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INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

February 2019

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Better Bones for A Better Life

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Translation Issues

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2019

Clinical Research

Protocol Writing Workshop

February 11-15, 2019

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Clinical Research
Protocol Writing Workshop Agenda

Monday, February 11

08.00 - 17.00
- Welcoming remarks
- Lectures on conceptualizing and defining ideas for a study protocol (e.g. key protocol elements, literature review)
- Lightning presentation of study concepts from participants (only for selected concepts)

Tuesday, February 12

08.00 - 17.00
- Review of day 1 concepts
- Lectures on developing specific sections of your protocol (e.g. overview of study designs, statistical concepts)
- Lectures on other aspects of protocol development (e.g. ethics, data management, funding

Wednesday, February 13

08.00 - 13.00
- Review of day 2 concepts
- Lectures of specific study designs and case studies of effective protocols

13.00 - 17.00
- Group exercise (only for selected concepts)

Thursday, February 14

08.00 - 17.00
- Group exercise

Friday, February 15

08.00 - 17.00
- Group exercise
- Overview of how to secure funding

Guest Faculty

- **Lori E. Dodd, Ph.D.** (National Institute of Allergy and Infectious Diseases Division of Clinical Branch Biostatistics Research Branch)
- **C. Jason liang, Ph.D.** (National Institute of Allergy and Infectious Diseases Division of Clinical Branch Biostatistics Research Branch)
- **Associate Professor Agus Salim** (Department of Mathematics and Statistics, La Trobe University)
- **Aaron Neal, D.Phil** (International Health Scientist at National Institute of Allergy and Infectious Diseases (NIAID))
- **Chuen-Yen, MD, MPH.** (National Institutes of Health | NIH · Division of Clinical Research (DCR))

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THANK YOU

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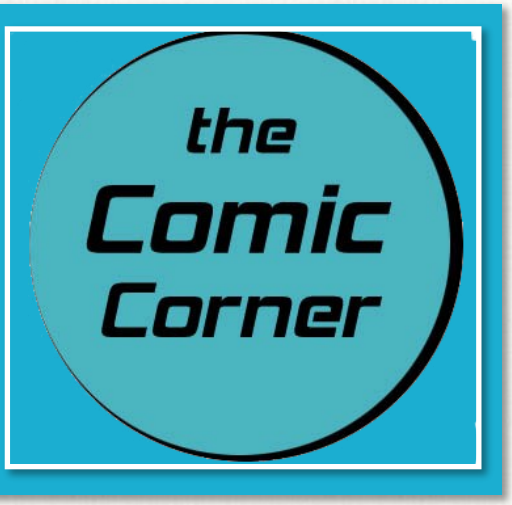

INA-RESPOND Newsletter

TRIPOD & INA-PROACTIVE Study Updates

By: ANANDIKA PAWITRI, EKA WINDARI R., LOIS E. BANG, MARIA INTAN JOSI, M. IKHSAN JUFRI, VENTY MULIANA SARI

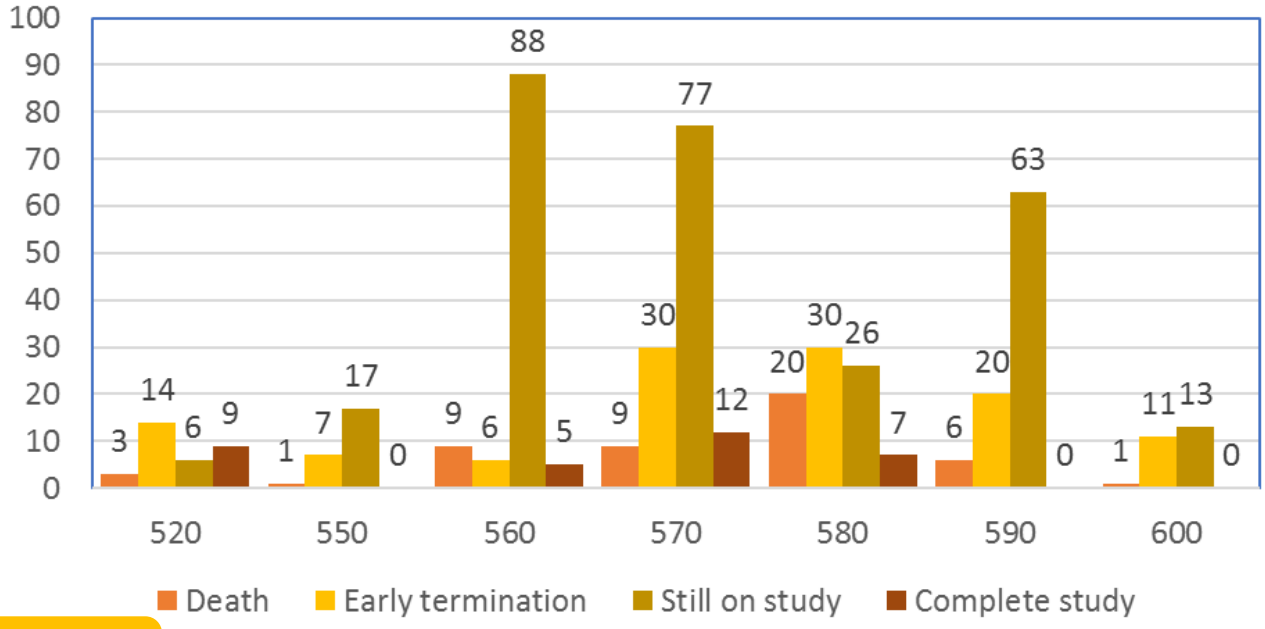

Figure 1. Participants Status Per Site Based On Uploaded CRF per 31 Jan 2019

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PARTICIPANT STATUS

Per 4 February 2019, the total number of ongoing participants in TRIPOD study is 290 (out of 490 enrolled participants.) 33 participants have completed the study while 200 participants were terminated early (including death). Therefore, there are still 59,1 % participants from the total enrolled participants in the follow-up status. From the uploaded CRFs, there are six participants from site 520 (RS Sanglah, Denpasar) who still need to be followed up, 17 participants from site 550 (RSUP dr. Wahidin Sudirohusodo, Makassar), 88 participants from site 560 (RSUP dr. Kariadi, Semarang), 77 participants from site 570 (RSUD dr. Soetomo, Surabaya), 26 participants from site 580 (RSUP dr. Sardjito, Jogjakarta), 63 participants from site 590 (RSUP Persahabatan, Jakarta), and 13 participants from site 600 (RSUP dr. Adam Malik, Medan).

