INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

September 2023

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Unveiling the Hawthorne Effect: When a Million Eyes Are Watching

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The Facts of High Risk Sports and Physical Activity in Female

HEALTH POLICY AGENCY
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2023

MASTHEAD

INA-RESPOND newsletter

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FEATURES

INA-RESPOND Newsletter

InVITE & PROACTIVE Study Updates

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

InVITE

As of September 4, 2023, of the 700 participants initially enrolled in the study, 414 (59.14%) have concluded their participation. This leaves 286 (40.86%) still actively engaged. The study is conducted across three distinct sites, all of which are currently focused on visits 4 and 5. A detailed breakdown of these visits per site is provided in Table 1.

There were some retention challenges faced during the study's course. Of the 414 participants who concluded their participation:

- 352 (50.29%) participants successfully completed the study.
- 45 (6.43%) chose to withdraw due to various reasons, including personal constraints or diminished interest.
- Three (0.43%) were unable to receive the full vaccine regimen within the stipulated 12 months post-enrollment, leading to their exclusion.
- Two (0.29%) were advised to discontinue based on concerns for their best interests.
- One (0.14%) participant was deemed non-compliant with the established study procedures.
- Unfortunately, one (0.14%) participant passed away during the study.
- Ten (1.43%) participants discontinued for other miscellaneous reasons.

Another focus of the study has been on the symptomatic visits among participants. Detailed data regarding these visits, as of September 4, 2023, is available in Table 2. It's crucial to note that the presence of COVID-19 symptoms in some participants does not necessarily indicate a confirmed diagnosis of the disease.

The first specimen shipment, using the credo box for InVITE local specimens from Site 02 (TC Hillers Hospital), took place on August 23. The specimens were received in good condition with an average temperature of -61°C. The credo box will be utilized next by Site 03 (Dr. Ansari Saleh Hospital).

Site	Symptomatic Visit		
	# of visit	Positive	Negative
01	104	61	43
02	14	6	8
03	2	1	1
Total	120	68	52

Table 2. Symptomatic Visit Details per Sep 4, 2023

Site	Screening / Visit 1	Enrollment Failure	Enrolled	Ongoing	Add. Visit 1	Visit 2	Add. Visit 2	Add. Visit 3	Visit 3	Agree Ext.	Not Agree Ext.	Ext. Visit 4	Ext. Visit 5
01	345	2	343	135	88	326	314	306	315	285	30	277	149
02	228	1	227	70	97	214	191	188	195	151	44	151	79
03	130	0	130	81		130			129	95	35	95	14
Total	703	3	700	286	185	670	505	494	639	531	109	523	242

Table 1. Details of Visits per site per Sep 4, 2023

INA104

In connection with the subject visit activities that have been completed at all sites, most of the sites have now been closed. Currently, only one site remains active, Site 680, which is preparing for a study close-out visit scheduled for October 2023. After the close-out activities, the site will address the action items and proceed with the document archiving process, also expected to be completed in October 2023.

The table below shows the site close-out visit activities in September: two sites have finalized their close-out activities, namely, Site 520 (Sanglah Hospital, Bali) and Site 540 (Sulianti Saroso Hospital, Jakarta). The remaining site, Site 680 (Soedarso Hospital, Pontianak), is set to conclude its study activities from 04-06 October 2023.

Upon completion of the site close-out visits, the focus of the study activities has shifted to the preparation of the study manuscript and the drafting of a final study report to be submitted to both central and local ethics commissions. In terms of manuscript preparation, three primary manuscripts are being drafted collaboratively by the Secretariat, study core team, and NIAID team, with contributions from the PI and Co-PI of each site. These manuscripts will cover the baseline characteristics and predictors for all death cases within 1 year and 3 years, as well as aspects of virology, immunology, disease progression, and clinical progression. Additionally, three more manuscript ideas are under consideration, focusing on late presenters, phylogenetic resistance analysis, and pediatric subject analysis. Currently, the Secretariat is prioritizing the manuscripts on baseline and late presenter characteristics. Once the core team and science team reach a consensus on the writing aspects, the concept plan will undergo further discussion with NIAID for refinement.

In addition to this concept plan, other plans have been submitted by the INA104 sites. Typically, these plans revolve around five main topics: viral load, immune response (CD4 and/or VL), comorbidities, coinfections, and opportunistic infections. These concept plans will be discussed in more detail once the components of the primary and supplementary manuscripts have been confirmed.

