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INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

October 2019

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

INA-PROACTIVE Site Preparation Visit at Site 520

8 October 2019

INA-RESPOND newsletter

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INA-RESPOND Newsletter

TRIPOD & INA-PROACTIVE Study Updates

By: Eka Windari R., Lois E. Bang, Maria Intan Josi, M. Ikhsan Jufri, Venty Muliana Sari

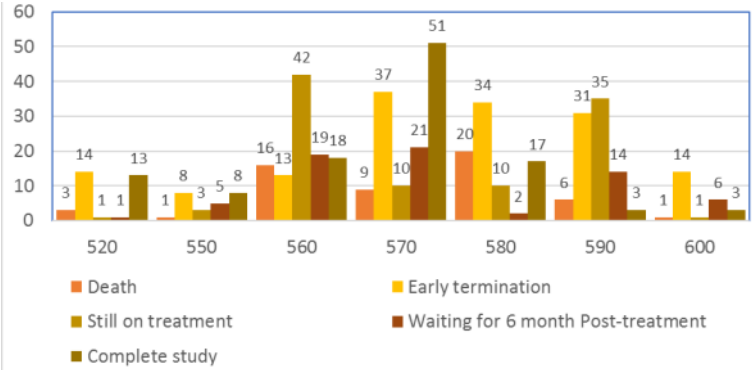

Figure 1.Participant status per site based on uploaded CRF per 31 Sept 2019

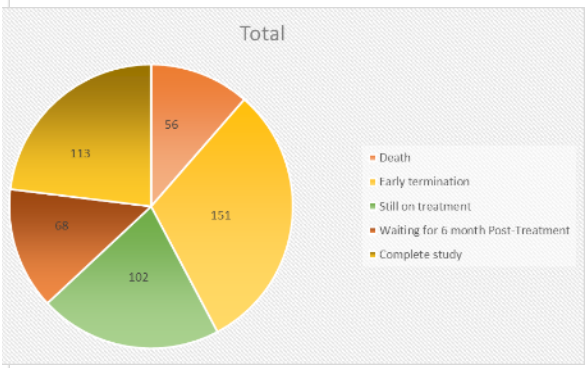

Figure 2. Total Participants Status based on uploaded CRF per 31 Sept 2019

STUDY UPDATES

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PARTICIPANT STATUS

Per 31 September 2019, the total ongoing participants in TRIPOD study are 170 out of 490 enrolled participants. From those 170 ongoing participants, 102 are still on TB treatment while 68 are waiting for 6-month post-treatment visit. One hundred thirteen participants have completed the study while 207 participants are terminated early (including death). Therefore, there are still 34.7 % participants from the total enrolled participants in the follow-up status. From the uploaded CRFs, there are 2 participants from site 520 (RS Sanglah Denpasar) who still need to be followed up, 8 participants from site 550 (RSUP dr. Wahidin Sudirohusodo Makassar), 61 participants from site 560 (RSUP dr. Kariadi Semarang), 31 participants from site 570 (RSUD dr. Soetomo Surabaya), 12 participants from site 580 (RSUP dr. Sardjito Jogjakarta), 49 participants from site 590 (RSUP Persahabatan Jakarta), and 7 participants from site 600 (RSUP dr. Adam Malik Medan).

Result for baseline culture and DST from all sites are not complete yet. The six sites that have all the full results for culture and DST are site 520, site 550, 570, 580, 590, and 600.

Site	Waiting for Baseline Study Culture Result	Waiting for Baseline DST Result
520 (n=32)	Complete	Complete
550 (n=25)	Complete	Complete
560 (n=108)	Complete	2
570 (n=128)	Complete	Complete
580 (n=83)	Complete	Complete
590 (n=89)	Complete	Complete
600 (n=25)	Complete	Complete

