INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

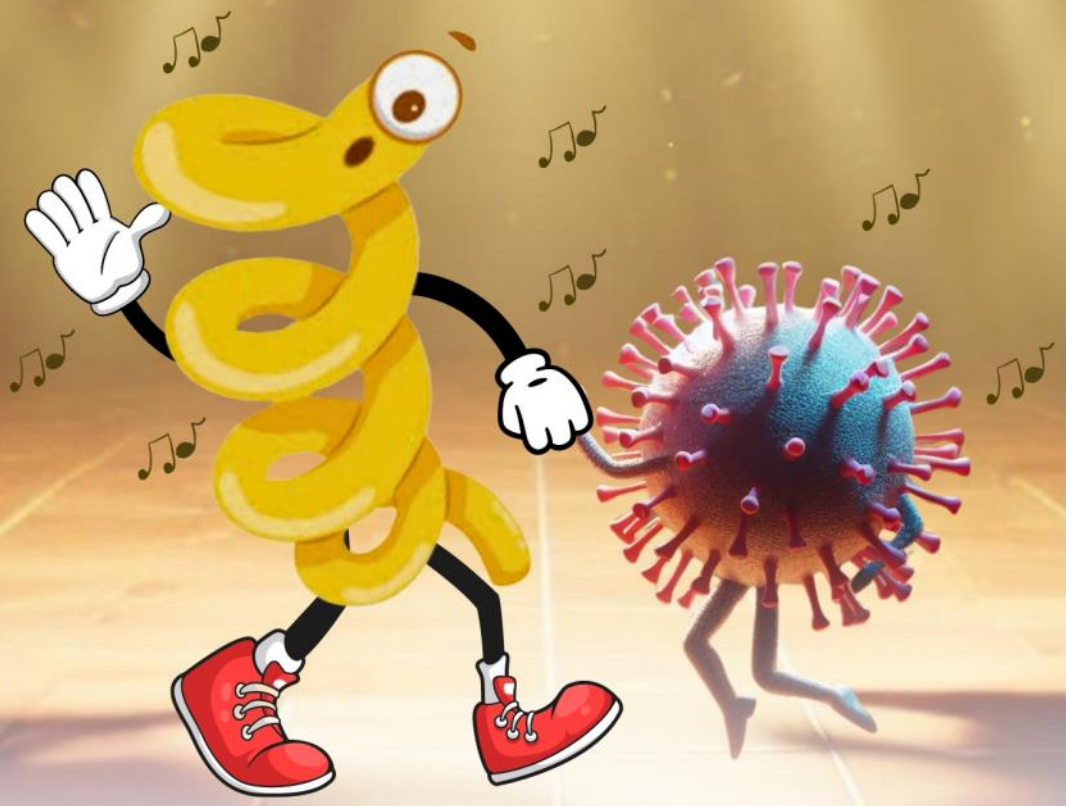
KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

April 2024

SCIENCE CORNER

Syphilis and HIV: A Risky Duo on The Dance Floor



COMIC CORNER — Beyond Facts: Crafting an Argument in Scientific Research

REPORT — RePORT International: TB RiCC Biomarker – Junior Investigator Training

SPORT & LIFESTYLE — Build Your Core to Build Your Health

HEALTH POLICY AGENCY

MINISTRY OF HEALTH REPUBLIC OF INDONESIA

2024

MASTHEAD

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newsletter

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INA-RESPOND Newsletter

InVITE & PROACTIVE Study Updates

By: Eka Windari R., I Wayan Adi Pranata, Lois E. Bang, Melinda Setiyaningrum, Nur Latifa Hanum, Restu Amalia, Riza Danu Dewantara

InVITE

The InVITE study in Indonesia has concluded its study period. All participants have completed their study visits, with the final visit occurring on January 24, 2024. Details of participant visit attendance are illustrated in Figure 1.

All specimens from the three sites—Tangerang District Hospital in Tangerang, TC Hillers Hospital in Maumere, and Dr. Moch. Ansari Saleh Hospital in Banjarmasin—have been sent to the INA-RESPOND Reference Laboratory. The InVITE Global laboratory team has provided instructions detailing the requirements for specimen shipment to the Central Laboratory. Currently, INA-RESPOND is preparing the necessary documentation for specimen shipment and is awaiting information related to the courier that will be used to send the specimens to the Central Laboratory. Specimen verification is conducted by the INA-RESPOND Reference Laboratory team for each specimen received from the sites. To ensure the quality and accuracy of the specimens in relation to the data, the team will also perform a final verification process before dispatching them to the Central Laboratory..

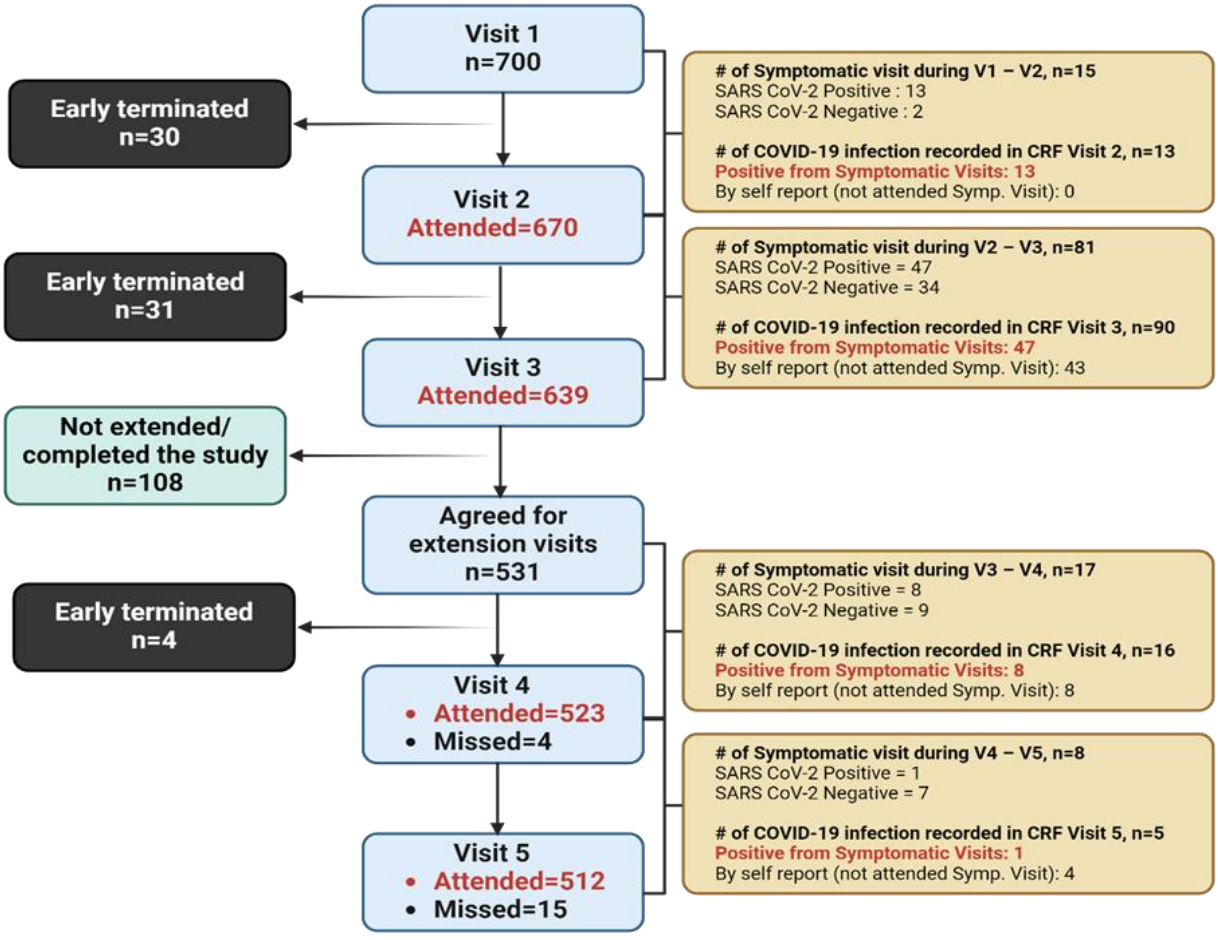

Figure 1. Participant Visit Attendance

INA-RESPOND has a Standard Operational Procedure (SOP) for Biosafety and Biosecurity, which governs the Quality Assurance (QA) process for the Study Specimen Inventory. This activity is carried out by the Clinical Research Associate (CRA) to ensure that the integrity of the specimens from ongoing studies is maintained and managed at the INA-RESPOND Reference Laboratory in accordance with the SOP and protocol. For the InVITE study, the execution of these activities is still in the preparatory phase, scheduled for May 2024. The QA process will be conducted for 10% of the samples, which will be randomly selected.