Site	Site Name	Scheduled	Actual
510	RS Hasan Sadikin, Bandung	Jun-23	15-16 Jun 2023
520	RSUP Sanglah, Denpasar	Sep-23	23-24 Aug 2023
530	RS Cipto Mangunkusumo, Jakarta	Jul-23	31 Jul – 1 Aug 2023
540	RS Sulianti Saroso, Jakarta	Sep-23	14 September 2023
550	RS Wahidin Sudirohusodo, Makassar	May-23	24-25 May 2023
560	RS Kariadi, Semarang	Mar-23	30-31 Mar 2023
570	RS Soetomo, Surabaya	Apr-23	13-14 Apr 2023
580	RS Sardjito, Yogyakarta	Apr-23	21 Mar 2023
590	RS Persahabatan, Jakarta	Jun-23	14-15 Jun 2023
600	RS Adam Malik, Medan	Jun-23	21-23 Jun 2023
610	RSU Kab Tangerang, Banten	Mar-23	08-09 Mar 2023
630	RSUD M. Ansari Saleh, Banjarmasin	Apr-23	05-06 Apr 2023
640	RS St. Carolus, Jakarta	Jun-23	05-06 Jun 2023
650	RS Budi Kemuliaan, Batam	Jun-23	07-08 Jun 2023
660	RSU Wahab Sjahranie, Samarinda	Jul-23	12-14 Jul 2023
670	RSUD dr. Zainoel Abidin Banda Aceh	Jul-23	12-13 Jul 2023
680	RSUD dr. Soedarso, Pontianak	Oct-23	TBD
690	Abepura	Jul-23	1-2 Aug 2023
700	RSUD Dr. TC Hillers Maumere	Aug-23	9-10 Aug 2023

INA-RESPOND Newsletter

STERILE COMPOUNDING – WHY IT MATTERS

By: DCR Pharmacy Team: Lucy Chung, Nayon Kang, David Vallée

FROM OUR PARTNER

In March of 2011, nine patients at six Alabama hospitals died from receiving parenteral nutrition that was contaminated with Serratia marcescens, a gram-negative bacterium. A total of nineteen patients were infected from receiving the contaminated product, which was later recalled.

Recently, in February 2021, the FDA was made aware of a 50-year-old female patient who was hospitalized and treated for suspected septic shock with multi-organ failure after receiving an IV-vitamin infusion in her home. The patient's blood cultures grew Pseudomonas fluorescens, a gram-negative bacterium. The IV-vitamin infusion was compounded by Age Management Institute Santa Barbara, CA.

What do two these situations have in common? Patients were harmed, some even died, due to lack of adherence to proper sterile compounding regulations, standards, guidelines, and best practices.

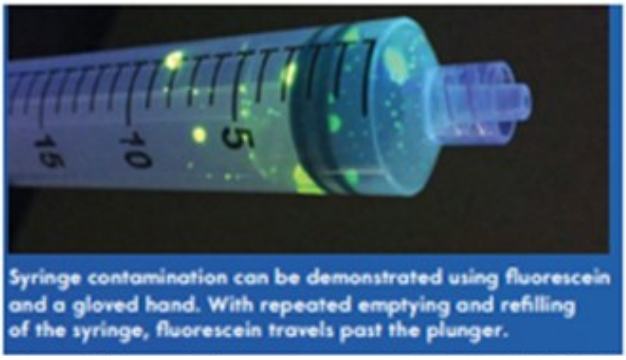
What is sterile compounding?

Sterile compounding is defined by the United States Pharmacopeia (USP) as "combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug or bulk drug substance to create a sterile medication"

The goal of proper sterile compounding is to minimize harm, including death, that could result from any number of components including:

- Microbial contamination or non-sterility
- Excessive bacterial endotoxins

USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations USP Education



Syringe contamination can be demonstrated using fluorescein and a gloved hand. With repeated emptying and refilling of the syringe, fluorescein travels past the plunger.

- Variability from the intended strength of correct ingredients
- Physical and chemical incompatibilities
- Chemical and physical contaminants
- Use of ingredients of inappropriate quality

In the US, compounding of sterile preparations is a practice that is typically dedicated to pharmacy personnel, however, some medical offices and clinics can perform limited compounding. Regardless, all compounding personnel are responsible for ensuring adhere to standards, regulations and guidelines regarding compounding and dispensing of sterile products in appropriate containers with accurate and appropriate labeling. Proper storage of compounded sterile preparations (CSP) is another important concern as extended storage and/or improper temperature conditions may allow for growth of a pathological burden of microorganisms with increased patient morbidity and mortality because of contaminated or incorrectly CSPs.

Legal Standards

As mentioned above, in the US the practice of compounding sterile preparations must adhere to legal standards, including the USP-NF General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. USP is an independent, scientific non-profit organization focused on building trust in the supply of safe, quality medicines. USP also develops standards for preparing compounded sterile medications to help ensure patient benefit and reduce risks such as contamination, infection, or incorrect dosing. USP's standards are enforceable by the U.S. FDA for medicines and their ingredients imported into or marketed in the United States and have been used in more than 140 countries globally, including Indonesia.