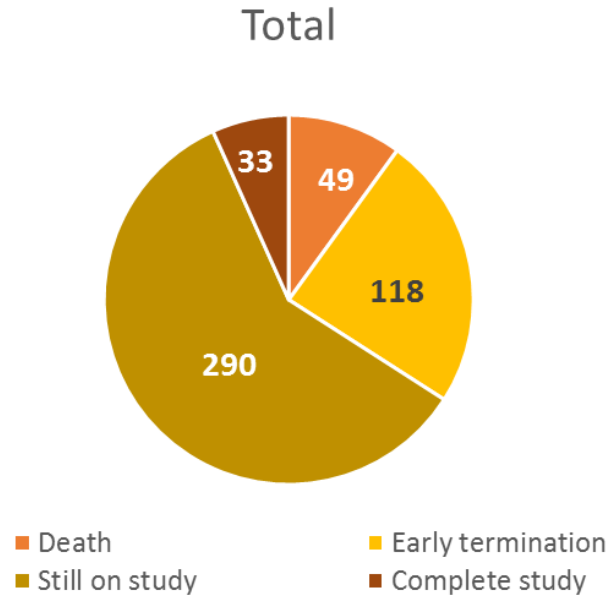

Figure 2. Total Participants Status based on uploaded CRF per 31 Jan 2019

Site	Waiting for Baseline Culture Result	Waiting for Baseline DST Result
520 (n=32)	Complete	Complete
550 (n=25)	Complete	Complete
560 (n=108)	9 (estimation: Feb 2019)	52 (estimation: Feb 2019)
570 (n=128)	11 (estimation: Feb 2019)	34 (estimation: Feb 2019)
580 (n=83)	7 (estimation: Feb 2019)	9 (estimation: Feb 2019)
590 (n=89)	28 (estimation: Feb 2019)	28 (estimation: Feb 2019)
600 (n=25)	6 (estimation: Feb 2019)	6 (estimation: Feb 2019)

Figure 3. Culture and DST result up to 24 January 2019.

AWAITING CULTURE AND DST RESULT

Not all sites have all the baseline culture and drug susceptibility testing (DST) results. As we can see in the table above, only site 520 and site 550 have all the tests results. DST results of the 52 samples from site 560 have not been released; the site's DST is referred to *Universitas Indonesia's* Microbiology laboratory, and site is waiting for the results to be published. DST for site 570 and 580 is referred to BBLK Surabaya. The sites have sent 34 and 9 samples respectively and are waiting for the results to be released. As for site 590 and 600, all culture and DST tests are conducted by the site's own laboratory. Site study team is waiting for them to be released.

TRIPOD MANUSCRIPT

Authors for TRIPOD manuscript have been selected. A meeting with NIH will be performed in the near future to initiate the manuscript writing process. The following are several manuscripts that were planned: a) focus on the baseline findings; b) treatment outcome and the related affected factors; c) related factors of TB and DM co-morbidity.

The authors will be sorted according to the number of enrolled participants. A discussion about TRIPOD manuscript will be set up during the Clinical Research Protocol Writing Workshop.

Site Number	Site Name	Author
520	RS Sanglah Denpasar	dr. I Gede Ketut Sajinadiyasa, Sp.PD
550	RSUP dr. Wahidin Sudirohusodo	Dr. dr. Irawaty Djaharuddin, SpP(K)
560	RSUP dr. Kariadi	dr. Banteng Hanang Wibisono, Sp.PD-KP
570	RSUD dr. Soetomo	dr. Tutik Kusmiati, SpP (K)
580	RSUP dr. Sardjito	dr Bambang Sigit Riyanto, SpPD-KP, FINASIM
590	RSUP Persahabatan	dr. Diah Handayani, SpP
600	RSUP H Adam Malik	Dr. dr. Bintang YM Sinaga, M.Ked(Paru), Sp.P(K)

Table 1. Author List of TRIPOD Manuscript

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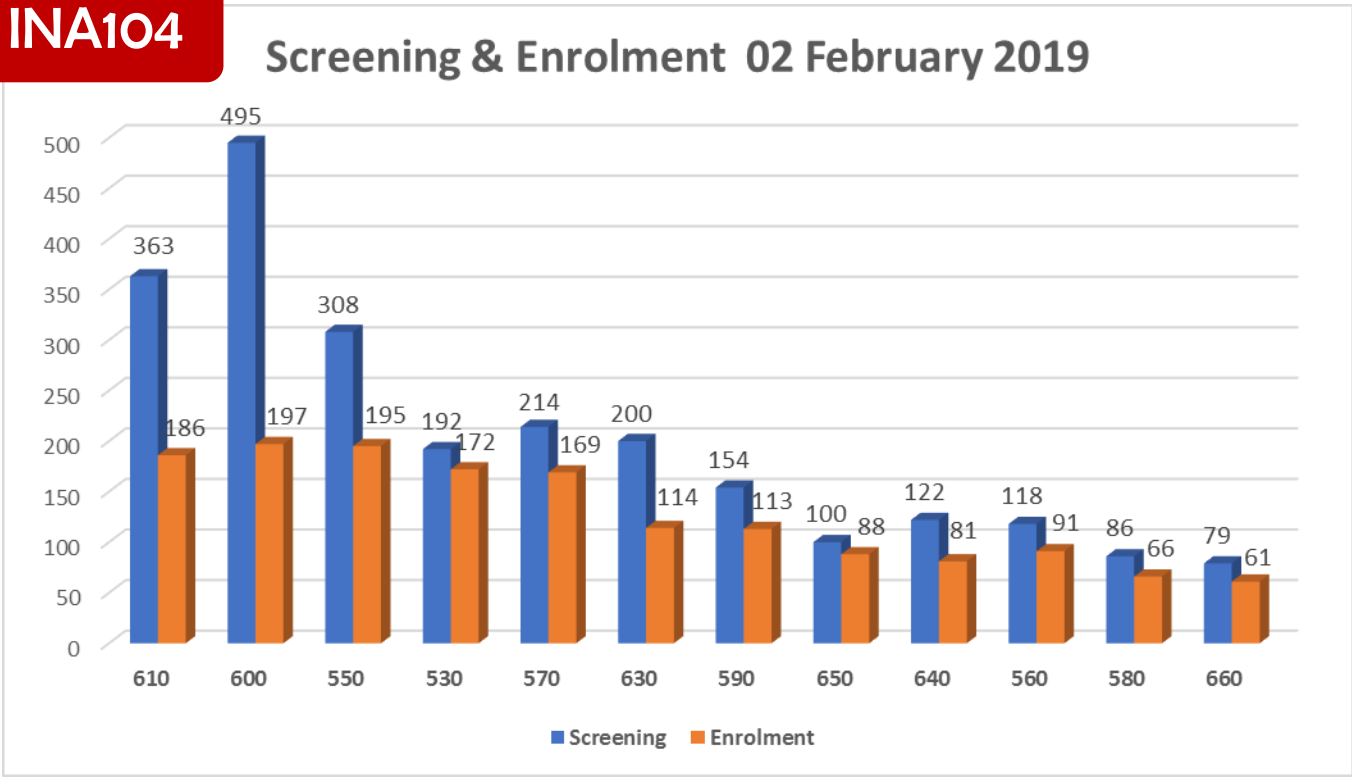


STUDY UPDATES

By 2 February 2019, all 12 sites as shown in the graphic above had enrolled 1,533 subjects consisting of 67 pediatrics and 1,466 adults. Sites enrolled 63,06% of screened patients (2,431 screened patients). Enrollment failure rate is 35,66% from total screening due to the reasons as stated in the table below.

Site 510 (Hasan Sadikin hospital) was activated on 4 February 2019. The total number of activated sites is now 13. The site is planning to start their first screening and enrollment on 7 February 2019. Site 540 (Sulianti Saroso hospital) is in the middle of completing some essential documents after its Site Initiation Visit (SIV). Hopefully, the site could also be activated this month.

