARTA - It was a pleasure to have dr. Direk, dr. Zen Hafy, and Ms. Emy Takahashi in Indonesia from August 17-22. In a very packed schedule, the guests visited RS Sardjito, Jogjakarta, RS. Wahidin Sudirohusodo, Makassar, and RSCM, Jakarta, and had meetings with INA-RESPOND team to enhance the partnership between SEAICRN and INA-RESPOND especially in the Sepsis Study (SEA050). Data Management issues and Publication policy are the 2 strongest concerns raised by the sites. Concerns were acknowledged, and there were several alternatives proposed by the SEAICRN Director, which will be discussed with the rest of the Executive Committee member. The team also discussed the study protocol and answered outstanding questions from Indonesian team. With things getting clearer and proceeding steadily, Indonesia will submit the protocol to NIHRB IRB this September.

Data Manager from INA-RESPOND and from FHI 360 met for 2 days to discuss about the data management process including how to complete CRF, how to manage data discrepancies, how to enter data to data management software, and how to integrate the database. -SK-

Makassar – Dr. Direk is sharing his opinion to the study members at RS. Dr. Wahidin Sudirohusodo

Sepsis Data Management – From left to right: Drg. Tince, Dr. Delima, Ms. Kanti, Mr. Erik, and Ms. Mila (as study monitor)

Best Wishes for INA101 team members celebrating their birthday in September:

5 Sept – drg Tince (NIHRD)
7 Sept – Ennycke Sary, S.Si (Lab Tech, Site 550)
10 Sept – dr Herman Kosasih (Secretariat)
14 Sept – Ernawati (Lab Tech, Site 510)
17 Sept – dr. Anis Karuniawati, SpMK, PhD (Co-PI, Site 530)
19 Sept – dr. Fatmawaty Ahmad (RA Site 550)
26 Sept – Kanti Laras (Data Manager, Secretariat)
28 Sept – Sri Hariastuti (Lab Tech, Site 570)

JOB OPPORTUNITIES

We are looking for 2 **Research Assistants** for each INA-RESPOND TB Study site. Visit our website for further information. To apply, please email your Resume / CV to Meity Siahaan at MSiahaan@s-3.com. Please write down the position that you'd like to apply in the subject line of your email. Interested candidates should respond immediately. Application closing date: 12 Sept 2014.

INA-RESPOND Newsletter

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