The FDA also has regulations for compounding in the FD&C Act, Section 501 and has published guidelines "Insanitary Conditions at Compounding Facilities. Guidance for Industry". Examples (not exhaustive) of insanitary conditions that apply to the production of sterile drugs include:

https://www.vecteezy.com/photo/13483331-rusty-scissors-with-black-handle

- Vermin (e.g., insects, rodents) or other animals (e.g., dogs) or evidence of their presence (e.g., urine, feces) in the production area or adjacent areas
- Visible microbial contamination (e.g., bacteria, mold) in the production area or adjacent areas
- Foreign matter in the production area (e.g., rust, glass shavings, hairs, paint chips)
- Engaging in aseptic processing wearing non-sterile gown components (e.g., gloves)

What can compounding personnel do to protect patient safety?

Proper aseptic technique, proper handwashing and garbing cannot be stressed enough. While there are many regulations and guidelines regarding the

> "The most important variable affecting microbial contamination of admixtures was the aseptic technique of personnel, not the environment in which the drugs were compounded."13

environment and equipment to provide a sterile environment, the greatest source of microbial contamination is people. People shed particles when sitting, moving head/arm/neck/leg, walking. The faster the movement, the more particles are shed.

While competencies can assess whether compounding personnel understand and can follow proper procedures, being mindful that every time a CSP is prepared, it is administered to a person. That person could be a stranger or a family member. Compounding personnel should work as though every product they manipulate/touch will be given to a loved one.

As described in the situations at the beginning of this article, the need for these regulations, standards and guidelines is clear. However, most people aren't even aware of that these exist, however not understanding and following these can lead to dire consequences. Sites that compound sterile preparations should have SOPs in place that align with the regulations and standards of their country. Competencies prior to engaging in sterile compounding and at least annually should occur. And finally, a sincere desire to produce a product that will not cause harm to patients is tantamount.

Questions? Ask DCR Pharmacy: DCRPharmacy@mail.nih.gov

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INA-RESPOND Newsletter

REPORT

UPDATES FROM THE 7TH REPORT INTERNATIONAL ANNUAL MEETING IN GOA, INDIA – FACING CHALLENGES TOGETHER TO CHALLENGE TUBERCULOSIS

By: Adhella Menur, Melinda Setiyaningrum

Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB), was the deadliest infectious disease until COVID-19 surpassed it in 2020. The COVID-19 pandemic disrupted the positive global trend of TB control, setting it back by roughly ten years. With the waning of the COVID-19 emergency and the rising incidence and death toll from TB, the latter is poised to reclaim its grim distinction. Multinational collaboration in research to achieve breakthroughs for TB elimination—spanning prevention, diagnosis, and treatment—is essential. Addressing this need, the National Institute of Allergy and Infectious Diseases (NIAID) established the Regional Prospective Observational Research in TB (RePORT) International network in 2013 to support the establishment of regional RePORT consortia in cooperation with host countries (https://reportinternational.org/). This platform facilitates future combined or comparative data analyses and serves as a vital resource for collaborations both within countries and internationally. Initially, Indonesia, coordinated by INA-RESPOND, along with India, South Africa, Brazil, and China joined the network. More recently, the Philippines, South Korea, and Uganda have come on board. The project has been implemented in two phases: Phase I (2013-2023, completed) and Phase II (2019-present).

The RePORT consortia are unified by a common data and specimen collection protocol. Each RePORT country focuses on bolstering local TB data and specimen repositories and related research. RePORT International has standard protocols for two study cohorts: Cohort A for active TB and Cohort B for household contact. Depending on their budgets, countries can participate in one or both cohorts. INA-RESPOND took part in Phase I, adopting Cohort A in the TRIPOD study (Tuberculosis Research of INA-RESPOND On Drug Resistance, NCT02758236). Annual meetings of RePORT International are convened to foster coordination among member countries, share updates in TB science, present junior investigators' research, and engage in high-level discussions. This year, the 7th RePORT International Annual Meeting spanned four days in Cavelossim, Goa, India, starting with a pre-meeting on September 5 and the main sessions from September 6-8, 2023. INA-RESPOND delegated Adhella Menur, a TRIPOD investigator, and Melinda Setiyaningrum, the TRIPOD Data Manager, to represent RePORT Indonesia.

The pre-meeting centered on data harmonization across the member countries. With Phase I completed, the RePORT International Data Manager team has been engaged in streamlining and storing the extensive database. Efforts have been made to harmonize data from bacteriologically confirmed TB adult patients from Cohort A in support of the RePORT International project titled "Epidemiologic factors associated with TB treatment outcomes across RePORT International consortia." This project aims to ascertain the impact of non-communicable diseases, such as prediabetes and diabetes, and communicable diseases like HIV on TB treatment outcomes and recurrence on both global and re-

gional scales. For this initiative, the TRIPOD study contributed data on 312 bacteriologically confirmed TB cases. The team is currently revisiting and finalizing data harmonization, targeting a database lock in October 2023, analysis in December 2023, and manuscript drafting in Q1 of 2024.