Site 680 (Soedarso hospital) made a new progress by having Site Preparation Visit (SPV) on 28-30 January 2019. The site team members are now scheduling its SIV. Meanwhile, site 670 Zainoel Abidin Hospital is preparing for SPV which is scheduled on 19-21 February 2019.

Assessment visits (SAV) are being conducted at hospitals in eastern Indonesia. SAV in Abepura Hospital was conducted on 23 January and will be followed by SAV at TC Hillers Hospital, East Nusa Tenggara on 28 February.

The 2nd Site Monitoring Visit (SMV) was conducted at site 590 (Persahabatan hospital) on 14-16 January 2019.

Reason	610	600	550	570	530	630	590	650	640	560	580	660	Total
1. Suspect HIV	6	-	2	-	-	1	-	-	-	-	-	-	9
2. Refuse to consent	3	-	4	4	3	-	6	1	-	4	-		25
3. Unwilling to comply with the study	2	25	2	3	11	-	-	2	1	13	3	1	63
4. Plans to move away	1	9	5	-	6	2	3	-	5	5	-	3	39
A. No show	99	256	30	4	16	48	14	-	5	2	2	3	479
B. Busy (in a hurry)	19	4	28	4	8	5	5	7	22	2	11	11	126
C. Has been enrolled	34	2	33	5	-	19	11	2	2	1	-		109
D. Participated in other CT											4		4
E. Hospitalized or unwell	-	-	4	-	-	-	-	-	-	-	-		4
F. Others (e.g. no referral letter from other health facility, equipment trouble)	2	-	-	-	1	6	-	-	-	-	-		9
Total	166	296	108	20	45	81	39	12	35	27	20	18	867

INA-RESPOND Newsletter

SITE 650: BUDI KEMULIAAN HOSPITAL, BATAM

By: ANGELINA FEBRINA

From left to right: Mr. Erwinsyah (KASPER HIV Center Staff), Mr. Yollis (KASPER HIV Center Staff), dr. Calvin, dr. Willy, Sp.PK, dr. Danang, Sp.PD, dr. Bratasena, Sp.PD, dr. Francisca, Mrs. Diana, dr. Angelina, and Mrs. Theresia (KASPER HIV Center Staff)

Budi Kemuliaan Hospital is a private hospital located in Batam, Riau Islands. Our hospital was pioneered by Mrs. Sri Soedarsono and was inaugurated on October 8th, 1984. Budi Kemuliaan Hospital has a quite long history of dealing with HIV/AIDS. HIV prevention program was first started in the 1990s until finally VCT Clinic was established ten years later. In 2004, Budi Kemuliaan Hospital was chosen as one of the first 25 referral hospitals for HIV/AIDS patients in Indonesia. With the generous support of some Netherlands Social Organizations, a new building was specifically constructed in 2006 for integrated HIV/AIDS patients services. Since then, this building has been used for HIV counseling and testing center, called "KASPER HIV Center," led by dr. Danang Legowo, Sp.PD, FINASIM; and for in-patient ward services for patients with HIV/AIDS and other infectious diseases.

Budi Kemuliaan Hospital, also known as Site 650, is one of the active sites of INA PROACTIVE Study. The first screening and enrollment at our site started on 2 August 2018. Our site consists of eight team members, and our activities are mainly associated with KASPER HIV Center and Clinical Pathology Laboratory. The following are some brief introduction of our team members:

dr. Bratasena, M.Ked (PD), Sp.PD had working experience as a doctor for International SOS before he finally decided to continue his study. His passion for infectious diseases led him to pursue Internal Medicine as his specialty. He was graduated from The University of Sumatera Utara in 2015, and since then he has been working as an Internist at Budi Kemuliaan Hospital. As a doctor, he sees his life as an opportunity to serve others.

dr. Nisa Trini Asnil, Sp.A is our head of Pediatrics Installation and also a member of KASPER HIV Center who is in charge of the prevention of HIV transmission from mother to child. She is an active person who really cares about children.

dr. Willy A I Wullur, Sp.PK, M.Min serves as the Head of Clinical Pathology Laboratory and is in charge as the vice-chairman of KASPER HIV Center. He has a wife and two daughters who are all doctors. Aside from his job, he enjoys photography and spending time with his family. He believes that life must become a blessing.

dr. Francisca L.Tanzil has the longest working history among us all related to HIV/AIDS. She has worked with Mrs. Sri Soedarsono in HIV/AIDS services since 1997 and for more than 20 years she has become one of our most experienced KASPER HIV Center Counselor Coordinators. She is a great cook and an amazing mother for her four children. During her leisure time, she enjoys fishing and gardening.

dr. Calvin Martin finished his internship at this hospital in February 2018. He has been involved in INA-PROACTIVE study since the site was activated. He has interest towards obstetrics and gynaecology and hopes to be an OB/GYN doctor soon. Besides his busy days working and studying, he likes to watch movies to fill in his leisure time.

dr. Angelina Febrina is our second RA who joined our team in October 2018. She finished her study abroad and finally decided to come back to Indonesia in 2014. INA-PROACTIVE is her first clinical research experience. Traveling over new places, exploring new things, and making new friends are things that please her.

Ms. Diana Sulastri Hutabarat, AMAK is our laboratory technician who started working in Clinical Pathology Laboratory of Budi Kemuliaan Hospital in 2003. She has more than ten years of experience dealing with HIV laboratory examinations. Travelling and sightseeing are the two things that she loves.

Mrs. Friska Sitorus started working as a nurse at Budi Kemuliaan Hospital in 2001, and since 2004 she has overseen all records and reports regarding ARV drugs. She has a beautiful voice, and singing is one of her hobbies. She also enjoys reading in her free time, and for her there is no beauty better than intelligence.

Site team members at Budi Kemuliaan hospital are excited to work with INA-RESPOND network. Let's all do our best!

From top to bottom:
dr. Bratasena, M.Ked (PD), Sp.PD, dr. Nisa Trini Asnil, Sp.A, dr. Francisca L.Tanzil, and Mrs. Friska Sitorus

INA-RESPOND Newsletter

HEPATITIS

By: DEWI LOKIDA

Hepatitis is inflammation of the liver which can heal by itself or can develop into fibrosis (scar tissue), cirrhosis, or liver cancer. The most common cause of hepatitis is hepatitis virus, and other reasons are toxic substances (e.g., alcohol, certain drugs) or autoimmune diseases.

The hepatitis virus consists of hepatitis A, B, C, D, and E. The hepatitis B and C viruses are major health challenges, affecting 325 million people worldwide. These viruses are the causes of liver cancer with 1.34 million mortality every year. Hepatitis B and C are chronic infectious diseases that may not show any symptoms for an extended period, sometimes years or decades. At least 60% of liver cancer cases are due to late testing and treatment of viral hepatitis B and C infections. The low test-and-treatment coverage is the most significant gap, and it is the focus of WHO to achieve global hepatitis elimination by 2030.