Figure 3.Culture and DST results up to 30 June 2019

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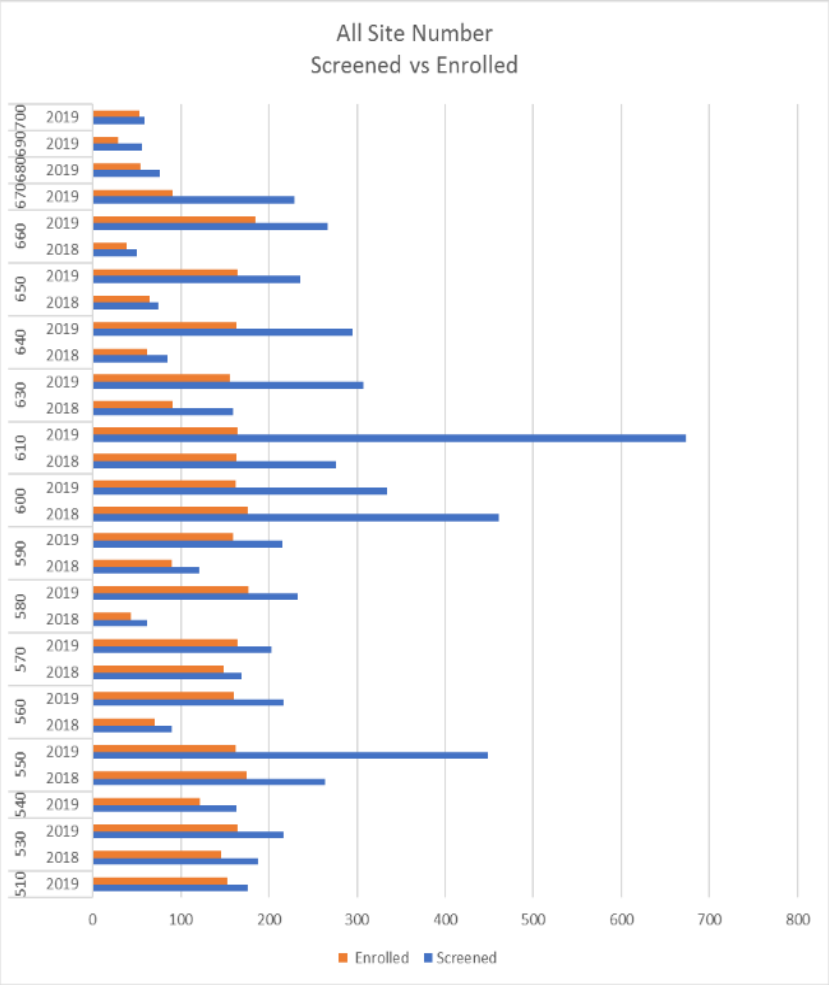
Screening and enrollment activities at all 18 sites is ongoing. As of Oct 13, a total of 3,748 subjects were enrolled which consist of 3,584 adults and 164 pediatrics from a total of 6,401 subjects screened. The enrollment rate was 58.55% from total screening, details are shown in Figure 1.

The total end of study and existing subject details is shown in Figure 2.

Several site visits for INA-PROACTIVE study has been conducted within this latest one month (between 12 September 2019 – 21 October 2019), the details are:

- NIHRD IRB Monitoring Visit to RSUD TC Hillers, Maumere on 11 September 2019
- 2nd Site Monitoring Visit to RSUP Hasan Sadikin, Bandung on 16-18 September 2019
- 4th Site Monitoring Visit to RSUP Wahidin Sudirohusodo, Makasar on 23-24 September 2019
- 2nd Site Monitoring Visit to RSPI Sulianti Saroso, Jakarta on 7-9 October 2019
- Site Preparation Visit to RSUP Sanglah, Denpasar on 7-9 October 2019
- Site Initiation Visit to RSUP Sanglah Denpasar on 15-16 October 2019

As a new site, Sanglah Hospital preparations are progressing. Equipment needed for the study has started to be delivered. The site is currently waiting for the delivery of the GeneXpert Viral Load machine. After this equipment is available on the site, training in the use of GeneXpert VL and PIMA Analyzer will begin. The Research Team at this site and also INA-RESPOND Secretariat are committed to preparing for the activation properly. It is hoped that this site can be activated in early November 2019.



Site Number	Subject		Total End of Study	Total Existing Subject
	Total Screened	Total Enrolled		
510	176	153	0	153
530	403	310	6	304
540	163	122	0	122
550	712	337	13	324
560	306	230	6	224
570	372	313	0	313
580	295	220	0	220
590	336	249	15	234
610	795	338	5	333
600	950	327	8	319
630	466	246	1	245
640	380	225	0	225
650	310	229	3	226
660	317	222	1	221
670	229	91	0	91
680	76	54	0	54
690	56	29	1	28
700	59	53	1	52
Grand Total	6,401	3,748	60	3,688

Figure 2. Total end of study and existing subject

INA-RESPOND Newsletter

NIHRD ETHICS COMMITTEE ONSITE MONITORING VISIT

By: Neneng Aini

NIHRD Ethics Committee Onsite Monitoring Visit to INA-PROACTIVE Study Site

TC Hillers Hospital, East Nusa Tenggara

The NIHRD Institutional Review Board (IRB) onsite monitoring visit was conducted on 11 September 2019, and the meeting was attended by the Chair of NIHRD IRB, Prof. Dr. M. Sudomo; NIHRD IRB member, Siti Sundari, MPH, D.Sc.; NIHRD representative, dr. Dona Arlinda; INA-RESPOND Secretariat representatives: Ms. Meity Siahaan, Ms. Lois Eirene Bang, and Ms. Neneng Aini; TC Hillers Hospital research team; the hospital Director; and management staffs. The purpose of the visit is to assess the performance and implementation of INA-PROACTIVE study, compliance with the approved study protocol, applicable regulation, and Good Clinical Practices guideline.

Prof. Sudomo gave presentation on Ethical Issues in Clinical Research. Since this site did not have local Ethics Committee (EC), they had a lot of questions during the discussion. They were planning to establish their own EC and requested the NIHRD IRB to train their staff.

This site is located in eastern Indonesia, in East Nusa Tenggara Province. Officially joined the INA-RESPOND Research Network in April 2019 as the 17th active sites for INA-PROACTIVE study. As on the NIHRD IRB standard of procedure for onsite monitoring, one of their selection criteria is a new site with no experience in conducting multi-center clinical research.

Prof. Sudomo said that a study protocol reviewed by health research EC or IRB is required by the international ethical standards governing research involving human participants. Review is also essential if the researchers intend to publish the results of their investigation, as most medical journals will not release the results of research without approval from a research ethics committee.