The RePORT International Data Manager team shared preliminary results and discussed challenges encountered during data harmonization. In Phase I, RePORT International merely provided guidelines for collecting study variables. Consequently, each country tailored its study Case Report Form (CRF), leading to varied data capture methods. Aligning CRF fields across countries proved challenging, with discrepancies most evident in areas like concomitant medications, non-TB disease history, and TB treatment compliance. Some CRFs also missed essential details or queries vital for effective data harmonization. For instance, the TRIPOD study's CRF overlooked demographic details such as occupation, income, and living conditions. Challenges also arose in harmonizing co-infections, comorbidities, and non-TB medication data. For the latter, while some countries recorded information at different visits, others lacked such data altogether. Technical issues, including incomplete dates, varying formats, and ambiguous blank values, further complicated the process.

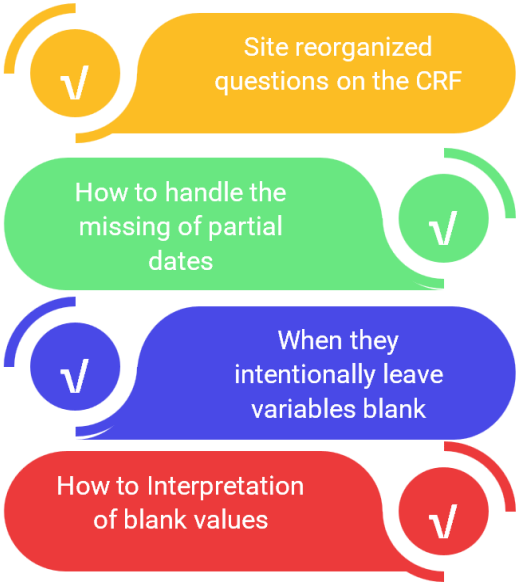


Fig 1. Challenges in RePORT International data harmonization

During the meeting, a productive discussion unfolded. The RePORT International team sought to address current challenges in data harmonization, draw lessons from them, and strategize for future projects, encompassing other cohorts and RePORT Phase II. For Phase II, collaboration is planned with the Frontier Science Foundation, a renowned non-profit research organization recognized globally for its trusted data management, statistical center, and publication support. Frontier Science will function as the central data-sharing hub, offering tools for secure data transfer. A specialized team will interpret the incoming data, ensuring thorough quality assurance and control, and addressing any issues directly with the data sender. The data will then be stored in a dedicated project database.

The second RePORT International project, titled "Analysis of host biomarkers associated with adverse TB treatment outcomes across RePORT International sites," was also deliberated upon. The objective is to broaden the validation studies of host biomarkers linked to TB treatment failure and to pinpoint a "cure" biomarker through a discovery-driven method. The TRIPOD study provided data on 11 failure cases and 22 cure cases for analysis. The TRIPOD team has secured IRB approval for this initiative from the Persahabatan Hospital Ethics Committee and is in the process of preparing the MTA for PAXgene RNA and Plasma shipment. This project is especially advantageous as RePORT International facilitates laboratory and data analysis training in Central Labs located in the United States, Brazil, India, and South Africa in 2024, aiming to enhance laboratory capacity across the member countries.

The subsequent three days comprised the main meeting. It offered extensive insights into the oper-

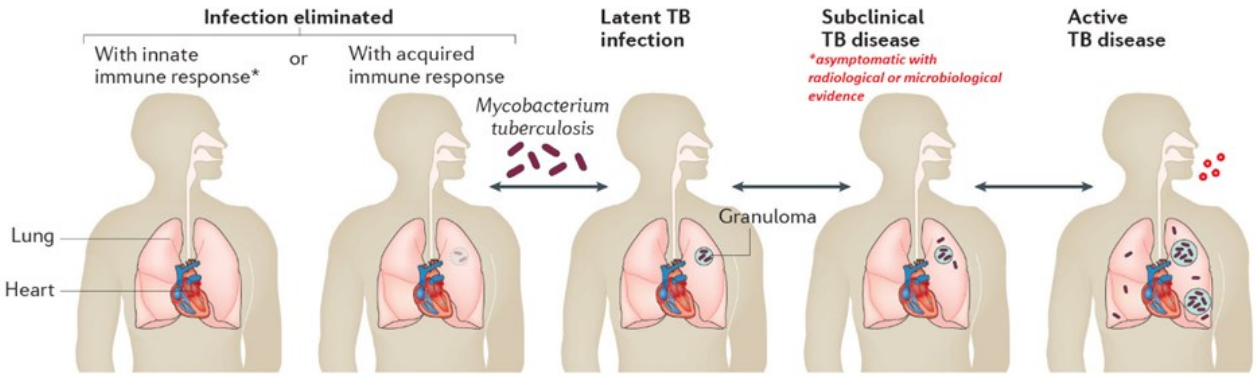


Fig 2. The spectrum of TB — from Mycobacterium tuberculosis infection to active pulmonary TB disease (Drain et al. Clin Microbiol Reviews, 2018 and Pai et al. Nat Review Dis Primers, 2017)