Source Document Verification (SDV) of critical variable data, such as vaccination dates and types received, as well as information on SARS-CoV-2 infection, is currently being performed by the INA-RESPOND secretariat team for all sites. This SDV is expected to be completed before the commencement of Global data cleaning specifically for Indonesia, which is scheduled to begin in June 2024.

The InVITE Global study design includes plans for multiple sub-studies, resulting in multiple manuscripts. Three manuscripts have been published, and plans for additional manuscripts are discussed periodically by the InVITE Publication Committee..

Manuscript Title	Publication Information	Indonesia Authors
Study protocol**:** Design of an observational multi-country cohort study to assess the immunogenicity of multiple vaccine platforms (InVITE)	PLoS ONE, published on September 15, 2022. https://doi.org/10.1371/journal.pone.02739	Dona Arlinda, Dewi Lokida, Muhammad Karyana, and Herman Kosasih
Challenges of conducting an international observational study to assess immunogenicity of multiple COVID-19 vaccines	PLoS Global Public Health, published on June 20, 2023. https://doi.org/10.1371/journal.pgph.0001918	Asep Purnama and Wiwit Agung Snc
SARS-CoV-2 seroprevalence in vaccine-naïve participants from the Democratic Republic of Congo, Guinea, Liberia, and Mali	International Journal of Infectious Diseases, published on February 25, 2024. https://doi.org/10.1016/j.ijid. 2024. 106985	Not involved

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Currently, INA-PROACTIVE The INA-PROACTIVE investigators, along with the Secretariat and partners, are currently preparing both primary and supplementary manuscripts. Meanwhile, in collaboration with the INA-RESPOND Warm Based Research Assistants (RAs), the Secretariat is conducting a scoping review on HIV research in Indonesia, covering all fields since the first reported case in 1987. The initial focus of this scoping review is on children living with HIV in Indonesia. The objective is to identify gaps in current research, provide scientific summaries for this age group, and support HIV control measures in Indonesia. This review will also assist in the preparation of a PROACTIVE manuscript focused on pediatric subjects.

In addition to the scoping review, the INA-RESPOND Secretariat and RAs are also engaged in journal club activities. The third journal club meeting took place on January 19th, 2024. The discussion centered on the article entitled "I can live a normal life": Exploring adherence


HIV Journal

Original Research

Open Access

"I can live a normal life": Exploring adherence to antiretroviral therapy in Indonesian adolescents living with HIV

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to antiretroviral therapy in Indonesian adolescents living with HIV", presented by Dr. Ivana Yulian from the Tangerang Site and Dr. Vitia Ajeng Nur Linda from the Yogyakarta Site. Here is a summary of the article:

According to the Joint United Nations Program on HIV/AIDS (UNAIDS) 2019 data, approximately 37.9 million people globally live with HIV, including 1.7 million children. In Indonesia, the Ministry of Health reports varying HIV prevalence among children by age group: 1.9% in

children under four years old, 0.9% in children aged 5-14, and 2.7% in adolescents aged 15-19. Adolescents in Indonesia are particularly at risk due to factors such as psychological immaturity, high curiosity, and susceptibility to peer influence. Antiretroviral therapy (ART) is the only treatment available for HIV infection. However, adherence to ART among adolescents presents significant challenges. A report from an infectious disease hospital in Indonesia in 2018 indicated that among 31 adolescents (aged 10-19) on ART, only 51.61% adhered to the treatment. Nonadherence not only affects the patients but also increases the healthcare burden. Therefore, it is essential to conduct a study to examine the challenges experienced by adolescents with HIV in undergoing ART.

The study aimed to explore and identify the experiences of adolescents with HIV in terms of challenges, strengths, and positive aspects related to ART adherence. Using a qualitative design with the Appreciative Inquiry (AI) approach, ten participants were recruited through purposive sampling. The inclusion criteria were adolescents aged 13-19 years old, unmarried, diagnosed with HIV for more than a year, consistently on medication, aware of their HIV status, able to communicate in Bahasa Indonesia, and cognitively able. Those experiencing health deterioration during data collection were excluded. Data were collected at a top referral hospital for infectious diseases in Indonesia from May to June 2020 through both offline and online in-depth interviews and analyzed using thematic analysis. Trustworthiness was ensured through thick description, member checking, and involving a supervisor as an external reviewer for instrument stability.

Six of the ten adolescents aged 13 to 19 had graduated from senior high school. Eight people contracted HIV through vertical transmission. Four individuals lived with their parents during data collection, whereas the others resided with only their father, mother, or other family members. The majority of participants declined to join the peer support group. Nine patients were still receiving first-line medication (Neviral and Duviral), while one received second-line therapy (Alluvia, Tenofovir, and Lamivudine). From this study, five main themes were obtained positively related to the adolescents' adherence to ART, termed (1) living a normal life, (2) setting an alarm for medication, (3) wanting to be healthy, (4) challenges in undergoing treatment, and (5) there is a hope.

Acceptance of their current status is crucial for adolescents with HIV as a positive coping technique; this is consistent with prior research that has identified a link between self-efficacy and ART adherence. Adolescents on ART can generally live their lives as if they were not HIV positive. Adolescents stated that setting an alarm for medication was the most crucial aspect of ART adherence. Medication reminders were critical in the study, whether via a mobile phone alarm or a watch. During ART, challenges include taking medication on time, experiencing drug side effects, forgetting to take medication, queuing to take medication, needing to take medication at the same time every day, being bored with taking medication, and handling large drug sizes. Adolescents who take ART do so because they want to live longer and be healthier. The participants stated that their desire to be well became their reason for taking ART.

There are also some issues regarding stigma, treatment availability, and future expectations. Concerning stigma, people living with HIV (PLWH) should not be shunned and should continue to receive support, as stigma and rejection appear to be prevalent in the lives of HIV-positive adolescents. In terms of treatment availability, it is hoped that ART will be accessible to them throughout their treatment. Regarding future expectations, participants hope to attain their ambitions, please their parents, and create a household free of HIV. The study's limitations include the exclusive characteristics of participants who mostly contracted HIV through vertical transmission, a qualitative study design with purposive sampling, and the use of online interviews as a methodological approach.

Finally, this study discovered that adolescents who value their independence and resist being controlled can still adhere to ART despite facing challenges. Adolescents require a unique approach; thus, the authors employed an appreciative inquiry approach to investigate the experiences of HIV-positive adolescents with ART. According to the findings, adolescents with HIV could live a normal life alongside those without HIV. This status is achievable because they are always motivated to be healthy and preserve their health to achieve their dreams and make their parents happy. Adolescents who successfully adhere to ART deserve recognition and rewards to celebrate their accomplishments and boost their confidence.