TRANSMISSION

Hepatitis B and C viruses are transmitted through blood. The transfer often occurs at a young age through needles or medical actions. The prevalence of hepatitis B virus is the highest in sub-Saharan Africa and East Asia, and around 5-10% of the adult population is chronically infected. In areas with a high prevalence of cases, the primary mode of transmission is from mother to child. Immunization is the most effective strategy for the prevention of hepatitis B virus infection. Hepatitis C is found throughout the world with the most affected areas are Central and Asia, East Asia, North Africa, and West Africa. Most infections are caused by needle injections and other unsafe medical procedures. Strategies for preventing hepatitis B and C virus infections should include guaranteed safe blood products, safe injection practices, reduced adverse effects on injection drug users, and the promotion of safe sex.

Hepatitis D is transmitted through contact with infected blood and only occurs in people who have previously been infected with the hepatitis B virus. Therefore, it can be prevented through hepatitis B vaccination and similar prevention efforts.

Hepatitis A and E viruses are transmitted through infected food and water and can cause outbreaks in communities where safe water are not available and poor sanitation. Hepatitis viral infections A and E do not cause chronic infection and do not require special treatment. Prevention of hepatitis A and E infections is through proper sanitation, food safety, and vaccination.

Dewi Lokida
Kepala SMF Patologi Klinik RSU Kabupaten Tangerang
Kepala Laboratorium INA-RESPOND

SYMPTOMS

1. Acute hepatitis

Symptoms caused by all hepatitis viruses in the acute phase are generally alike, starting from influenza-like symptoms, abdominal pain to the emergence of severe symptoms from mild jaundice to fulminant hepatitis.

a. Prodromal phase

The symptoms are usually anorexia, nausea, vomiting, mild fever, malaise, myalgia, headache, and mild pain on the right side of the abdomen. This period lasts 3-7 days but may continue for three weeks. In children, patients can feel severe headaches.

b. Icteric phase

The icteric phase usually occurs after the prodromal phase. In this phase, the color of the urine becomes darker while the color

of the feces becomes brighter, and jaundice/icterus appears throughout the body. Body temperature returns to normal, appetite improves, abdominal pain goes, but sometimes pruritus appears. In some patients, the prodromal phase can end without an icteric phase.

c. Convalescence phase (healing phase)

This phase occurs after the icteric phase, and most patients heal by themselves. In children the healing period is faster, the color of the stool returns to normal, appetite is normal, pruritus decreases. After jaundice disappears, malaise can last for several days. Clinical and biochemistries level are back to normal six months after the onset of disease in hepatitis A, Hepatitis B (95%) and hepatitis C (15-20%)

2. Chronic hepatitis

The symptoms of chronic viral hepatitis infection are generally unclear and cannot be distinguished between chronic hepatitis caused by hepatitis B, C, and D viruses. Clinical symptoms may include malaise, decreased stamina, abdominal pain, decreased appetite, nausea, muscle pain, and joint pain. Many hepatitis patients do not experience any symptoms until hepatic cirrhosis occurs and are accidentally identified through a blood check or medical check-up. Jaundice rarely occurs in chronic hepatitis except when a liver failure occurs.

LABORATORY EXAMINATION

1. Hepatitis A virus (HAV)

In day-to-day clinical practice, the diagnosis of hepatitis A virus infection is done by serological examination of specific Anti-HAV IgM antibodies. That can be detected in serum during acute illness. a. It can last 3-6 months after infection.

In some cases, infection can recur in a few weeks or months, because of repeated HAV excretion. Anti-HAV IgG will appear gradually and persist in the serum and provide protection against the possibility of reinfection.

2. Hepatitis B virus (HBV)

Acute hepatitis B infection lasts six months after exposure to this virus, and it can become chronic if the virus persists for more than six months. HBV can be detected in the blood or other body fluids. Serological examination for HBV is carried out based on pair detection of antigens and antibodies namely Surface Ag (HBsAg) and its antibodies (Anti HBs), and HBe antigen and AntiHBe. For HBc, we only do the anti-HBc as HB core Ag (HBcAg) does not circulate in serum. PCR can be performed to detect HBV-DNA.

a. HBsAg

HBsAg is a product produced by the hepatitis B virus S (surface) gene which circulates with high concentrations in the serum (up to 1,013 particles/mL). HBsAg in serum can be detected 1-10 weeks after infection and 2-8 weeks before the onset of clinical symptoms. HBsAg is the first serological marker to be examined for the diagnosis of hepatitis B virus infection. HBsAg can disappear as the healing process or can persist causing chronic infection. Positive HBsAg results indicates that the patient can transmit the virus to other people.

b. Anti HBs

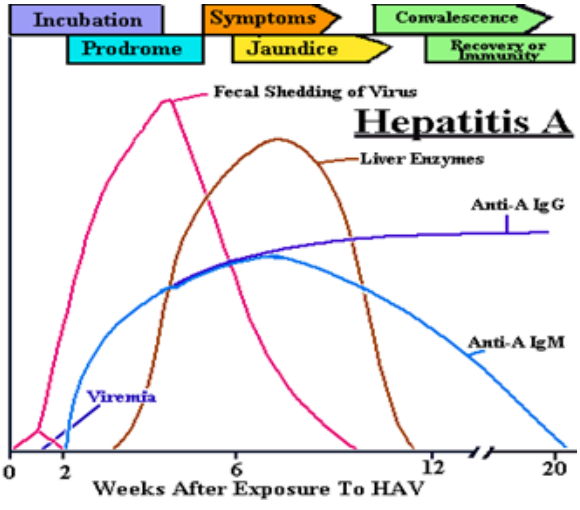
During the healing process, HBsAg becomes undetectable while anti-HBs begins to appear. HBsAb is a neutralizing antibody associated with long-term immunity. Anti HBs can also appear as a response to hepatitis B vaccination. The Anti HBs concentration of at least 10mIU may protect against infection.

c. HBcAg and anti-HBc

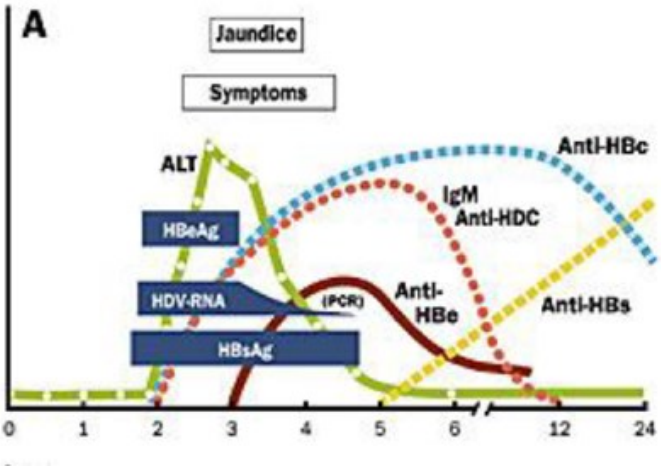
Hepatitis B core Ag is a viral nucleocapsid component that does not circulate in the serum, so it cannot be detected by serology. During acute infection, anti-HBc IgM appears immediately after HBsAg and can last for six months. Anti-HBc IgG will gradually increase to replace anti-HBc IgM. Anti HBc examination is an alternative examination to determine immunity to the hepatitis B virus and help determine the need for vaccination.

d. HBeAg

Hepatitis E Ag is a product of the nucleocapsid gene which is secreted to the serum, a marker of viral replication activity related to liver effectiveness and damage. HBeAg can be detected early in the infection, together or immediately after the appearance of HBsAg, and it usually disappears within a few weeks in acute infection. Detection of HBeAg in serum over 3-4 months indicates chronic hepatitis B infection.