ations of the RePORT International Coordinating Center (TB RiCC), updates on TB science, and potential collaborations with other networks, such as TB-SRN of IeDEA. The TB RiCC undergoes restructuring every five years. Representing the leadership group, Jerrold Ellner introduced the revamped organizational structure, TB RiCC 3.0, for 2023-2028. A notable addition to the organization is the Scientific Review Committee (SRC), entrusted with overseeing scientific activities within the RePORT network, like concept sheet reviews, grant proposal evaluations, and more. The TB RiCC 3.0's roadmap encompasses updating the common protocol to reflect current knowledge, which includes integrating new procedures, visits, data, and specimens, conceptualizing RePORT Phase 3, introducing separate cohorts like diagnostics, early biomarkers, lung health, pediatrics, and studies on extrapulmonary TB, and drafting a Bylaws document that will detail regulations for RePORT projects. Ellner also showcased the current standing of the RePORT network, highlighting 32 study sites across six countries, encompassing 13,534 participants, 391,605 stored specimens, and over 140 associated publications, with a significant contribution from India, Brazil, and South Africa. He expressed optimism regarding the network's continued growth and productivity.

The sessions updating TB science covered a spectrum from basic research, subclinical TB, post-TB lung health, to vaccines. These also included presentations by Junior Investigators from the RePORT countries network. Subclinical TB emerged as a focal point in the scientific discussions. This category denotes a condition caused by viable MTB that doesn't manifest as clinical TB symptoms but triggers detectable abnormalities through existing radiologic or microbiologic assays. The progression from subclinical TB to active TB varies greatly, ranging from approximately 5-7 months to possibly 16 months. Intriguingly, many cases resolve spontaneously, while some individuals remain asymptomatic for extended periods (yet might be infectious). Subclinical TB is believed to account for nearly half of all transmission, and treatments might curb this spread. A study from Yogyakarta, Indonesia (Ananda NR, Trop. Med. Infect. Dis. 2023, 8(9), 447; https://doi.org/10.3390/tropicalmed8090447) disclosed that of the 47,735 individuals who participated in the active case finding (ACF) program via chest X-rays, 393 were diagnosed with TB. Remarkably, 176 of these 393 cases (44.8%) were asymptomatic, with 52 of the 176 (29.5%) being bacteriologically confirmed. This underscores the pressing need to comprehend and formulate data-driven guidelines for diagnosing and managing subclinical TB.

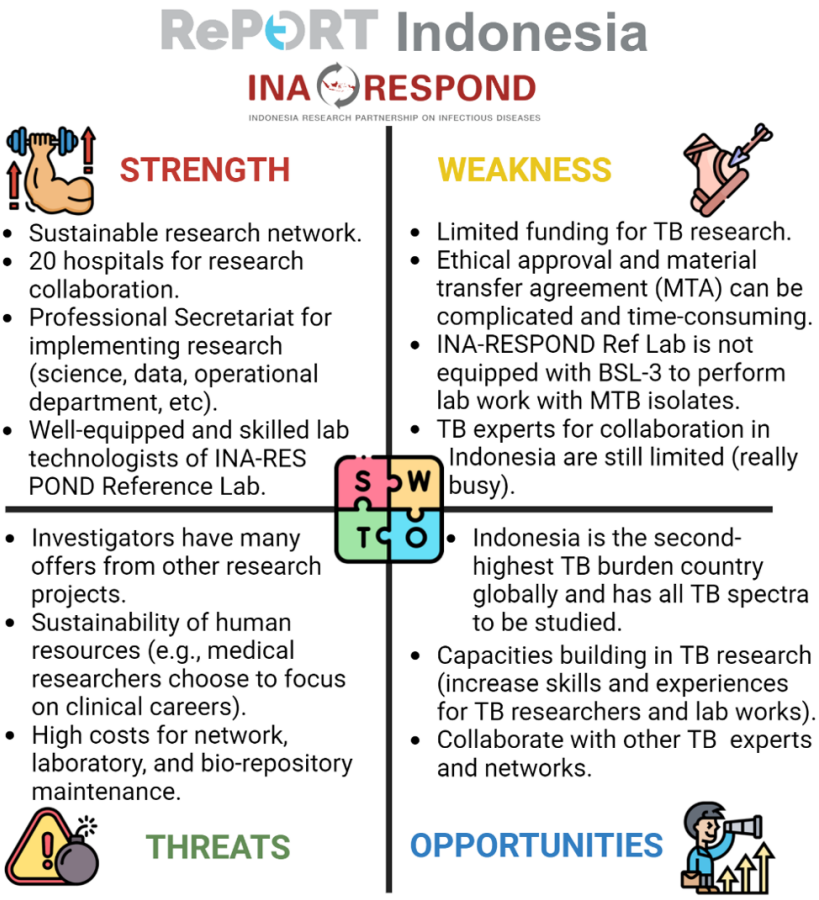
A significant area of scientific interest was lung health following TB treatment. According to Dodd et al. in Lancet Infect Dis., as of 2020, an estimated 155 million TB survivors were alive worldwide. The pooled standardized mortality ratio for TB survivors stood at 2.9 compared to individuals without TB. TB survivors face risks of TB recurrence and other diseases, including post-TB lung disease, cardiovascular disease, lung cancer, and autoimmunity. Post-TB lung disease is a chronic respiratory condition, with or without symptoms, largely attributed to prior TB. This ailment can lead to COPD, restrictive ventilatory defects, aspergilloma, exacerbations of bronchiectasis, and pulmonary hypertension. Overcoming TB is a prolonged journey that doesn't conclude with the final dose of anti-TB medication. Continuous monitoring after TB treatment is essential to enhance survivors' health and quality of life. There's an anticipation for studies focusing on lung health post-TB treatment, which would delve into the degree of lung injury, markers, prevention, and management.