The primary responsibility of a health research EC or IRB is to protect potential participants in the research, but it must also consider potential risks and benefits for the community in which the research will be carried out. The ultimate goal is to promote high ethical standards in research for health. The purpose of initial EC review is to contribute to safeguarding the dignity, rights, safety, and well-being of all actual or potential research participants, while the purpose of a continuing review is to monitor the progress of the study which was previously approved; not only for the changes but also to ensure continuing protection of the rights and welfare of research subjects. The continuing review activities involve review of the progress of the study, annual reports, protocol deviations/violations, serious adverse event monitoring, and on-site monitoring. International and national regulations and guidelines for continuing review state that it is an opportunity for the EC to be assured that risks to subjects are minimized and is are reasonable in relation to anticipated benefits if any to the subjects and the knowledge it will generate.

INA-Proactive study obtained ethical approval from the NIHRD IRB prior the study starts on 10 January 2018 with Ethical Clearance Number LB.02.01/2/KE.012/2018. The continuing review for study progress was submitted bi-annually and obtained the extended ethical approval prior to its expiration date. Of 18 active sites for INA-Proactive study, 3 sites chose to use their own local IRB as their IRB of record while the other 15 sites chose to rely on the NIHRD IRB as on the signed reliance agreement for each site. Site TC Hillers Hospital choose NIHRD IRB as their IRB of record.

During the visit, NIHRD IRB reviewed study documents, including source documents, study standards of procedure, site's facilities, and specimen management. At the end of site visit, they gave recommendations to the site and INA-RESPOND Secretariat that could improve study implementation at this site and other INA-PROACTIVE study sites.

The recommendations were related to the specimen management and specimen testing result reporting procedure and additional information in the bi-annual study progress report. This visit is vital for NIHRD IRB, the site, and INA-RESPOND Secretariat. As part of capacity building for NIHRD IRB, this visit gives experience and opportunity to get the full picture on how INA-RESPOND implement the approved study protocol and ensure the same standards were implemented at each site since. It also indirectly ensures quality assurance and training for research staff and most importantly ensures that there are no breaches or lapses in the integrity of data. Active on-site monitoring helped the IRB to identify problems related to the implementation of GCP which could not have been detected by the passive ongoing review of study-related documents carried out routinely. For the site and INA-RESPOND Secretariat, this visit gives us new experience on the IRB point of view to ensure the safety and well-being of the study participants. The recommendation will be appropriately implemented at the site.

INA-RESPOND Newsletter

CORRECTIVE ACTION PREVENTIVE ACTION PLAN

By: Susan E. Vogel, RN, BSN

"To address this mistake we need to utilise our thorough system of root cause analysis. I will begin, if I may, by pointing out that it's not my fault"

FROM OUR SPONSOR

As the saying goes, "into every life a little rain may fall, into every study something will go wrong." When they do go wrong, a corrective action and preventive action (CAPA) plan can provide a structure for finding the root cause of the issue/problem identified, solving the issue, documenting, and providing solutions to prevent the re-occurrence. Corrective Action is the elimination of the cause or causes of the existing issue to prevent a recurrence. Preventive Action is the identification and elimination of the cause(s) of potential issues to prevent occurrence. Implementing a corrective action would be considered a reactive approach to the issue that would also include a preventive component. A preventive action, though, can be considered as a proactive approach resulting from analysis of information and data. With a good quality management structure in place, often the preventive action precedes corrective action. A quality management assessment will identify potential risks so processes can then be put into place to mitigate the risks before they occur. But when something does go wrong, a corrective action and preventive action (CAPA) plan needs to be put into place.

To ensure a robust CAPA plan is written, the EXACT principle should be used.

Examine the root cause.

eXecute the specific plan.

Adequately document the action plan.

Carry out for future subjects/studies.

Timely review of the effectiveness of the plan.

It is critical to determine the root cause of what went wrong and the process(es) that lead to it. Remedial action addresses only the visible indicator of the protocol and not the actual cause. To just say "participant signed the wrong consent form" is not getting to the root cause of the issue. Use the "5 Why Questioning" as an effective method to obtain all the information as well as help determine if this is an isolated event or more significant and has the potential to recur. Below is an example of the 5 Why Questioning.

1. "Why did the participant sign the wrong consent form?" It happened because the study team member quickly grabbed the incorrect version that was in the clinic.

2. "Why is that?" They keep a stack in the clinic to have readily available and the consents were the wrong version.

3. "Why is that?" The version was recently updated, and the consents did not get switched out before the participant was to be consented.

4. "Why is that?" It is not anyone's particular job to ensure that it is done in a very timely fashion.

5. "Why is that?" The SOP does not clearly state that a particular staff member upon receipt of a new version must immediately update the consents in the clinic area.

In executing a corrective plan, the plan should clearly define targets and timelines, determine staff who will implement the plan, identify any additional documentation that is needed or required to address the issue. Be sure to determine the solution that will prevent a recurrence.

Adequately document the action plan using a template CAPA plan applying the EXACT method when writing it. The CAPA plan should include: Protocol title and number, Site name, Principal Investigator name, name of person completing the document, date CAPA plan written within the header of the document. The body of the document would have the following sections: 1) Date of problem; 2) nature of the problem; 3) problem root cause analysis, problem risk analysis, 4) correction action (s), 5) preventive action(s) and 6) follow-up/effectiveness of action plan.