INA-RESPOND Newsletter

REPORT INTERNATIONAL: TB RICC BIOMARKER – JUNIOR INVESTIGATOR TRAINING

By: Gustiani Salim

PART TWO

TRAINING AT SALVADOR, BRAZIL

As part of the RePORT international consortium, research at RePORT Brazil focuses on conducting experiments to evaluate the immune response of individuals, translating research findings into clinical practice, and identifying promising and effective strategies for disease treatment and prevention. Specifically, for this training program, the lab provided hands-on and theoretical training in TB biomarker development by performing high throughput cellular phenotyping and protein quantification in a diverse range of biospecimens using Luminex technology. Moreover, the facility offered training in data handling, cleaning, standardization, and analysis, in addition to designing analytical figures for manuscripts and grant applications. The training was hosted at RICC Luminex Referral Lab, managed by FIOTEC/FIOCRUZ in cooperation with the Centro Universitário Faculdade de Tecnologia e Ciências (UniFTC), in Salvador, Bahia state.

Photo: Participants with the Brazil team

1. Protein-based Biomarker Study in Tuberculosis Disease

TB proteomics signature discovery has been a rapidly growing area of research that aims to identify potential protein biomarkers for the early detection, diagnosis, and treatment monitoring of tuberculosis disease. One common approach is the discovery of host-derived biomarkers, especially host immune responses to Mycobacterium tuberculosis (Mtb) infection such as identification of proteins associated with cytokine signaling, complement activation, cell adhesion, or other pathways associated with pathogen sensing and inflammatory responses, such as cytokines, chemokines, and acute phase proteins. This approach involves assessing relative differences in protein quantity, for example, which proteins are differentially expressed between treated versus untreated patients.

2. Luminex Technology for Assessing Protein-based Biomarker Discovery

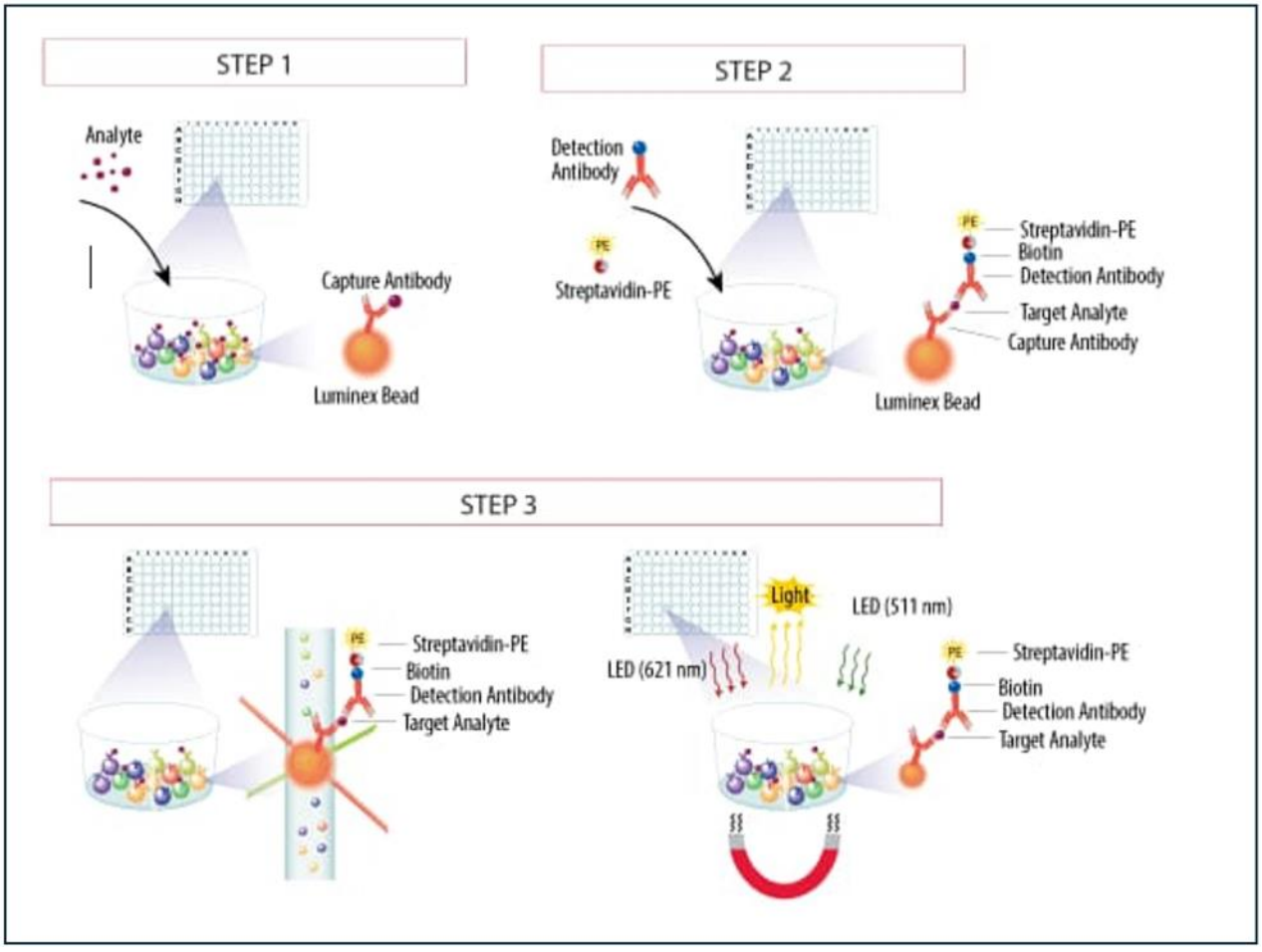
Several different technologies have been used to profile proteins in biological samples. The gold standard and widely used assay for protein detection and quantification is the Enzyme-linked immunosorbent assays (ELISA). Although ELISA is simple and robust, its capacity is limited as it only measures one analyte at a time from each sample. It's also time-consuming and costly when we need to perform multiple target analytes for multiple samples. Nowadays, the dynamic range of ELISA-based assays is narrower than that of other technologies such as multiplex assays like Luminex.

Luminex technology is a type of immunoassay that uses magnetic microsphere beads to simultaneously measure up to 100 analytes in a single experiment. Furthermore, the advantages and strengths of Luminex include:

- **Familiarity of the process** - Specific like a sandwich ELISA
- **Efficiency** - Analyze up to 100 analytes in one single sample
- **Reduced sample volume** - Much less sample requirement (25 uL)
- **Time saving**
- **Bespoke** - Study analytes involved in a disease or a pathway in the same assay plate with the analyte profile specific to individual needs.
- **Low Variability** - Minimizes experimental variability with multiple data points derived from a single experiment.

Luminex assays use color-coded microspheres, or beads, that are internally dyed with different proportions of red and infrared fluorophores that correspond to a distinct spectral signature, or bead region. This allows Luminex to create up to 500 different bead colors. The unique color combination gives the bead a "Spectral Address" that can be identified by the instrument. The beads are very small, of uniform size—6.5 micron, suspended in liquid, and therefore exhibit kinetic behavior that is essentially liquid-phase.

On this opportunity, the participants were trained using the Luminex xMAP Intelliflex® system machine. The system provides fast read times for both 96-well and 384-well plates format. Like other quantitation methods, Luminex requires a standard curve generated from a series of standard controls of known concentration to determine the concentration of tested samples. The basic principle of



processing samples using Luminex technology is summarized as follows:

1. Antibodies specific to a desired analyte are coupled to color-coded beads and are incubated with sample plasma or serum. The antibodies bind to the analytes of interest.
2. After washing away unbound materials, samples are incubated with a mixture of biotinylated detection antibodies specific to the analytes of interest and Phycoerythrin (PE)-conjugated streptavidin reporter to form an antibody-antigen sandwich.
3. Using a Luminex instrument, beads are excited by one laser to determine the bead region and corresponding assigned analyte. Another laser determines the magnitude of the PE-derived signal, which is proportional to the amount of analyte bound. Multiple readings are taken at each bead region, ensuring robust detection.