Updates from the VPM1002 study by the Serum Institute of India PVT. LTD., concerning a next-generation BCG vaccine, were also noteworthy. VPM1002 is a genetically modified BCG vaccine, promising enhanced immune activation and greater safety compared to traditional BCG. The vaccine successfully cleared phase I clinical trials in Germany and South Africa, proving its safety and immunogenicity in young adults. It was also validated in a phase IIa randomized clinical trial involving healthy South African newborns and a phase IIb trial with both HIV-exposed and unexposed infants. Subsequent trials are underway, including a phase III efficacy study in newborns to prevent MTB infection, trials in pulmonary TB patients post-successful TB treatment to avert TB recurrence, and in healthy household contacts of recently diagnosed sputum-positive TB patients to guard against MTB infection.

Six Junior Investigators, three from RePORT India, two from RePORT Brazil, and one from RePORT South Africa, showcased their research using data and specimens from their respective countries. These nations have matured in TB research, boasting advanced laboratory testing and academic collaborations. The presentations covered a range of topics, from TB recurrence, the influence of pre-existing nutritional status on TB severity, to the pharmacokinetics of Moxifloxacin in MDR-TB patients. The inclusion of Junior Investigator presentations is a staple at the RePORT annual meetings, aiming to foster scientific zeal among emerging researchers and ensure generational continuity. RePORT Indonesia aspires to send a larger contingent of young, gifted researchers to subsequent meetings, hoping for an even greater contribution.

On the concluding day of the RePORT Goa assembly, the network addressed updates and challenges encountered by each country. Representatives from every country provided a 20-minute brief on the status of ongoing projects, related scientific endeavors, SWOT analysis, and the potential to pursue studies on subclinical TB and its long-term ramifications. Representing Dr. Erlina Burhan for RePORT Indonesia, Adhella Menur showcased the TRIPOD study and associated publications. She elaborated on RePORT Indonesia's endeavors in dissecting the TRIPOD data, pursuing collaborations, securing funding, and fortifying laboratory capabilities. A noteworthy collaboration involved fungal experts Retno Wahyuningsih and David W. Denning, culminating in the publication titled "The seroprevalence of anti-Histoplasma capsulatum IgG among pulmonary TB patients" in the PLOS NTD Journal. Sadly, several attempts to secure TB research grants were unsuccessful. As part of their laboratory capacity-building efforts, the INA-RESPOND Reference La-

boratory has been actively performing TB tests on specimens from the TRIPOD repository, utilizing techniques like whole genome sequencing with Oxford Nanopore's MinION and Sanger sequencing. Adhella also presented RePORT Indonesia's SWOT analysis, emphasizing the commitment of INA-RESPOND and its hospital networks to advance TB elimination. By contributing more to the RePORT International network and participating in TB studies, RePORT Indonesia is geared up to collaboratively combat tuberculosis.



See you at the RePORT annual meeting in Brazil next year!

TB RiCC 3.0 Pilot Proposal Program

The Request for Application (RFA) soon will be announced. This program will fund two TB proposals. It must include at least two RePORT networks using RePORT data and specimens—the application deadline in December 2023.