Once the plan is written, it is important to not only carry out the actions for all current protocols but for all future protocols by ensuring that all updated applicable documents such as SOPs, templates, and forms are available for use by the staff. Ensure the implementation of new processes and that appropriate staff are aware of the implementation dates. Any training that is done whether self-training through review of updated documents or in person training needs to be well documented and filed in protocol site files.

A timely review to verify that the actions continue to be effective and that the problem does not recur is critical. As mentioned before, the CAPA plan should contain a timeline of the assessment of quality control mechanism (s) to determine if the plan needs to be adjusted further.

Example of a CAPA Plan

Date of problem: 27 Sept 2019

Nature of Problem: Participant ABC-123 signed the incorrect version of the consent, version 3.0 signed when version 4.0 was the approved version.

Root Cause Analysis: It was determined that no one person was assigned the task to update the consent forms that are kept in the clinic area causing an older version to be used as it was not replaced when the new version was approved.

Problem Risk Analysis: A review was performed to ensure no other participants signed the wrong version and it was determined this was a single error. No other protocols had the incorrect version of the consent in the clinic area.

Corrective Action: Participant was re-consented to the most current version of the protocol and an explanation provided to participant about what was different between the versions. This has been documented in the participant's chart. All incorrect versions of the consent have been removed from the clinic and replaced by the correct version.

Preventive Action: The SOP has been updated to reflect that the study coordinator is responsible to ensure that the most current version of the consent is placed in the clinic as soon as it is available and will destroy all old versions. Staff has reviewed and signed off on new SOP regardless of what study they are working on. Staff, who consent participants, also trained to check version of the consent to ensure it is the most current one prior to consenting a participant.

Effectiveness of Action Plan: All consents within the clinic will be QC'd on an every other week schedule by an assigned staff member to ensure that the correct version for a given protocol consent is on file for use.

INA-RESPOND Newsletter

PNEUMOCOCCAL VACCINE FOR CHILDREN: A LONG ROAD OVER A CENTURY TO FIND A WAY BACK

By: dr. Adhella Menur

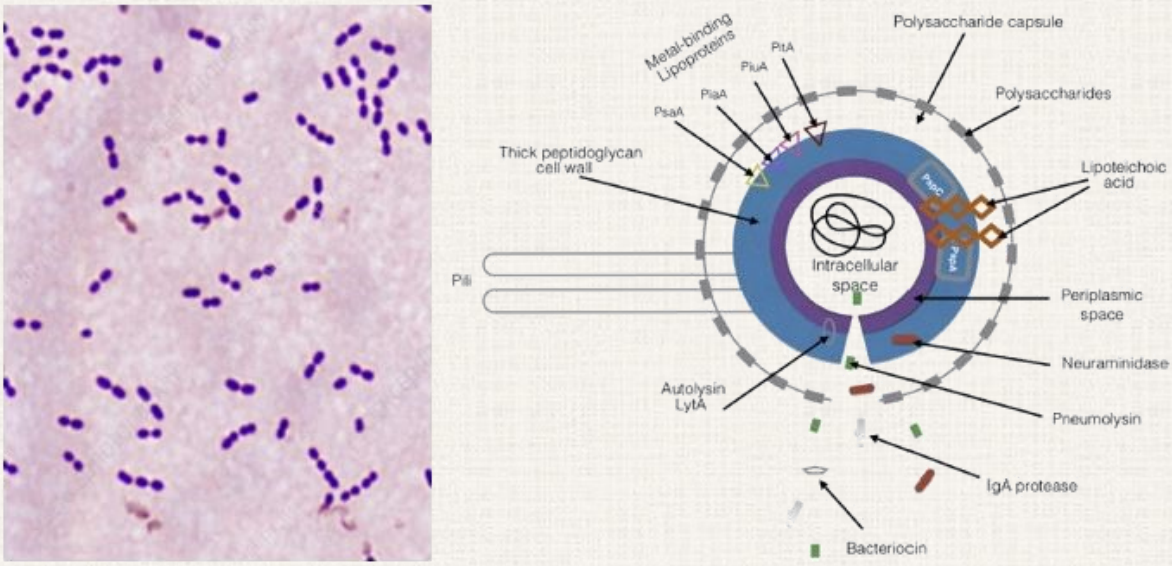


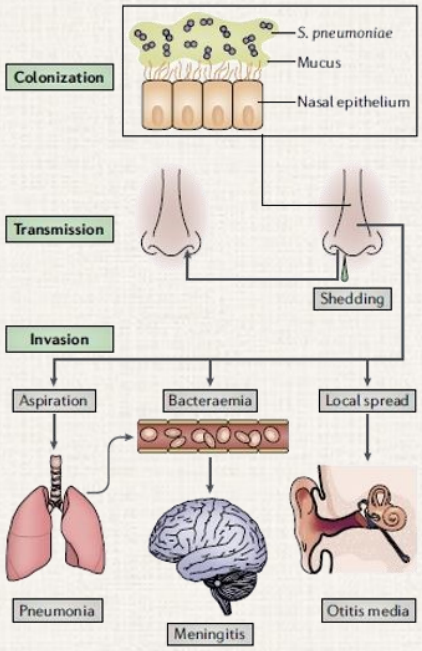
Figure 1. Pneumococcus under the microscope (gram-positive) and the schematic figure of its virulence factors[6]