Photo: Luminex xMAP Intelliflex® system machine

For data evaluation, the quality of raw data was initially assured using Belysa software. The output data was obtained in the form of a table including the concentration of each tested analyte along with standard curve data. Subsequent data processing was performed using R studio software for quality control, statistical analysis, graph creation, and presentation needs.

3. Visiting the Biorepository Facility of RepORT Brazil

During the training schedule at the lab, participants had the opportunity to visit the biorepository facility that supports the storage of biological study specimens of TB from RePORT Brazil. This biorepository provides centralized storage facilities managed by the José Silveira Foundation. Located at the Bahia Rehabilitation Institute (IBR), the biorepository facility occupies an area of 24 m2 that houses nine -80C freezers and two liquid nitrogen tanks. To date, more than 275,000 specimens have been collected and stored including MTb isolates, sputum, blood, urine, DNA, and plasma at baseline and during follow-up sent from the three enrollment sites participating in the study: Rio de Janeiro, Manaus, and Salvador. All specimens are managed using the FreezerPro tracking system, a software that provides access to sample information from anywhere. The biorepository system is also connected and integrated with clinical, epidemiological, and laboratory data in a single REDcap-RePORT-Brazil database system.

After undergoing training for two full weeks, the participants returned to their respective countries. The next training will be continued at Rutgers - New Jersey Medical School (NJMS) Laboratory, Newark, New Jersey, United States of America from May 6 – 17, 2024.

INA-RESPOND Newsletter

SYPHILIS AND HIV: A RISKY DUO ON THE DANCE FLOOR

By: Ivana Yulian Hendarsin, Cintya Naya Danastri, Adhella Menur

The blaze of syphilis amidst the HIV epidemic

Syphilis, an age-old sexually transmitted disease (STD), has a history marked by stigma and blame. The disease became an outbreak among French soldiers during their invasion of Naples in the first Italian Wars in 1495, two years after Columbus's return from Hispaniola in 1493. The disease was stigmatized as disgraceful due to promiscuity, and various countries blamed each other for the outbreak. For example, the French referred to it as the 'Neapolitan disease' or the 'Spanish disease'; the English and Italians called it the 'French disease'; the Russians named it the 'Polish disease'; the Polish and the Persians called it the 'Turkish disease'; and the Turks called it the 'Christian disease'. At that time, the disease was more severe and deadly, possibly because of its novelty and the lack of immunity in the population. The name "Syphilis" was introduced in 1530 by the Veronese poet and physician Girolamo Fracastoro. In his poem Syphilis sive morbus gallicus, Fracastoro recounts the tale of a mythical shepherd named Syphilus who offended the Sun God by blaming him for a drought and insulting him. As punishment, the Sun God afflicted Syphilus and his community with a horrendous new illness. Fracastoro's poem gained attention among scholars, leading to the adoption of the term "Syphilis" to describe the disease.

In 1905, Schaudinn and Hoffman identified spiral-shaped bacteria in syphilis lesions (both fresh and Giemsa-stained specimens) as the etiologic agent, naming them Treponema pallidum. Several diagnostic methods were introduced in the following years, such as Landsteiner's dark-field microscopy, August Wassermann's serologic test, and the specific T. pallidum immobilization test (TPI) by Nelson and Mayer. However, the only available treatment at that time involved using toxic metals like mercury and arsenic, often leading to severe side effects and even death. The disease can be devastating, and congenital cases can cause miscarriage, lifelong medical issues, and infant death. Fortunately, penicillin was approved in 1943 and, in combination with aggressive public health interventions including case finding and contact tracing, contributed to a significant decline in the incidence of syphilis in the subsequent decades. Furthermore, in 2000, syphilis cases reached their lowest point in the United States, with an incidence rate of 2.1 cases per 100,000 persons.

Unexpectedly, syphilis has re-emerged as a significant global public health concern. In 2016, an estimated 6 million new cases of syphilis were reported worldwide. Among pregnant women, approximately 7 in every 1000 were found to have syphilis, which led to an estimated 143,000 early fetal deaths and stillbirths, 61,000 neonatal deaths, 41,000 preterm or low-birth-weight births, and 109,000 infants with clinical congenital syphilis. The incidence of syphilis in the U.S. has surged to levels not seen in more than two decades. Reported cases to the U.S. Centers for Disease Control and Prevention (CDC) increased by 81% from 2014 to 2018. More than half of men with new syphilis cases reported having sex with men (MSM), and 20-70% of whom were people living with HIV (PLWH).

Syphilis and HIV co-infection rates have been on a marked rise worldwide in recent years. This rise can

be attributed to the fact that both are systemic STDs which share common risk factors, including high-risk sexual activities. Several studies have also highlighted a reciprocal synergistic interaction between syphilis and HIV. The question is, **since the HIV epidemic began around the 1980s, why has syphilis surged in recent years?** Initially, during the early HIV epidemic, the implementation of syndromic treatment for STDs and widespread adoption of safer sexual practices due to fears of HIV infection contributed to a decline in syphilis prevalence. However, the successful introduction of antiretroviral therapy (ART), pre-exposure prophylaxis (PrEP), and improved survival rates among PLWH have influenced sexual behavior. This high-risk sexual behavior has created opportunities for the resurgence of syphilis as prevention measures have been relaxed or overlooked.

The dancing duo trend between syphilis and HIV should also be a concern for Indonesia. The country stands out as the only one in the Asia Pacific region experiencing a rise in HIV prevalence. As of 2022, there were estimated 540,000 PLWH in Indonesia, with 79% aware of their status and only 33% receiving ART. Concurrently, there has been an increase in syphilis cases in the country due to uninterrupted transmission and improvements in screening efforts. According to the Indonesia Ministry of Health, the number of syphilis cases surged by around 70% between 2016 and 2022, rising from 12,000 to nearly 21,000. Most of these cases were identified among MSM group (28%) and pregnant women (27%). Unfortunately, comprehensive data on the incidence and prevalence of syphilis among PLWH are still lacking. This underscores the urgent need for intensified efforts to address the dual challenges of syphilis and HIV in Indonesia.

The interplay of syphilis and HIV

Syphilis: Brief description

Syphilis is a highly infectious STD caused by the extracellular spirochete bacterium, *Treponema pallidum*, which spreads through contact with infectious lesions or body fluids. The crucial initial step of infection is the attachment to host cells and the extracellular matrix. Once beneath the epithelium, the spirochetes multiply locally and disseminate through the lymphatics and bloodstream. *T. pallidum* is one of the few pathogens capable of crossing specialized endothelial barriers such as the retinal, placental, and blood-brain barriers. Transmission of syphilis occurs primarily through sexual contact or in utero, from mother to child. Given the lack of animal reservoirs, syphilis theoretically could be a disease that we could eradicate. The average incubation period of syphilis is approximately three weeks (10–90 days). Syphilis is often referred to as the "Great Imitator" or "Great Mimicker" because of its varied and sometimes subtle presentations, which can resemble other infections. The classic clinical manifestations of syphilis are divided into early syphilis (primary, secondary, and early latent stages), which is highly infectious, and late syphilis (late latent and tertiary stages). How the pathogen burden is eventually decreased, and how latency is maintained remains a mystery. Equally mysterious is where *T. pallidum* resides during latency. Its ability to survive for extended periods while evading humoral defenses makes it a "stealth pathogen."