Hepatitis A



Hepatitis B

e. Anti HBe.

Anti HBe produced by the immune system can be transient during acute infection or persist permanently after substantial viral replication. The presence of Anti HBe seroconversion is a predictor of hepatitis B clearance in patients receiving antiviral therapy and shows low levels of hepatitis B virus. Its appearance indicates good prognosis.

f. HBV DNA

HBV DNA examination is performed on serum specimens using the real-time PCR to determine replicative or non-replicative chronic HBV infection using 105copy/mL cut off and to monitor the response to antiviral therapy.

3. Hepatitis C Virus

Diagnostic tests for HCV infection include serological examinations based on antibody responses and detection of viral genomes in the blood.

a. Anti HCV

Anti HCV tests can be used as screening or diagnosis. Anti HCV can be detected in 60% of acute phase patients, and in 35% of patients, within a few weeks or several months after the onset of infection.

b. HCV RNA

HCV-RNA examination using real-time PCR can be used for the diagnosis of acute hepatitis C, confirmation of chronic hepatitis C, showing the presence or absence of perinatal transmission, exposure detection and monitoring of anti-viral responses.

4. Hepatitis D Virus

Hepatitis D virus infection (HBD) occurs only at the time of hepatitis B virus infection. Unlike HBV, HDV only infects hepatocytes and only replicates in the liver (intrahepatic). Confirmation of hepatitis D infection is done by examining HDV Ag or HDV-RNA in serum or liver tissue, but examination to date is limited to research only.

5. Hepatitis E Virus

Hepatitis E infection in the initial phase is diagnosed by the detection of IgM anti-Hepatitis E, that can last up to 6 weeks after peak symptoms while IgG anti-HVE can remain detected for up to 20 months. However, no FDA-approved commercial serological examination is yet available. Identification of viruses, viral antigens or viral nucleic acids in feces can be done but rarely used for diagnosis.

PREVENTION

In addition to lifestyle and maintaining cleanliness and hygiene, vaccination is the best way to avoid hepatitis, in this case, hepatitis A and B. Hepatitis A vaccine is given two doses on children at least 12 months of age, and the second dose is given at intervals of 6-18 months. Hepatitis B vaccine is given three times in a row with a certain period. Newborns whose mothers are infected with hepatitis B must be vaccinated three times immediately; 24 hours – seven days after birth for the first vaccination. This dose shows the effectiveness of 89-98%.

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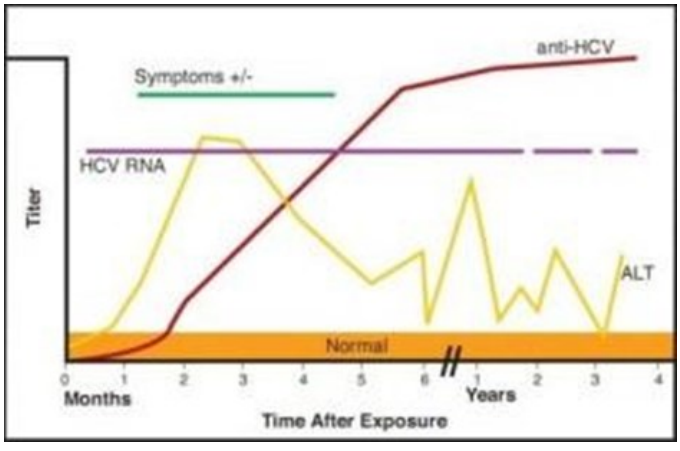
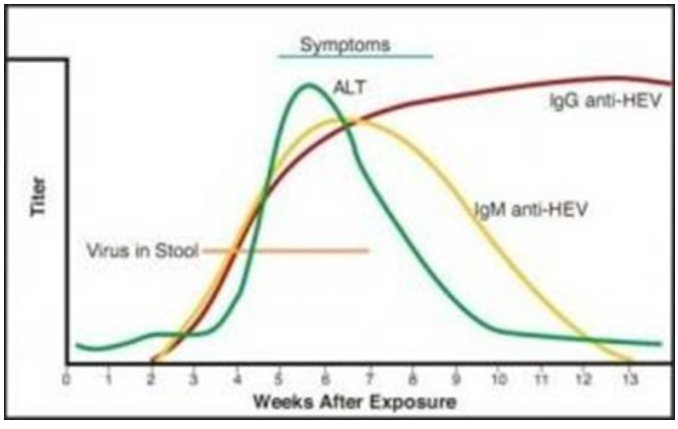
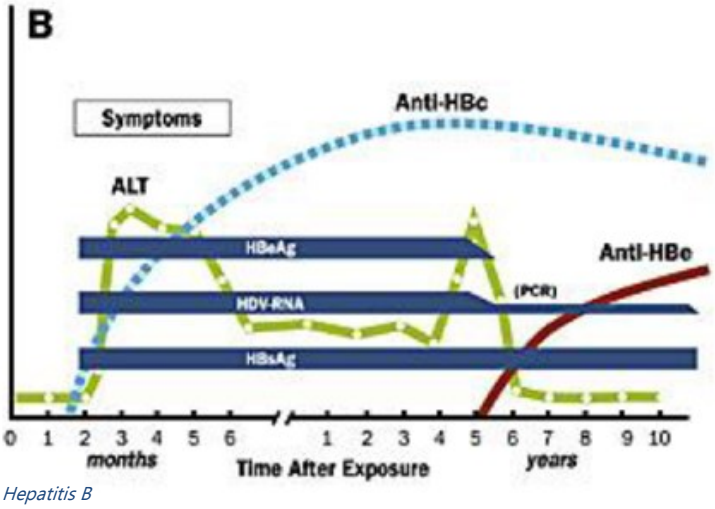




Hepatitis C (above) and Hepatitis E (below)



Hepatitis B

INA-RESPOND Newsletter

Ending HIV in Indonesia: Test and Treat

By: RUDI WISAKSANA

SCIENCE & HEALTH

The term Test and Treat for HIV infection, often called TnT, has been gaining more popularity lately. It is often claimed to be able to end the spread of HIV in the world, including in Indonesia. Is this claim accurate? For more details, continue reading the article below.

What is Test and Treat?

HIV Test and Treat, a.k.a. Universal Test and Treat, is a strategy that allows someone with HIV (often called ODHA: *Orang Dengan HIV AIDS* or PLHIV: People Living with HIV AIDS) to get antiretroviral treatment (ARV) as soon as they are diagnosed. We know that currently available antiretroviral treatment cannot eliminate the virus completely from the body, so PLHIV must take the drug as long as they live. This is one of the reasons why previous HIV treatment guidelines only regulated the administration of ARVs for PLHIV who had had the infection for a long time, characterized by CD4 cell counts of less than 200 or 350 cells/ml or advanced clinical symptoms known as Acquired Immunodeficiency Syndrome (AIDS). Delays in the administration of ARVs in the previous guidelines were also based on the fact that ARV drugs were very complex. The medicines were not in fixed-dose combination, so patients had to consume a large number of pills every day. In addition, they possessed many side effects. Treatment access was still limited/not available in all health facilities, and the drugs' prices were high. All of the above reasons made health workers to be very careful (and may even be too careful) when starting an ARV treatment. Considering the benefits and the risks of the treatment, the previous guidelines required health workers to wait for patients to enter the advanced immunodeficiency period before starting the treatment.