Streptococcus pneumoniae or pneumococcus is a 0,5-1,25 um "lancet-shaped," gram-positive, extracellular bacterium that can act as commensal or pathogen in human. In 1881, George Sternberg and Louis Pasteur isolated the pneumococcus from the septicemia rabbit independently. In 1918, the year of the influenza virus pandemic, secondary pneumococcus pneumonia infection contributed to the highest number of mortalities.[1]

The clinical spectrum of pneumococcus infection is ranging from mild to severe and lethal disease. Pneumococcus infection is divided into non-invasive pneumococcal disease (NIPD) that limited to human mucous such as otitis media, sinusitis, and pneumonia without bacteremia and invasive pneumococcal disease (IPD) that invade the sterile body area like pneumonia with bacteremia and/or empyema, sepsis, and meningitis. Children under two years who are still developing the immune response are the most prone population for the pneumococcal infection with 700,000-1 million mortality numbers annually worldwide.2 Pneumococcus is contributing in 15% children pneumonia cases and 22.5%-41% meningitis cases worldwide with high numbers of case fatality rate.[3,4]

Pneumococcus has several virulence factors that make it a harmful pathogen, including polysaccharides capsule, surface proteins, excreted proteins, and cytoplasmic proteins. The major virulence factor is polysaccharides capsule that protects pneumococcus from complement-mediated opsonophagocytosis. It is also the basis of epidemiological pneumococcus categorization based on the serotype and serogroup. A serotype is defined as pneumococcal strains producing a polysaccharides capsule with unique chemical structure and immunologic properties. A serogroup is defined to include serotypes that share many immunologic properties like cross-reactive antibodies. To date, 48 serogroups with 97 separate capsular serotypes have been identified according to the Danish nomenclature system. Six serogroups (1, 3, 6, 14, 19, and 23) are identified as the most cause of IPD in children.[5]

The first important step of the pneumococcus infection is colonization in the nasopharynx. The main bacterial features that facilitate colonization are adherence to host cells and tissues, subversion of mucosal innate and adaptive immunity, and evasion of clearance by the mucociliary flow. Once the immune system is disrupted and/or imbalanced normal flora happens, the colonization will become infection. 27%-65% of healthy asymptomatic children are carriers and transmitters for the pneumococcus. Colonization rates are higher in situations of overcrowding such as in day-care centers, orphanages, winter, recent viral respiratory infection, maternal pneumococcal carriage, and passive smoke. The carrier rate is reduced in adolescents (6%-10%) to 3%-4% in adult population. However, adults and elderly who are living with children in house can have high-



er colonization. There was a spike in pneumococcus infection among elderly persons in the first week of the year following the holiday season, suggesting that it was transmission of these types from young children to their grandparents. Those facts make children as important population who role as epidemiological driver for this infection[6,7]

The management of pneumococcus infection becomes complicated as there is increasing numbers of antibiotic resistance pneumococcus strains. Multidrug resistance pneumococcus strains numbers in Asia are reaching up to 59.3%.8 Pneumococcal vaccine is an amenable choice upon the high numbers of morbidity and mortality accompanied by those increased rates of antibiotic resistance.

There was a quite interesting history of pneumococcal vaccine development. Started in 1911, British physician Sir Almroth Wright conducted three large clinical trials of the whole killed cell pneumococcal vaccine among young South African gold miners. In his third trial, a dose of 500 million organisms reduced pneumonia incidence by 25–50% and the death rate by 40–50%. During his trials, serotyping methods with a classification system were developed by other researchers, and serotype -specific pneumococcal polysaccharide vaccine (PPV) took over the show. Franz Neufeld and Ludwig Handel developed a method to distinguish serotypes of pneumococcus known as quellung (swelling) reaction. Independently, F. Spencer Lister developed a distinct typing system based on phagocytosis and specific agglutination. Lister used his typing system in 1914 to develop the first serotype-specific whole-cell pneumococcal vaccines, containing his serotypes A, B, and C (now known as serotypes 2, 1, and 5).[1]

From 1942 to 1945, Heidelberger, Colin M. MacLeod, and Paul Kaufman tested a PPV against serotypes 1, 2, 5, and 7. Among more than 5000 vaccine recipients, the research team calculated a 90% reduction in pneumococcal pneumonia and bacteremia. In 1947, E.R. Squibb & Sons obtained a license in the US to distribute two forms of hexavalent PPV (adult formula against serotypes 1, 2, 3, 5, 7, and 8, while children formula against serotypes 1, 4, 6, 14, and 18). Unfortunately, Squibb's vaccines ceased because of the preferable usage of penicillin that was discovered by Nobel prize winner Alexander Fleming, a former Sir Wright's assistant.[1,9]

In early 1970, the interest of vaccine development arose again as antibiotic-resistant contributed to 17%-30% of pneumococcus infection mortality. Briefly, results from several separated trials conducted by US National Institute of Health (NIH), Merck Sharp and Dohme (MSD), and Ian Riley et al. supported the urgency of PPV to reduce morbidity and mortality from pneumococcus infection. In the 1983, the World Health Organization recommended 23-valent vaccines (PPV23) with serotypes covering about 87% of pneumococcus infection in the US. However, it has some limitations, with the major issue being poor immunogenic in children under two years old. Antibody concentrations after subsequent doses of PPV23 appeared to be lower than those after primary vaccination that are related to the large amounts of polysaccharides, which exhaust the memory B-cell pool without replenishment.[1]