The primary stage of syphilis manifests as a solitary chancre, indurated and ulcerative, with a clean base at the site of contact or inoculation. The chancre is usually painless and may occur at extragenital sites such as the perirectal area, the rectum, or the oral cavity. Secondary syphilis is a systemic disease resulting from bacteremia, with clinical manifestations including a mild, nonpruritic rash, fever, generalized lymphadenopathy, mucosal lesions, alopecia, periostitis, and occasionally hepatitis or nephritis. Secondary syphilis is followed by a period termed latent syphilis in which no symptoms are present, and diagnosis can only be achieved through serological testing. Latent syphilis is subdivided into early latent (≤1 year after infection) and either late latent or latent syphilis of unknown duration. Tertiary syphilis de-

scribes a broad range of manifestations but most commonly includes gummatous (soft, tumor-like growths of the tissues that are highly destructive), cardiovascular, and/or neurological effects and can also cause death. Of note, neurosyphilis can occur at any stage of the disease. Early neurosyphilis includes meningovascular diseases (e.g., meningitis, strokes, seizures), brainstem or cranial nerve abnormalities, ocular syphilis (e.g., blurred vision or blindness), and otosyphilis (auditory vestibular abnormalities). Although there can be substantial overlap, late neurosyphilis typically affects the brain and spinal cord parenchyma, presenting as dementia, tabes dorsalis, general paresis, sensory ataxia, or bowel or bladder dysfunction.

A detailed history and physical examination construct the diagnosis of syphilis, and both direct and indirect testing are used to establish the diagnosis. Currently, indirect testing with serological assays remains the cornerstone for diagnosis. The traditional serological screening algorithm begins with a non-treponemal test (e.g., a rapid plasma reagin [RPR] or Venereal Disease Research Laboratory [VDRL] test), with reactivity confirmed by a highly sensitive and specific treponemal test (e.g., the *T. pallidum* hemagglutination assay [TPHA], rapid test [TP rapid], an automated enzyme or chemiluminescence immunoassay). Penicillin remains the drug of choice for all stages of syphilis due to its high effectiveness, and no reports of resistance to it in *T. pallidum* have been found. Alternative options include ceftriaxone, doxycycline, and erythromycin. Azithromycin should no longer be used due to the detection of global resistance..

The non-treponemal test also provides titers that are necessary for clinical management and evaluation. With adequate treatment, most patients will return to a non-reactive non-treponemal antibody. Serological cure is defined as a seroconversion (from positive to negative) or as a 4-fold (or two dilutions) decline in non-treponemal antibody titer 6 to 12 months after

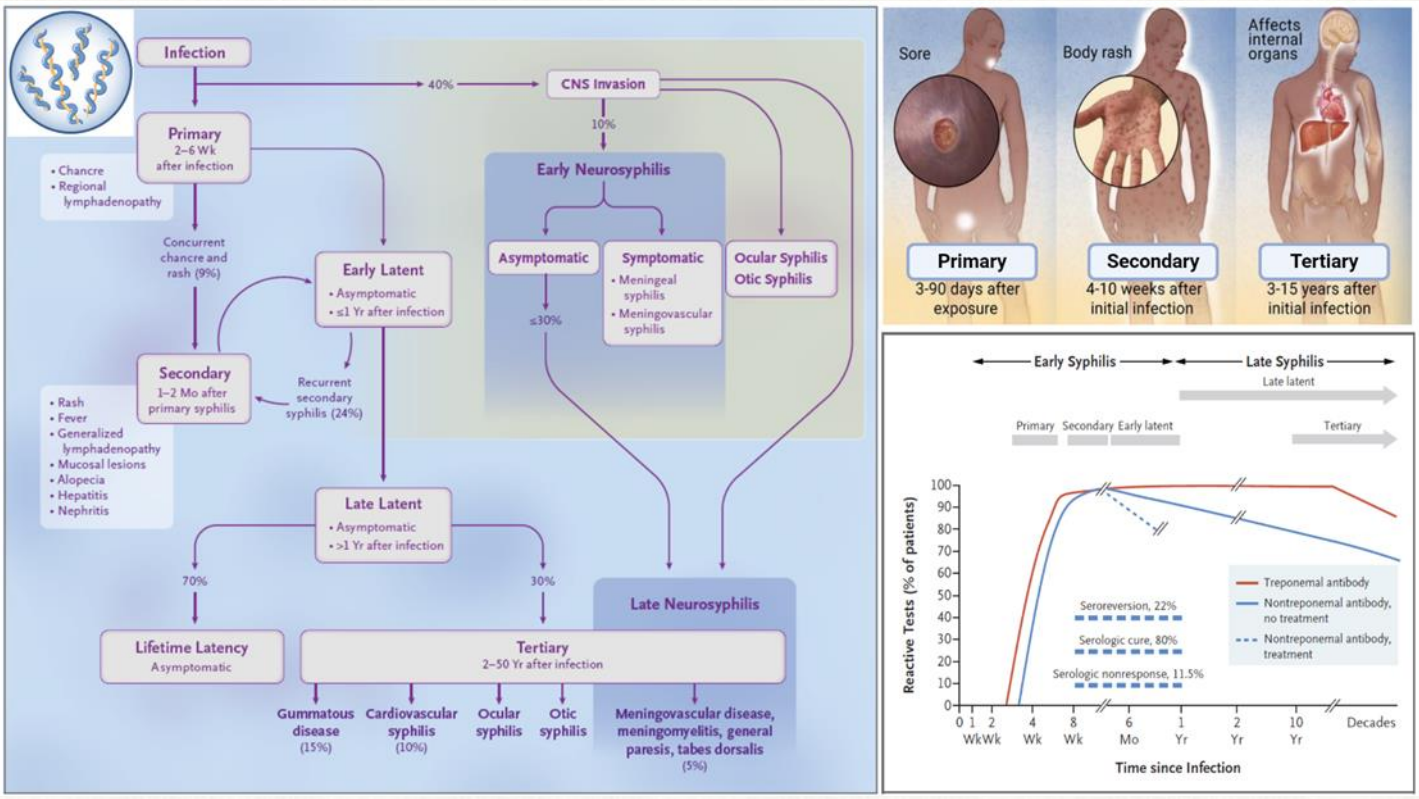


Figure 1. Natural history of untreated syphilis (Ghanem KG, et al, 2020, DOI: 10.1056/NEJMra1901593).