This guidelines are no longer in accordance with the recent scientific development. ARV treatment has become affordable, covering the primary health care level. The medicine is more simple now. Fixed-dose combination drugs that can be taken once a day for adults are now available. The side effects are also less severe and less common. The evolution

of the treatment guidelines also allows the medicines to be given without the need for complex laboratory preconditions examinations, which allow PLHIV to start ARVs early without waiting for the disease to develop further.

Another benefit of early ARV treatment is reducing HIV transmission in the community. We know that there is a long period from a person is infected with HIV until the clinical symptoms appear, which in many cases is the reason why they come to health facilities to get a diagnosis and ARV treatment. This asymptomatic period can last from seven to ten years. Although this asymptomatic period is not dangerous for the infected person, the chance of an infected person to transmit HIV to others through his/her risky behavior is high. An HIV+ drug user who shares unsterile needles with his friends may not be aware that he has been spreading the virus until the HIV clinical symptoms appear. Depending on how often and how long he is on drugs, a lot of people may have been infected. Let's see another example of an infected female sex worker who, because of the pressure of her customers, is forced not to use condoms while she is working. Imagine how many people can get infected in this period that lasts up to ten years. So, it is clear that there is actually a lost opportunity to prevent HIV transmission if we only treat PLHIV who have had symptoms of HIV or have entered the AIDS stage. If we can provide treatment for PLHIV who have just been infected or have not shown any clinical symptoms, in addition to preventing PLHIV from entering the stage of AIDS or death, we can prevent them from transmitting HIV to the people around them including close relatives such as partners (husbands or wives) and babies.

HPTN 052, a large study conducted in 2011 in nine countries around the world including one in Thailand, published very promising results from this Test and Treat strategy. The study that prospectively followed 1,764 serodiscordant couples, where one partner is infected by HIV and the other is not, found that early ARV administration clearly reduced mortality from HIV and AIDS. Immediate ARV administration regardless of CD4 value in the HIV+ partner also benefits to reduce the risk of transmission to his/her sexual partner by 96% when compared to couples who only start ARVs after the CD4 count drops between 200-250 cells/ml. This was also confirmed by other major studies such as START and Temprano. The Temprano study, which divided PLHIV into two groups, the group receiving ARV regardless of their immunodeficiency status and the group given ARV after the CD4 dropped to below 500 cells/ml, found that there was a decrease in mortality or AIDS incidence by half in the group given antiretrovirals immediately. In addition, the study also found that there were no differences in the incidence of side effects in either group. The benefits of Test and Treat in preventing HIV transmission cause this strategy to sometimes be referred to as Treatment as Prevention (TasP). Their activities are basically the same; they just have different points of view and goals.

Seeing the results above, the World Health Organization (WHO) recommends all countries including Indonesia to implement this HIV test and treat strategy to reduce the incidence of HIV. WHO estimates that with this strategy, every country will be able to end HIV epidemiology in approximately 20 years.

So, that is a little information about HIV Test and Treat or Treatment as Prevention. Hopefully, this article can provide motivation so that we all strive to immediately provide ARV treatment for PLHIV who have been diagnosed. Doing Test and Treat in our country may pose some challenges because, in addition to resource problems, HIV is closely related to social issues and stigma. Next time we will look into the efforts Indonesia has made in the implementation of this HIV Test and Treat.

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INA-RESPOND Newsletter

Better Bones For A Better Life

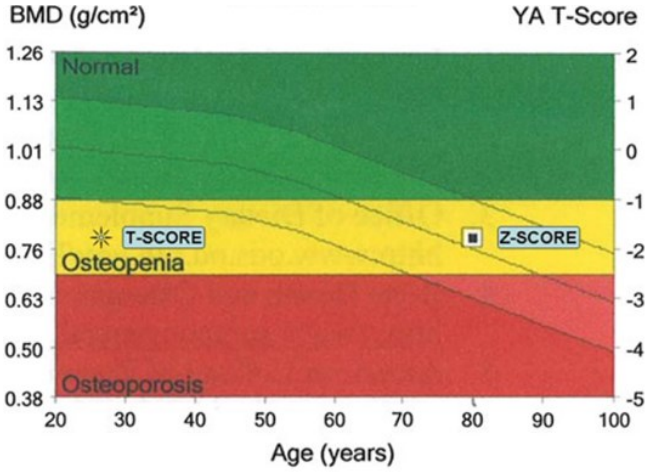
By: CALEB LEONARDO HALIM

A healthy bone system is one of the factors that affect our overall quality of life. Bone development begins when we are in the womb of our mother, reaches its peak at early adulthood or the end of our puberty age, and declines at menopause age in women. Bone development is affected by many factors such as genetics, nutritional intake, medicine, diseases, and exercise. Because puberty is the peak time for our body to increase bone density, this period is crucial to having healthy bones later in life. During this time, if a person is suffering from malnutrition, gets some diseases, or does not have enough exercise, bone density structure will be compromised.

All of these may increase the occurrence of bone loss or osteoporosis. Osteoporosis has caused more than two million cases of fracture each year in the US, and it was estimated that over 10 million people in the US suffered from this disease with another 34 million suffered from low Bone Mineral Density or osteopenia which increases the likelihood of osteoporosis.[1,2] Osteoporosis is a risk factor for fracture just as hypertension is for stroke, and it affects a large number of populations in the world for all genders and races. People who are living in a subtropical country and have dark skin have a higher risk due to the lack of UVB (Ultraviolet B). Fifty percent of women and 25% of men over age 50 will suffer a fracture related osteoporosis during their lifetime.2 Osteoporosis is a silent disease which we are rarely aware of until fracture occurs and causes a major secondary health problem or even death.[3]

Fifty percent of women and 25% of men over age 50 will suffer a fracture related to osteoporosis during their lifetime.[2] The most prevalence sites of fracture are hips, spine, and forearms.[3] Bone tissue will continuously be lost by resorption and rebuilt by formation. Unfortunately, those who have passed their peak period no longer can build a denser bone. The only thing we can do is to reduce the rate of bone resorption, and this is where nutrition and exercise play an important part.

Bone strength can be measured with a DXA (Dual-energy X-ray Absorptiometry) device. The result of this measurement is in the form of Bone Mineral Density (BMD). This device



DXA printout showing BMD value for an 80-year-old white female, and her T -score and Z-score values calculated from the reference population curves[4]

will calculate the T-score or Z-score. According to the National Osteoporosis Foundation (NOF), if you have a T-score >-1, you have an average bone density (the higher, the better).[5] A T-score between -1 and -2.5 shows you have osteopenia/ a weaker bone than ordinary people, so you have a higher chance to get a fracture related to bone weakness.[5] A T-score below -2.5 shows that you have osteoporosis.[5] Based on NOF's recommendations, you should take a bone density test if:

* You are a woman aged ≥65
* You are a man aged ≥70
* You break a bone after age 50
* You are a woman of menopausal age with risk factors
* You are a postmenopausal woman aged <65 with risk factors
* You are a man aged 50-69 with risk factors

How do we fight this silent debilitating disease? The answer to that is by having the right amount of healthy nutrition and exercises. However, if you happen to have a T-score of less then -2.5, diet and exercise alone may not be enough. You need to seek your doctor immediately for medical assistance and you need to take some medicine.