Third-generation vaccines, pneumococcal conjugate vaccine (PCV), in which capsular polysaccharides are conjugated to a protein were developed to improve the immune response to the capsular polysaccharide in young children. PCV7 (4, 6B, 9V, 14, 18C, 19F, 23F) was introduced in 2000, followed by PCV10 (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F) in 2009 and PCV13 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in 2010. PCV routine vaccination of infants and young children has led to a significant reduction of pneumococcus infection. High PCV efficacy also gives a positive public health impact with indirect protection to unvaccinated population (herd immunity). This herd-protection effect is the result of reduced transmission of vaccine-type pneumococcus in the community as a result of decreased carriage.1 In 2017, Indonesia had begun the PCV pilot project in Lombok and planned to add the vaccine into the national immunization program like other 134 countries worldwide.[10]

Meanwhile, the 'serotype replacement' issue becomes the challenge in PCV glory. The new emergence of serotype 19A infection after introduction of PCV7 and then 35B infection after introduction of PCV13 were identified. Pneumococcus is like an enemy who can change their capsule under antibody pressure to escape from the vaccine soldier. PCV15 with two serotypes (22F and 33F) added in PCV13 is under clinical trial. The PCV manufacture is complex with limited serotypes contain because

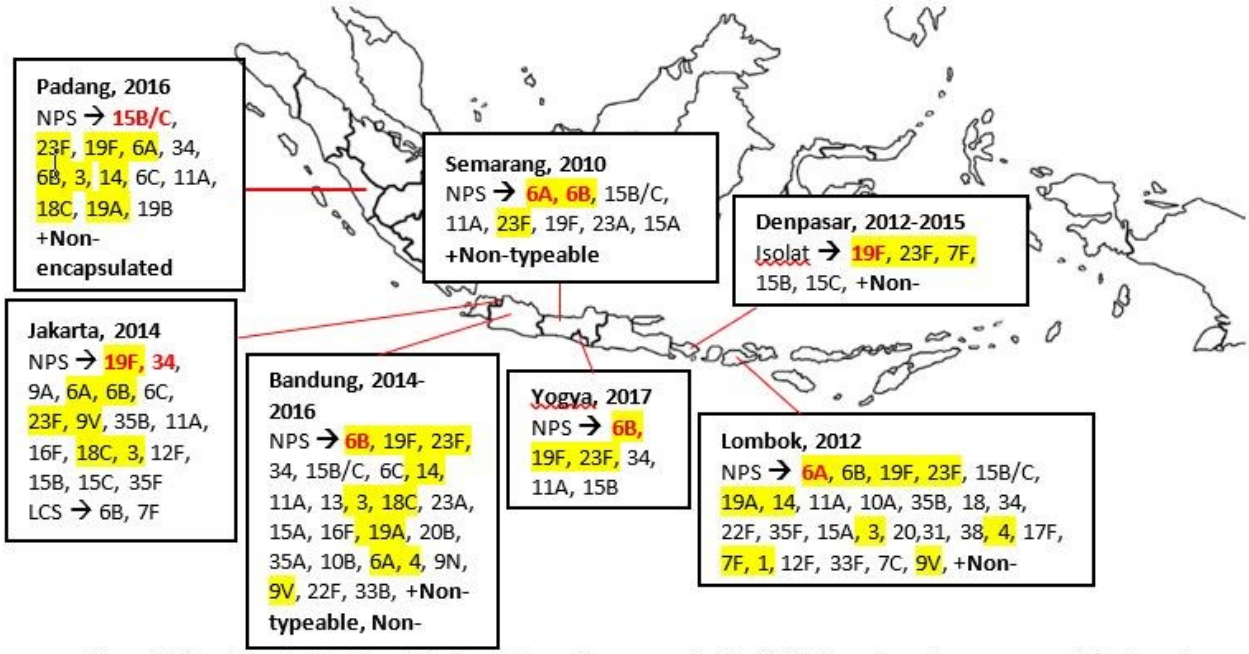


Figure 3. Serotype distribution in Indonesia based on many studies.[13-20] The red numbers represent dominant serotype and the yellow blocks represent serotypes in PCV13 coverage. NPS: *nasopharyngeal swab*, LCS: *liquor cerebrospinal*

excessive amounts of polysaccharides can reduce the immune response.[11] Another concern is that 3%–19% of pneumococcus infections are due to non-encapsulated strain which cannot be tackled by the current vaccine.[6]

Serotype-independent future vaccines are now being investigated. These include protein (i.e PspA, inactivated pneumolysin), protein and polysaccharide combination, live attenuated vaccine (the SPY1 strain), and 'back to future' whole-cell vaccine, as animal data suggest that whole-cell non-encapsulated pneumococcal vaccine may protect against a variety of serotypes.[1,6] Ongoing trial of SPWCV (Streptococcus pneumoniae Whole Cell Vaccine) in Indonesia is trying to give alternative for current issues and the fact that coverage of PCV13 is estimated 60% because of variative serotype distribution in Indonesia as an archipelago country.[12] This never-ending vaccine development reminds the researchers to always learn from history and combine it with current knowledge for the better future.

REFERENCES

Grabenstein JD, Klugman KP. A century of pneumococcal vaccination research in humans. Clin Microbiol Infect. 2012;18 Suppl 5:15-24.