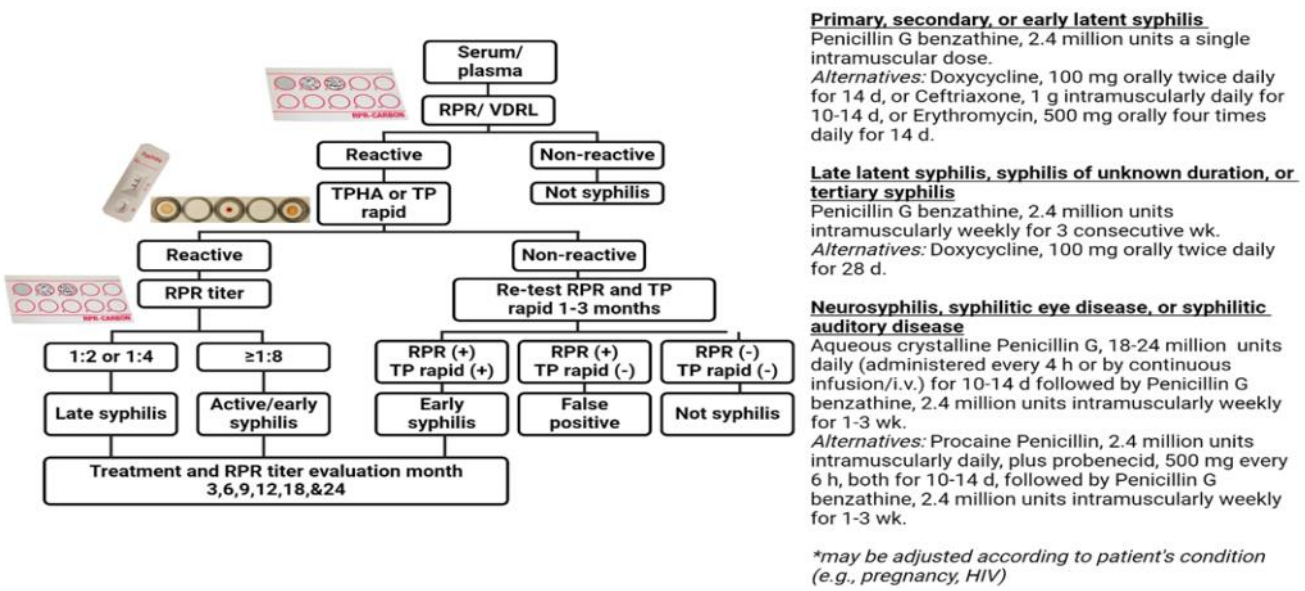


Figure 2. Traditional approach of syphilis serological testing algorithm according to Indonesia Ministry of Health. Syphilis treatment recommendations according to WHO and Indonesia Ministry of Health (2016).

therapy for early syphilis and 12 to 24 months for late syphilis. Some patients may maintain a low non-treponemal antibody titer for life despite adequate treatment (serofast). Treatment failure is defined as a ≥4-fold rise in non-treponemal titers after

treatment in the absence of re-infection. An individual with a previous serological cure might be considered as "re-infected" if a new seroconversion (from negative to positive) or a 4-fold or greater increase in non-treponemal antibody titer occurs. Conversely, antibodies detected in treponemal tests usually remain detectable for life even after successful treatment. Thus, a reactive treponemal test can indicate current or past syphilis infection.

Syphilis and HIV: What's the dance they play?

The understanding of the interaction between syphilis and HIV has continued to evolve and increase clinical importance, given the rising rates of co-infection and the unique synergy between the duo. Untreated syphilis can increase the risk of transmitting and ac-

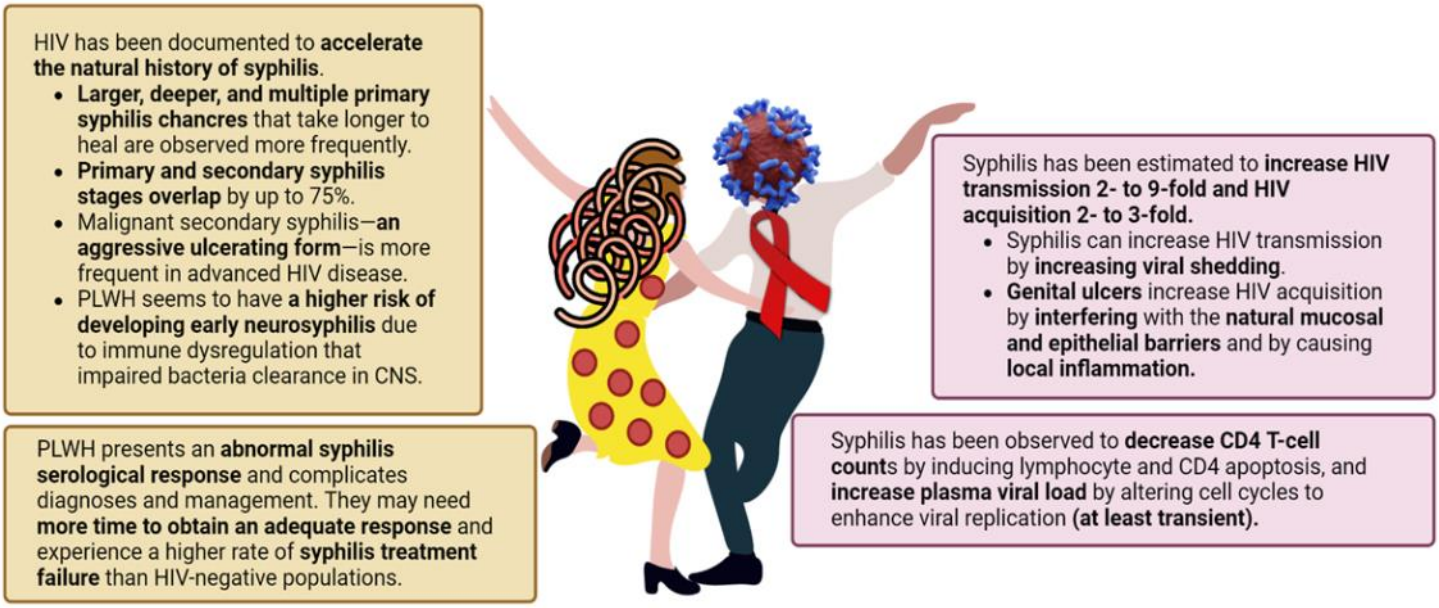


Figure 3. Reported interaction between syphilis and HIV, which needs further research. Created with: Biorender.com.

quiring HIV infection. In turn, co-infection with HIV can affect the manifestations of syphilis and make it harder to distinguish between its stages, potentially leading to misdiagnosis. Syphilis infection does not lead to immunity against reinfection, and repeated episodes of syphilis can occur predominantly in PLWH, especially in an asymptomatic form. A study in one center reported syphilis reinfections in PLWH, ranging from one to seven episodes. Patients with the duo infection may also face a higher risk of syphilis treatment failure, and their genital ulcers typically take longer to heal compared to those with syphilis alone, which can increase transmission and the risk of exposure to other STDs.

Neurosyphilis in PLWH requires special attention, but diagnosing it remains challenging due to the lack of highly sensitive and specific tests to distinguish cerebrospinal fluid (CSF) findings compatible with neurosyphilis from common abnormalities in PLWH. While a reactive CSF nontreponemal test is highly predictive, it's less than 80% sensitive. One study found that combining a serum RPR of 1:32 or greater with a CD4+ T cell count of 350 cells/μL or less increased the likelihood of neurosyphilis. Until more data are available, neurosyphilis should be considered in all PLWH with syphilis, and a lumbar puncture is suggested for those with neurological symptoms, evidence of active tertiary syphilis, late latent syphilis, syphilis of unknown duration, or treatment failure.

The hurdle to stop the risky dance

Iceberg phenomenon

Both HIV and syphilis are stigmatized illnesses, often evoking avoidance and fear in people. The stigma surrounding these diseases persists in society, fueled by many misconceptions about their transmission and the implications of living with HIV and syphilis. Notably, stigma and shame often deter housewives and pregnant women from seeking help. A lack of information, awareness, and outdated beliefs contribute to the unease surrounding these infections, leading to significant underreporting of cases. The complexities of managing syphilis further compound the iceberg phenomenon of dual infection. As previously discussed, syphilis's reputation as the "Great Imitator" often leads to misdiagnosis, particularly in the early stages when it can mimic other skin or genital diseases. In people living with HIV (PLWH), syphilis diagnosis frequently occurs during the latent stages, resulting in delayed treatment. Additionally, routine laboratory culture media cannot culture T. pallidum, and direct methods like molecular or specialized microscopy techniques are limited by their performance, availability, and costs. Clinicians also struggle with the lack of specificity of nontreponemal tests and the poor correlation of treponemal tests with disease activity.