TB RiCC 3.0 Capacity Strengthening Working Group Programs

E-learning TB courses and a 2-year mentored Post-Doctoral Fellowship Program for early-stage investigators (MD and/or Ph.D with <10 years' experience since recent graduation). The mentorship program will fund two fellows annually from RePORT countries network. Applications open in January 2024.

INA-RESPOND Newsletter

THE FACTS OF HIGH RISK SPORTS AND PHYSICAL ACTIVITY IN FEMALE

By: Risky Dwi Rahayu

SPORTS & LIFESTYLE

Over the past decade, female participation in sports has seen a significant rise. This was evident in the 2023 FIFA Women's World Cup in Australia/New Zealand, where 32 teams competed. This is an increase from the previous Women's World Cup, which featured only 24 teams.^1 The 64 matches attracted nearly two million spectators, averaging 30,911 attendees per stadium. Additionally, records from the United States marathon reveal that the percentage of female finishers surged from 11% in 1980 to 45% in 2017.^2

However, increased participation in sports also introduces risk. Studies have confirmed that injury patterns differ between male and female athletes. A retrospective cohort from the National Collegiate Athletes Association (NCAA) Division III, spanning 1980-1995, highlighted that female athletes aged 18-22 years in sports such as basketball, cross country running, soccer, tennis, track, and water polo experienced injuries less frequently than their male counterparts. The injuries these females encountered were predominantly located in the shoulder, hip/groin, and lower leg areas.^3 More recent data from elite athletes aged 16 and above across several team sports revealed that while female athletes generally suffer fewer injuries, they exhibit a higher incidence rate ratio of ACL sprains compared to male athletes.^4 Furthermore, ACL sprains from non-contact mechanisms account for 55% of all ACL injuries, with a higher occurrence in females, particularly during competitions and among adolescents.^5 In track and field events, data from 14 elite international championships between 2007 and 2014 indicated that male athletes have a higher injury rate per 1000 athletes compared to females.^6 Yet, injury types vary: male athletes primarily reported hip/groin, thigh, and lower leg injuries, with strains and cramps being predominant, while female athletes reported a higher incidence of stress fractures. Another NCAA study noted that between 2004 and 2009, female athletes had a 1.4 times higher concussion rate in ball sports than males and needed more recovery time.^7

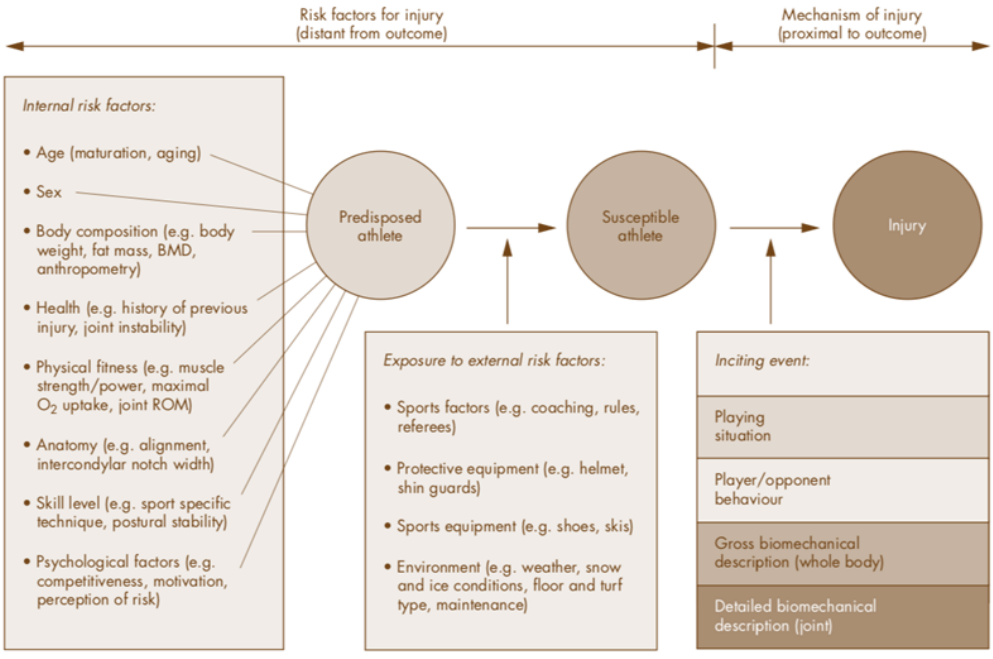


Figure 3 Comprehensive model for injury causation. BMD, Body mass density; ROM, range of motion.