O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009;374(9693):893-902.

Lin TY, Shah NK, Brooks D, Garcia CS. Summary of invasive pneumococcal disease burden among children in the Asia-Pacific region. Vaccine. 2010;28(48):7589-605.

Collaborators GBDM. Global, regional, and national burden of meningitis, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2018;17(12):1061-82.

Geno KA, Gilbert GL, Song JY, Skovsted IC, Klugman KP, Jones C, et al. Pneumococcal Capsules and Their Types: Past, Present, and Future. Clin Microbiol Rev. 2015;28(3):871-99.

Brooks LRK, Mias GI. Streptococcus pneumoniae's Virulence and Host Immunity: Aging, Diagnostics, and Prevention. Front Immunol. 2018;9:1366.

Weiser JN, Ferreira DM, Paton JC. Streptococcus pneumoniae: transmission, colonization and invasion. Nat Rev Microbiol. 2018;16(6):355-67.

Kim SH, Song JH, Chung DR, Thamlikitkul V, Yang Y, Wang H, et al. Changing trends in antimicrobial resistance and serotypes of Streptococcus pneumoniae isolates in Asian countries: an Asian Network for Surveillance of Resistant Pathogens (ANSORP) study. Antimicrob Agents Chemother. 2012;56(3):1418-26.

Berical AC, Harris D, Dela Cruz CS, Possick JD. Pneumococcal Vaccination Strategies. An Update and Perspective. Ann Am Thorac Soc. 2016;13 (6):933-44.

NTB DKP. Pencanangan program demonstrasi imunisasi pneumokokus konyugasi 2017 [cited 2019 05 Sep]. Available from: https://dinkes.ntbprov.go.id/berita/pencanangan-program-demonstrasi-imunisasi-pneumokokus-konyugasi/.

Swanson DS, Harrison CJ. Playing "Whack-a-Mole" With Pneumococcal Serotype Eradication. Pediatrics. 2017;140(5).

Sundoro K. Immunization programme in Indonesia: Overview (focusing on Streptococcus pneumonia wholecell vaccine). J Vaccines Vaccin 2014.

Dunne EM, Murad C, Sudigdoadi S, Fadlyana E, Tarigan R, Indriyani SAK, et al. Carriage of Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Staphylococcus aureus in Indonesian children: A cross-sectional study. PLoS One. 2018;13(4):e0195098.

Safari D, Kurniati N, Waslia L, Khoeri MM, Putri T, Bogaert D, et al. Serotype distribution and antibiotic susceptibility of Streptococcus pneumoniae strains carried by children infected with human immunodeficiency virus. PLoS One. 2014;9(10):e110526.

INA-RESPOND Newsletter

OUR INDONESIAN PUBLICATION HEROES

By: Aly Diana

Indonesia seems to rely on the students and the academics as the publication heroes. It does make sense as every year, there are more than 1.5 million students enrolled in universities across Indonesia, and there are increasing numbers of academics. This large number of students and scholars should be a potential source of scientific publication. The government pushes it further with the regulation from the Directorate General of Higher Education no.152/E/T/2012 and Joint Regulation of the Minister of Education and Culture and Head of the National Civil Service Agency no.4/VIII/PB/2014 regarding students and academic publications, respectively. Undergraduate students have to publish one paper in any journal, master's students must publish one article in a nationally accredited journal, and Ph.D. students must publish one paper in a nationally accredited journal and one paper in an international journal. The academics have to publish as well to be promoted.

These regulations should have some positive effects on increasing the number of papers published, particularly in international journals, which is currently still very low even compared to that of some Southeast Asian countries. However, to accommodate this publication demand, good-quality journals need to be established in Indonesia. According to the data released by the ISJD in 2010, there are more than 7,000 scientific journals in Indonesia, but only 5,900 scientific journals can be accessed through the database, and only 16 journals are categorized as international journals and are registered in international indexes.

There is not enough space out there in the accredited journals for all the students and academics to publish their works. The government needs to make a significant effort to improve the quality of journals, particularly in terms of increasing the number of national/international class journals, to accommodate the increasing demand for student and academic publications. Otherwise, the regulation will have a negative effect on a student's length of study and academic career.

As of 2017, the Ministry of Research, Technology, and Higher Education, as well as most universities and research institutions in Indonesia, use the Scopus and Web of Science databases to evaluate the research performance. Using this approach, as expected, the regulations are too difficult to follow. Therefore, the government thinks that a new measurement tool for assessing research performance in Indonesia is required.

COMIC CORNER

A new metric, referred to as the S-score, to measure the research performance in Indonesia is then developed. The score has eight evaluation items, which are: 1) journal title, aims, and scope; 2) publisher, 3) editorial and journal management; 4) quality of article; 5) writing style; 6) format of PDF and e-journal; 7) regularity; and 8) dissemination. The development of a new metric has been considered important, because evaluation system should be based on country's academic circumstances. Again, most scholarly journals published in Indonesia are not listed in Scopus or Web of Science. Therefore, a new local system incorporating locally appropriate metrics is required. This new S-score is then incorporated in the Science and Technology Index (SINTA) website. Briefly, using S-score has shown a considerable improvement in research performance of Indonesian scholars, as more and more journals have been accredited using this new metric. So far, this step has been regarded suitable for a country where most journals are not indexed in Scopus. Hopefully, this approach will let our publication heroes shine and improve the quality of journals in Indonesia.