Furthermore, advancements in HIV management with highly effective antiretroviral therapy (ART) and the understanding that undetectable HIV cannot be transmitted through sex (Undetectable = Untransmittable) have led to declines in previously practiced safer sex behaviors and promoted syphilis transmission. The impact of condomless sex has been further augmented by the introduction of Pre-exposure Prophylaxis (PrEP) and behaviors like "serosorting" (selecting partners with the same HIV status). Increased use of online applications to find sexual partners has also been associated with high-risk behaviors, including having multiple partners and engaging in injectable substance use during sex. Additionally, the misconception that oral sex is "safer" sex and rarely associated with HIV transmission may also play a role in the transmission of syphilis. In Indonesia, syphilis screening is recommended for triple elimination programs

(targeting HIV, syphilis, and Hepatitis B) in pregnant women, women in labor, women with a history of miscarriage or stillbirth, sex workers, MSM groups, and all STD patients. Public health authorities are still working to optimize screening efforts. These issues contribute to enlarging the iceberg base and require prompt attention.

Ping-pong Phenomenon

Sex partners frequently infect and re-infect each other with syphilis, referred to as the "ping-pong phenomenon" or "ping-pong syphilis." The phenomenon may be more frequent in patients with the duo infection since PLWH experienced more delay in diagnosis, treatment failure, and recurrent cases of syphilis. It is such a really risky duo on the dance floor—high frequency of syphilis re-infection highlighting the need for regular STD screening in sexually active PLWH. The notification of recent sex partners of patients with syphilis and, in particular, of patients with concordant HIV infection is a critical component of disease prevention and control. Early identification and treatment of contacts can potentially prevent the continued spread of both infections. Individuals who had sexual contact within 90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner might be infected, even if their serological test is negative. Therefore, these individuals should receive presumptive treatment with Penicillin G benzathine (2.4 million units intramuscularly) once. If the exposure occurred more than 90 days before the diagnosis of early syphilis in a sex partner and serologic results are unavailable or follow-up is uncertain, presumptive treatment is also recommended. Other sex partners are considered at risk and should undergo clinical and serologic evaluation to reduce the likelihood of the ping-pong phenomenon occurring.

Future directions

Improvements in clinical management of HIV and syphilis co-infection are needed in two key areas: enhanced syphilis diagnostic methods and increased efforts in managing and preventing both diseases. While rapid treponemal testing has improved syphilis identification, its limitation in distinguishing active from past infections remains. Developing rapid tests of syphilis combining non-treponemal and treponemal antibodies is promising but requires validation. PCR is being optimized for single syphilis detection or multiplex detection of multiple STDs, though FDA approval and cost remain obstacles. Therefore, up to now, tailoring diagnostic approaches based on understanding syphilis clinical stages is crucial.

The development of syphilis vaccines is imperative, but viable candidates like whole inactivated cell, live attenuated, or genetically engineered vaccines are still years ahead. In the meantime, the use of Doxycycline for prophylaxis in high-risk groups could be considered, with careful attention to antibiotic resistance. Ongoing studies are evaluating the effectiveness of these interventions. Therefore, routine periodic syphilis screening remains the cornerstone of prevention, especially among PLWH, with recommendations every 3 to 6 months. PLWH should receive treatment akin to the general population, with adjustments made for specific scenarios like neurosyphilis or treatment failure. Further research is needed to establish optimal treatment and ensure a cure for syphilis in PLWH.

Integrating syphilis and HIV care is crucial. The dance between the duo is harmful rather than joyful. All the public layers should participate in controlling syphilis and HIV. Health authorities must develop policies that facilitate rational and accessible testing for screening and monitoring while

raising awareness about both diseases using innovative media platforms. Clinicians and social workers play a vital role in educating patients, counseling them on safe sexual activities, and regularly screening those at increased risk. Ending the stigma surrounding syphilis and HIV is crucial to creating an environment where people feel comfortable discussing their sexual health and seeking assistance when needed. Together, we can perform a safe and healthy dance!

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INA-RESPOND Newsletter

BUILD YOUR CORE TO BUILD YOUR HEALTH

By: Monica Surjanto

Understanding the Core

The core muscles, essential for maintaining spinal stability, can be divided into two groups based on their functions and attributes. The first group includes the deep core muscles, also known as local stabilizing muscles. This group primarily comprises the transversus abdominis, lumbar multifidus, internal oblique muscle, and quadratus lumborum. The second group consists of the shallow core muscles, or global stabilizing muscles, which include the rectus abdominis, both internal and external oblique muscles, erector spinae, quadratus lumborum, and hip muscle groups.

The Benefits of Strengthening Your Core

Strengthening your core muscles offers numerous benefits:

1. Improved Posture: A strong core helps maintain spinal alignment, reducing the risk of slouching and back pain. Good posture not only enhances appearance, making you look taller and more confident, but also prevents muscle imbalances and joint strain.

2. Enhanced Balance and Stability: Core muscles are crucial for maintaining balance and stability, whether you're standing, walking, or performing dynamic movements. Strengthening these muscles reduces the risk of falls and injuries, especially as you age.

3. Better Athletic Performance: For both casual enthusiasts and seasoned athletes, a strong core is vital for optimal performance. It improves your ability to generate power and transfer energy between different body parts, enhancing agility, speed, and endurance.

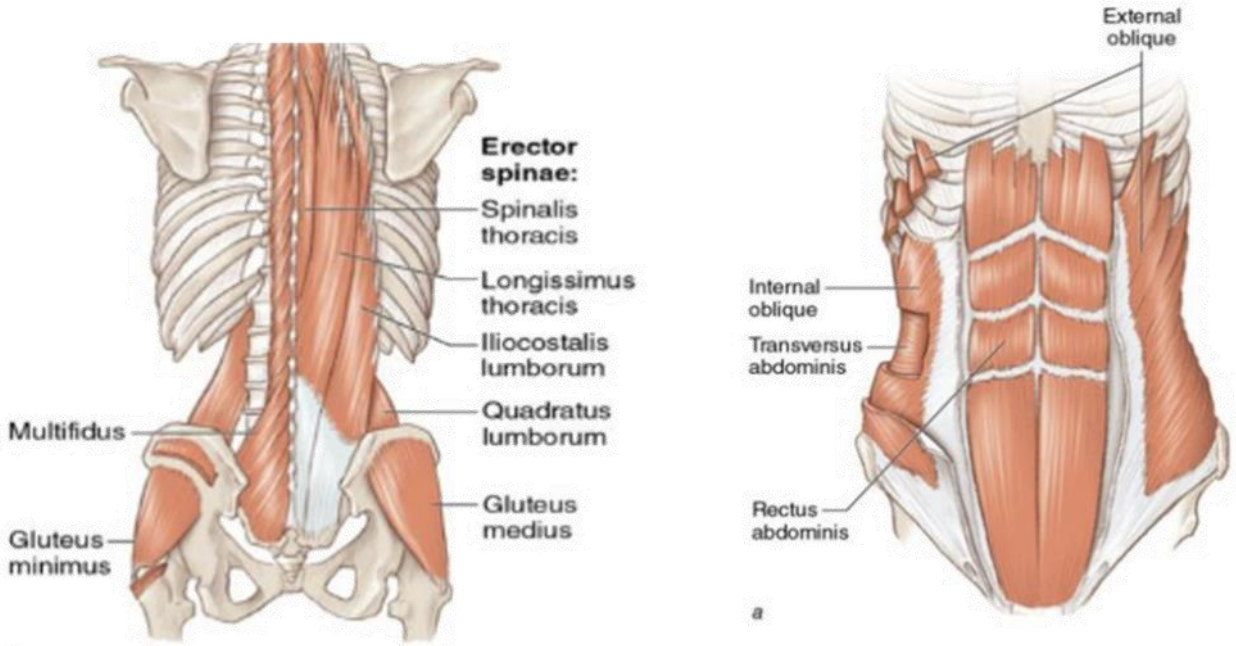


Fig 1. Core muscles

4. Reduced Risk of Injury: Weak core muscles can lead to poor movement mechanics and compensatory patterns, increasing the likelihood of strains, sprains, and other injuries. By strengthening your core, you build resilience against injuries and improve overall movement efficiency.