There are multifaceted reasons behind the incidence of injuries in female athletes. These can be grouped into internal risk factors, external risk factors, and inciting events.^8 Anatomically, females typically possess a wider pelvis and increased Q angles, coupled with smaller ligaments, which result in more anterior knee laxity.^8-10 Poor neuromuscular control during activities like running, jumping, and quick directional changes can lead to dynamic valgus, especially if there's a deficit in attention during high-pressure situations.^11,12 This may cause high-risk knee movements. Females might also utilize different stabilizing strategies during body contact, possibly due to factors such as lower neck strength and higher impact forces.^13,14 Furthermore, long-term energy deficits—either from inadequate energy intake or excessive training—can cause hormonal imbalances, menstrual dysfunctions, and impaired bone health, all part of the female athlete triad.

Given the data, various sports and physical activities pose injury risks to female athletes. Activities that involve contact, are team-based, or require sudden changes in direction, such as many team sports, heighten the risk of ACL injuries. Conversely, sports that emphasize a lean body physique, have revealing uniforms (like gymnastics, figure skating, and martial arts), categorize participants by weight classes (as in certain martial arts), or demand high energy expenditure (as seen in athletics or track and field) tend to increase the risk of stress fractures for female athletes.^15,16

Recognizing these inherent risks underscores the importance of prevention over treatment and rehabilitation. Regular screenings that evaluate a female athlete's anatomy, biomechanics, metabolic health, energy availability, training regimen, and psychological well-being in relation to her sports performance are crucial. Any female engaged in these high-risk physical activities is strongly advised to consult with a sports and exercise medicine physician. This not only helps in identifying and assessing injury risks but also ensures prompt treatment, if needed. Moreover, ongoing evaluation can optimize performance and significantly reduce the likelihood of injuries.

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COMIC CORNER

UNVEILING THE HAWTHORNE EFFECT: WHEN A MILLION EYES ARE WATCHING

By: Aly Diana

The Hawthorne Effect, initially observed in a workplace setting, extends its influence to medical research across various domains. Named after the Western Electric Hawthorne Works where it was first discovered, this phenomenon suggests that individuals adjust their behavior when they know they are being observed. In medical research, the Hawthorne Effect can sometimes persist despite conventional techniques like randomization and blinding, causing headaches for researchers when it is not anticipated from the beginning. In this article, we briefly explore the Hawthorne Effect's impact on medical research and discuss strategies for addressing its persistence to better prepare our research strategies.

The Hawthorne Effect, evident in various forms in medical research, poses persistent challenges despite rigorous attempts to mitigate it through techniques such as randomization and blinding. This phenomenon can erode the credibility of medical research, notably when it compromises the effectiveness of interventions by influencing participant behavior. Such shifts in health practices, driven by awareness of being studied, can introduce bias and skew study outcomes. Beyond participants, healthcare providers and caregivers may also exhibit behavior modifications, as emphasized in prior research, underscoring the broad reach of this effect in the medical field.

To address the persistent Hawthorne Effect in medical research, several strategies can be employed. Long-term surveillance is one approach, involving extended monitoring of participants beyond the initial study period. This extended obser-

vation allows participants to acclimate to the research environment, potentially reducing the influence of the Hawthorne Effect over time. Additionally, prioritizing the use of objective measures, such as biomarker levels or disease progression, can minimize the impact of the Hawthorne Effect, as these data are less susceptible to participants' awareness of being observed. Employing a mixed-methods research approach, which combines quantitative data with qualitative insights gathered through behavioral surveys or interviews, can provide a comprehensive understanding of behavior changes among both participants and healthcare providers. Finally, conducting post-study debriefing sessions with participants and healthcare providers offers an opportunity for open and transparent discussions about the Hawthorne Effect's impact on their behavior, yielding valuable insights for future research endeavors.

The Hawthorne Effect has long been a topic of debate and discussion in the realm of research and social sciences. While it is widely acknowledged that individuals may alter their behavior when they know they are being observed, the extent and significance of this effect continue to be subjects of scrutiny. Some researchers argue that the Hawthorne Effect can be substantial, leading to notable changes in behavior that can influence research outcomes significantly. Others contend that its impact may be more subtle or context-dependent, suggesting that not all studies are equally susceptible to its influence. Additionally, there is ongoing debate regarding the ethics of the Hawthorne Effect—whether it is an unintended bias that should be minimized or a valuable phenomenon that can offer insights into the psychology of human behavior. This ongoing discourse underscores the complexity of the Hawthorne Effect and the need for careful consideration when designing and interpreting research findings.

Amid the debates surrounding the Hawthorne Effect, what remains paramount for researchers is a keen awareness of potential influences on their studies. Being well-prepared and anticipating various factors that may affect research outcomes is a fundamental aspect of robust research design. By planning meticulously and considering the potential impact of the Hawthorne Effect or other sources of bias, researchers can aim to minimize unexpected surprises and ensure the credibility and validity of their findings. In essence, a proactive and thoughtful approach to research planning and execution can be the key to avoiding later regrets and enhancing the quality of research outcomes.

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