The nutrition we are referring to in this case is calcium. We often do not have enough of this mineral in our diet. We do not drink or consume dairy products as regularly as when we were a kid. I know some of us still do, but many don't.[6] Calcium in our body helps to reduce the rate of bone loss/ resorption as we are getting older. Calcium will not help our bone to become denser like before, but it will certainly help maintain the condition of our bone. However, calcium does not work alone. It needs vitamin D. Guess what? We also lack this vitamin! Dietary source of this vitamin comes from fish, eggs, and dairy. Nevertheless, these sources only provide a small amount of vitamin D much needed for our body.[6] The largest source of vitamin D is from the sun (UVB), from 11 am to 1 pm. Unfortunately, many of us do not go outdoors during these hours because of the heat. A study in cities in southeast Asia recommends exposing our face and both arms at around 9 o'clock for 25 minutes (three times a week) to obtain adequate vitamin D for our body.[7]

A sedentary lifestyle is a risk factor for osteoporosis, among other diseases. To have healthy bones, we also need to do some exercise or at least physical activities to keep our lives "active." Weight-bearing activities significantly contribute to maintaining healthy bone. They increase bone mass as well as strength and reduce the risk of falling.[6] In early childhood to adult, the goal of our physical activities should be to improve and maintain our bone density, and in older adults, the goal should be fall prevention and ensuring safe exercise.[6] For us to get the most of our training, the exercise we do should be dynamic, not static; achieve adequate strain intensity; consist of discrete, intermittent bouts; and include variable loading patterns.

Many studies shown weight-bearing exercise such as running and weightlifting is superior to non-weight-bearing activities such as swimming; and high impact exercise such as jumping and basketball is superior to low impact exercise such as badminton or yoga to stimulate bone formation in the body.[2,8] One report from Sweden found that athletes had higher bone density compared to non-athletes, and non -athletes who exercise had a higher bone density compared to a non-exercising group. Another exciting finding is that among all athletes tested; weightlifter had the highest bone density followed by runners, soccer players, and swimmers. We can see that the higher the impact done to the body, the denser the bone will become. Interestingly, a little gain to bone density will benefit a lot to our strength. A 5.4% increase in BMD is equal to 64% increase in ultimate force and a 94% increase in energy before we become fatigued.[6] This information should give us a better understanding of choosing the proper exercise to do.

Conclusion

Bone certainly has a significant role in keeping one's quality of life high. Bone loss/osteoporosis increases the risk of fracture which lowers our quality of life or even worse, causes death. Please take this note to home as you continue to live your daily lives:

If you belong in one of the six categories from NOF to do a bone density test, do not wait any longer to come and make an appointment with your doctor to run the test.

Nutrition and exercise play a vital role in making and keeping our bone healthy. Keep your calcium intake checked by consuming enough dairy products or other food containing high calcium. For vitamin D, it seems that it is not enough to rely solely on our food, we have to expose ourselves to the sunlight, ideally from 11 am to 1 pm. However, for convenience purpose and for the sake of not catching skin cancer, we can expose ourselves at around 9 am for 25 minutes, three times a week.

Lastly, exercise more regularly! Exercise gives benefit not only for your bones but also your muscles, heart, and overall mood. Each person needs to adjust and select their exercise based on their health profile, preference, and the availability of the exercise. Do this three to five times a week for weight -bearing cardio training and two to three times a week for high impact resistance/strength training. Weight-bearing and high impact exercise are superior to maintaining bone density but keep in mind to start slow and make steady progress, always remember to prioritize safety.

Let us build a healthy bone for a better life.

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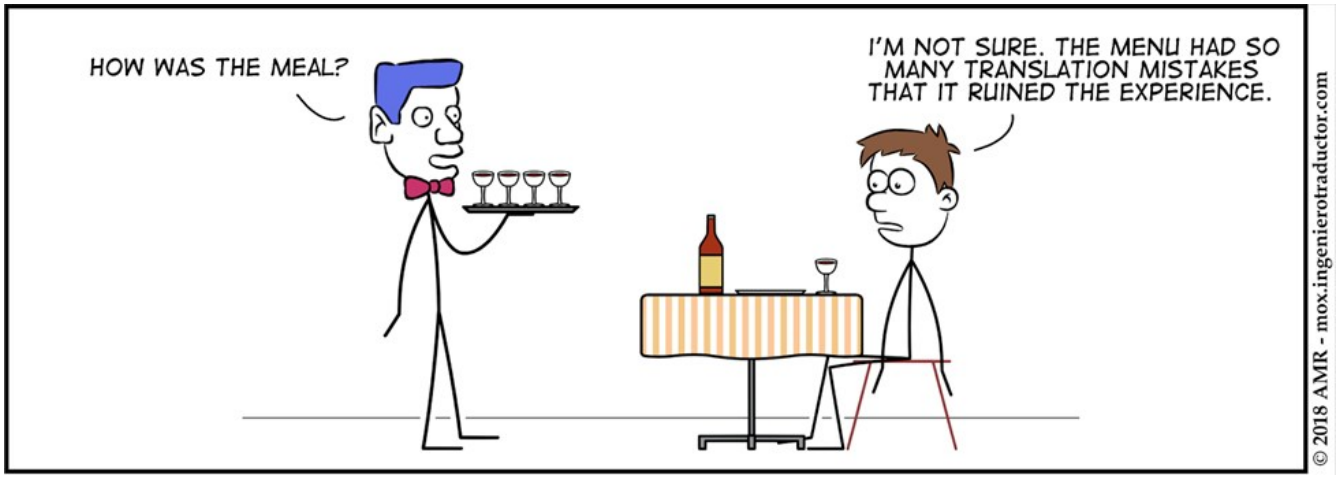
INA-RESPOND Newsletter

Ideas to Sentences; Source Language to Targeted Language: Translation Issues

By: AMELIA GHANI



WRITING CORNER

As a researcher, we often have to write about a topic to be published in an international journal. Almost all recognized international journals require writers to submit their paper/manuscript in English. Researchers who do not use English as their first language will most likely write their paper/manuscript in their native language and then translate it into English. Some journals that are written in English but not published in English-speaking countries require the paper/manuscript to be written in both English and the native language of the country. The translation results from the source language to targeted language (English) often have mistakes and errors (spelling, punctuation, grammar, or usage), either minor or major, which can affect the meaning of sentences or paragraphs, thus changing the message you want to convey.

In general, mistakes and errors in translation can be categorized into totally wrong translations, slightly-off translations, wrongly-approached translations, strange-sounding/awkward translations. There are several main factors that cause translation to be wrong, among others, is the limited knowledge and ability of a person in language (either Indonesian or English), cultural differences, and the inappropriate selection of the target language. Most major errors are fatal and will directly affect the process of transferring information. On the other hand, small/simple errors in large numbers, although not fatal, will affect a person's overall reading experience.