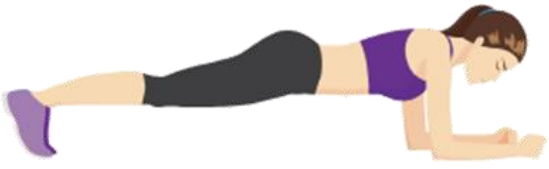
5. Enhanced Functional Fitness: Core strength is essential for everyday activities, from lifting groceries to bending down to tie your shoes. Developing a strong core makes these tasks easier and reduces the risk of strain on your spine and joints.

Efficacy of Core-Strengthening Exercises for Treatment of Back Pain

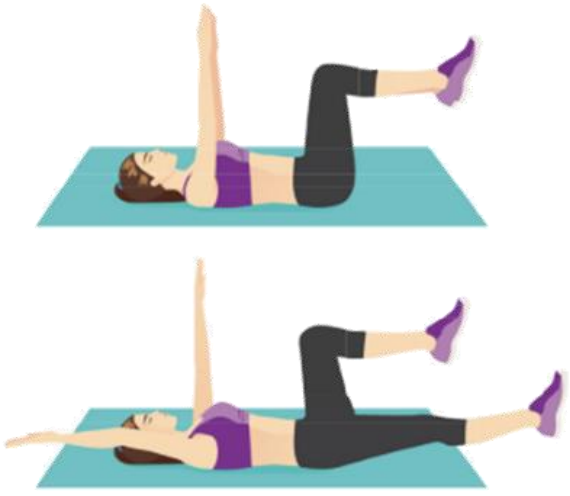
There is substantial evidence that individuals with chronic low back pain (LBP) and sacroiliac pain exhibit improper recruitment of core muscles and display core weakness. Research also shows increased fatigability, decreased cross-section, and fatty infiltration of paraspinal muscles in patients with chronic LBP. Even high-level athletes may experience core instability, predisposing them to musculoskeletal injuries. Female athletes, in particular, may be at increased risk of injury to the anterior cruciate ligament if core weakness is present. Additionally, patients with back pain often overactivate superficial global muscles while control and activation of the deep spinal muscles are impaired. Thus, core stability exercises have a strong theoretical basis for the prevention and treatment of various musculoskeletal conditions and spinal disorders.

Building Your Core

Contrary to popular belief, endless crunches are not the most effective way to strengthen your core. Instead, focus on exercises that target all the core muscles, including the deep stabilizers. Here are some exercises to consider:



Plank: Lie on your stomach and raise yourself up on your elbows and toes, with your elbows below your shoulders. Engage your core muscles to keep your body straight from shoulders to heels. Hold this position for 60 seconds, or as long as you can.



Dead Bug: Lie on your back with your arms extended towards the ceiling and your legs bent at a 90° angle. Extend your right arm and left leg away from your body, then bring them back to the center. Repeat this action with your left arm and right leg. Aim for 12 to 15 repetitions.

Side Plank: Lie on your right side and raise your body onto your right elbow, ensuring your elbow is below your shoulders. Engage your core muscles to keep your body straight from head to heels. Hold for 60 seconds, or as long as you can, then switch to the left side and repeat.

Bridge: Lie on your back with your knees raised so your feet are flat on the floor. Place your hands along your

sides. Lift your hips upwards, tilting your pelvis as you go, until your body and legs form a straight line. Hold for ten seconds, then return to the starting position. Work up to 12 to 15 repetitions.

Conclusion

Core-strength exercises strengthen the core muscles, which include the abdominal muscles, back muscles, and the muscles around the pelvis. Strong core muscles make it easier to perform many physical activities. Core strengthening has a strong theoretical basis in the treatment and prevention of LBP, as well as other musculoskeletal afflictions, as evidenced by its widespread clinical use. Studies have shown that these programs may help decrease pain and improve function in patients with low back pain (LBP).

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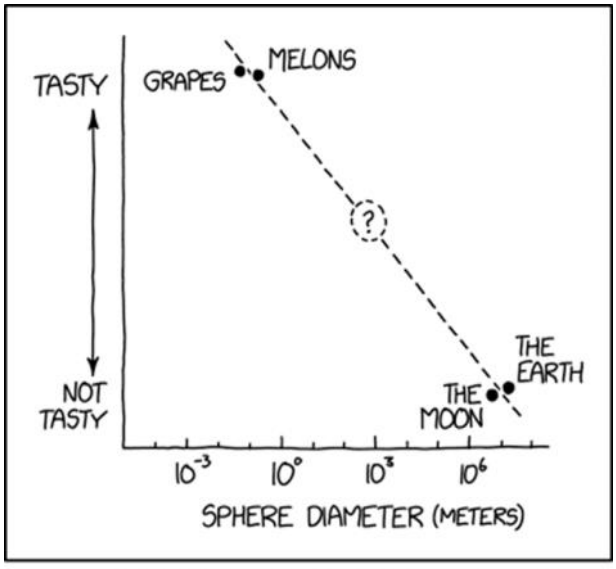
INA-RESPOND Newsletter

COMIC CORNER

BEYOND FACTS: CRAFTING AN ARGUMENT IN SCIENTIFIC RESEARCH

By: Aly Diana



MY RESEARCH SUGGESTS THE EXISTENCE OF AN 800-METER SPHERE THAT TASTES OKAY.

Source: https://xkcd.com/2893/

Research is more than just collecting a heap of information; it involves finding answers to significant issues. This piece serves as a reminder of the importance of shaping a persuasive research argument, transforming basic data into a narrative that clearly outlines problems and supports solutions. It highlights essential steps in discussing research, including the vital interplay between claims, reasons, and evidence in the advancement of scientific understanding.

The impact of our research is determined by our ability to make a compelling argument for a chosen viewpoint or solution. Research is an active search for answers, not merely gathering information. Sharing our findings means more than offering a list

of facts; it involves explaining why these findings are important and how they can address pressing issues. This explanation is the foundation of a research argument.

Data doesn't make sense on its own; it requires a context and interpretation to be meaningful. A thorough discussion includes a summary of our findings and a comparison to existing research, providing a clear explanation of our results and their broader relevance. Encountering unexpected hurdles in research is common. Openly discussing these challenges enriches our analysis. It is also important to consider other possible explanations for our results. Simply matching our results with prior studies or showing agreement or disagreement with previously published research isn't enough for a well-rounded discussion.

We must steer clear of typical errors, such as introducing results without discussing them, disconnecting our explanation from the data, presenting information in the order it occurred rather than in a logical sequence, overlooking evidence that challenges our conclusions, or making claims without solid, logical support. Our paper relies on a convincing argument, composed of a claim, a reason, and evidence. The claim is the main statement we're putting forward; the reason explains this claim; and the evidence consists of the factual data that supports the reason. Preparing for and responding to potential questions and objections strengthens our argument. These steps not only reinforce our main point but also improve the discussion about our research topic.

In the realm of research, the outcome can be described as an answer, a solution, or in terms of argument, a claim. Understanding the type of claim we're making is key. As we refine our argument, we must constantly evaluate whether our claim is detailed and significant enough to warrant an argument and withstand scrutiny.

Creating a research argument involves more than displaying figures and data; it's about forming a narrative that convincingly supports your point. This means carefully evaluating our claim to ensure it's clear and substantial. By doing this, we move our scientific conversation from simple data presentation to meaningful argumentation, adding value to the scientific dialogue. Embracing these principles enriches our collective knowledge. In the creation of a research argument, we find the merger of thorough analysis and effective communication, driving science forward.

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