Some Examples of Translation Mistakes and Errors in Manuscript

Source language: Indonesian. Targeted language: English

S: "*Serum retinol dan hemoglobin diukur pada awal sebelum fortifikasi minyak goreng dan 12 bulan setelah intervensi.*"

T: "**Serum retinol** and hemoglobin were measured **by HPLC and hemocue respectively at baseline** before the fortification of cooking oil and 12 months after **at endline.**"

C: Retinol serum and hemoglobin were measured at baseline, before the fortification of cooking oil, and 12 months after the intervention.

The English form of the phrase "serum retinol" is "retinol serum", This kind of mistake happens a lot because in the Indonesian language the noun modifier comes after the modified noun (*diterangkan-menerangkan*) whereas in English, the noun modifier comes before the modified

noun (*menerangkan-diterangkan*). In this case, the source language's culture influences the result of the translation.

The phrase "by HPLC and hemocue respectively at baseline" is not mentioned in the source sentence. When translating a sentence, avoid adding words/phrases that are not included in the source sentence as they may change the meaning of the sentence.

The phrase "at endline" is not the English for "intervensi". However, the phrase "at endline" might refer to the same thing as "12 months after the invention".

S: "*Enzim metabolik yang sering berperan dalam kejadian resistensi insektisida antara lain adalah esterase dan monooksigenase*".

T: "Metabolic **enzyme** which **often involved** in insecticide resistance are esterase and monooxygenase".

C: "Metabolic enzymes which are often involved in insecticide resistance are esterase and monooxygenase".

The word "enzyme" must be in plural form because there are two kinds of metabolic enzyme. In addition, the verb for the subject (enzymes) is already written in plural form. This mistake is caused because the Indonesian language does not have 'subject-verb agreement' rule.

The phrase "often involved" is written in active voice. The predicate should be written in passive voice (to be + past participle). Many Indonesians often make this kind of mistake especially when the past form (V2) of the verb is the same as the past participle form (V3). Also, we often think that V3 is passive.

Example of active and passive sentences:

Jack will eat the sandwich later. (Active)
The sandwich will be eaten later by Jack. (Passive)

S: "*EWARS diterima dengan baik di Lampung, Bali, dan Kalimantan Selatan, dan memberi manfaat untuk meningkatkan kinerja pada fungsi peringatan dini*".

T: "EWARS was well accepted in Lampung, Bali, and South Kalimantan, and **gave beneficial** to increase performance on early warning function".

C: "EWARS was well accepted in Lampung, Bali, and South Kalimantan, and was beneficial to increase performance on early warning function".

The focuses of the problem are inappropriate word choice and word form, and also the translator's tendency to translate word per word resulting in unusual or strange translation. In this case, the translator used the phrase "gave beneficial" instead of "was beneficial".

What Can We Do To Reduce Translation Mistakes and Errors?

Check the source language. Make sure the sentence in the source language is written in a good/formal structure, and all words are spelled correctly. Also, use punctuations accurately to prevent translation mistakes and errors, which may affect the meaning of the sentence.

When translating, the information conveyed should not change from the source. However, this does not mean we have to translate word per word. If we do not know the translation of a word, we can use other ways to convey the information as long as the meaning remains the same. This should be taken into account especially when we are using jargons or proverbs. For example, "Bagai pinang dibelah dua" is translated word per word to "like a nut cut in half." However, it should be translated to "like peas (two peas) in a pod."

Find out how a word is usually used. Every language has words that have similar meanings. Find out the use of these words to determine which words are most appropriate to describe the actual situation/condition. Using a collocation dictionary may further help you to avoid mistakes and errors

Ask someone (an editor or a proofreader) with excellent English skills to review your translation. Communicate well with the person who is helping you so that he understands well what you want to convey. Also, inform him who your target reader is.

To sum up, mistakes and errors in the translation process are common and most likely cannot be avoided. However, with a lot of practice and attention to details, we can minimize them to a state where the results of our translation are acceptable and accurate. Use all available resources (human or non-human) to help you get the best results. Good luck!

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INA-RESPOND Newsletter

Our Clinical Trial Guardian – the Data Safety and Monitoring Board

By: ALY DIANA

A clinical trial is a demanding and ambitious trial, and it can be dangerous for the participants. That's why we need our guardian, the Data and Safety Monitoring Board (DSMB). Many things can go wrong during a clinical trial, for example, no effect at all, high risk/severe side effects, clear benefits on trial group (which means we need to give the same treatment to placebo group as soon as possible). Therefore, to make sure that the respondents/ patients are protected from any harm, the DSMB is needed.

The sponsor or the Trial Steering Committee generally appoint members of a DSMB. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations, and should reflect the disciplines and medical specialties necessary to interpret the data and to fully evaluate the patient safety. The number of DSMB members depends on the phase of the trial, the range of medical issues, complexity in design and analysis, and the potential level of risk. However, it generally consists of three to seven members including, at a minimum: experts in the clinical aspects of the disease/patient population being studied, one or more biostatisticians, and investigators with expertise in current clinical trials conduct and methodology.

The primary responsibilities of the DSMB are to 1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and 2) make recommendations to the research team concerning the continuation, modification, or termination of the trial. The important thing, before initiating any data review, the DSMB is responsible for defining its deliberative processes, including event triggers that would call for an unscheduled review, stopping procedures that are consistent with the protocol, unmasking (unblinding), and voting procedures. Pre-established statistical guidelines should be followed. The DSMB is also responsible for maintaining the confidentiality of its internal discussions and activities as well as the contents of reports provided to it.

The DSMB should review each protocol for any major concern prior to implementation. During the trial, the DSMB should review cumulative study data to evaluate the safety, study conduct, and scientific validity and integrity of the trial. As part of this responsibility, DSMB members must be satisfied that the timeliness, completeness, and accuracy of the data submitted to them for review are sufficient for evaluation of the safety and welfare of study participants. The DSMB should also assess the performance of overall study operations and any other relevant issues, as necessary.

The DSMB should conclude each review with their recommendations to the research team as to whether the study should continue without change, be modified, or be terminated. Confidentiality must always be maintained during all phases of DSMB review and deliberations. The DSMB should review data only by masked study group (such as X vs. Y rather than experimental vs. control) unless or until the DSMB determines that the group identifiers are necessary for decision-making.

Closing remark: The involvement of DSMB is a critical part of any clinical study. Providing the DSMB all required data in a timely manner is vital to make sure that everybody is safe and the quality/credibility of the research is well maintained.

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"It was more of a '*triple-blind*' test. The patients didn't know which ones were getting the real drug, the doctors didn't know, and, I'm afraid nobody knew."

INA-RESPOND Newsletter

The Indonesia Research Partnership on Infectious Disease newsletter is an internal bulletin of INA-RESPOND research network intended to disseminate information related to the network's studies, activities, and interests to all members of the network as well as its sponsors and related parties.

The INA-RESPOND newsletter welcomes all network members and stakeholders to contribute by submitting articles related to the network's studies and interests. Send your articles or subscribe to our latest newsletter by sending an email to INA.Secretariat@ina-respond.net