References:

Direktorat Jenderal Penguatan Riset dan Pengembangan, Kementerian Riset, Teknologi, dan Pendidikan Tinggi. Pedoman Akreditasi Jurnal Ilmiah 2018. Jakarta, Indonesia.

INA-RESPOND Newsletter

EXERCISE AND MENTAL HEALTH

By: Maria Lestari

LIFESTYLE & SPORT

Lifestyle modification might be one of the ways to increase health and quality of life in this "metabolic syndrome" era. Furthermore, lifestyle changes can make a significant impact on people with serious mental conditions. Many of these people are at high risk of chronic disease associated with sedentary behavior and medication side effects, including diabetes, hyperlipidemia, and cardiovascular disease.[1]

An essential component of lifestyle modification is exercise. The importance of exercise is not adequately understood or appreciated by patients and mental health professionals alike. Evidence has suggested that training may be an often-neglected intervention in mental health care.[2]

TONS OF BENEFITS

It is now clear that exercise reduces the likelihood of depression and also maintains mental health as people age. Getting active does more than keeping your body strong and healthy. Training can also be a great way to boost your mood, reduce stress, and rev up your energy. Moreover, exercise helps to improve mental health by reducing anxiety, depression, negative mood, and improving self-esteem and cognitive function. Also, exercise has been proven to decrease symptoms like low self-esteem and social withdrawal. Thirty minutes of exercise of moderate intensity, such as brisk walking for three days a week, is enough for these health benefits. Moreover, these 30 minutes need not be continuous; three 10-minute walks are believed to be as equally useful as one 30-minute walk.[3]

In 2017, the researchers of Psychiatry Rehabilitation journal found that schizophrenia patients who participated in a 3-month physical conditioning program showed improvements in weight control and reported increased fitness levels, exercise tolerance, reduced blood pressure levels, increased perceived energy levels, and enhanced upper body and handgrip strength levels.[4]

Exercise directly affects the brain. Regular exercise increases the volume of specific brain regions—in part through better blood supply that improves neuronal health by improving the delivery of oxygen and nutrients, and one of critical importance for mental health is the hippocampus—an area of the brain involved in memory, emotion regulation, and learning. Studies in other animals convincingly show that exercise leads to the creation of new hippocampal neurons (neurogenesis), with preliminary evidence suggesting this is also true in humans.[5]

Much mental sickness health is characterized by a cognitive inflexibility that keeps us repeating unhelpful behaviors, restricts our ability to process or even acknowledge new information, and reduces our ability to use what we already know to see new solutions or to change. It is therefore plausible that exercise leads to better mental health in general, through its effects on systems that increase the capacity for mental flexibility.[6]

WHAT KIND OF EXERCISE AND HOW LONG?

The best exercise is the kind that you enjoy doing, that you can maintain, and that has your body's longevity in mind. Different types of exercise may bring about different responses, both physically and mentally. The most important thing is a balanced exercise routine. It is a combination of resistance training, where we're strengthening our muscles and joints under load, and aerobic training, where our cardiorespiratory system is challenged.

Group activities such as team sports, cycling, aerobic exercise, and gym workouts have the highest associations with good mental health, according to a large observational study published in The Lancet Psychiatry journal in 2018. Weight or resistance training also has a significant impact on reducing depressive symptoms when done for around 30-45 minutes. Furthermore, there's currently rising popularity in mindful exercises, such as yoga and pilates, which can also be great choices to add to the exercise routine. Studies have suggested both may help reduce symptoms of depression.[7]

British Journal of Occupation Therapy suggested that exercising for 30-60 minutes, three to five times per week, is associated with better mental health. Exercise is particularly beneficial as a treatment for mental health when supervised by a health professional with specific training in exercise prescription, like an exercise physiologist.[8]

Published in 2018 in the American Journal of Psychiatry, the study was the largest and most extensive of its kind. It involved almost 34,000 Norwegian adults, whose exercise levels and symptoms of depression were monitored over 11 years. Based on these results, the international research team suggested that 12% of episodes of depression could be prevented with just one hour of exercise each week, regardless of age, gender, or even the intensity of exercise.[9]

HOW CAN EXERCISE BE A MOOD BOOSTER?

Researchers have studied several theories about how physical activity might trigger mood improvements. Exercise may:

- Subdue responses from both the sympathetic nervous system (responsible for the fight-or-flight reaction) and the hypothalamic-pituitary-adrenal (HPA) axis, the hormonal feedback system that reacts to stress.
- Work as an antidepressant, increasing levels of neurotransmitters (chemical messengers) like serotonin and norepinephrine in the brain, thus boosting mood.
- Prompt the release of endorphins, naturally occurring opioids produced by the body.
- Enhance people's sense of self-efficacy (belief in oneself as capable), which reduces anxiety.
- Distract from thoughts and stressors, which also reduces anxiety.[10, 11]

CONCLUSION

The beneficial effects of regular physical activity on health are indisputable in the field of modern medicine. Exercise is not only the first step in lifestyle modifications for the prevention and management of chronic diseases but also has positive benefits in individuals with mental illness.

REFERENCES

1. Richardson CR, Faulkner G, McDevitt J, Skrinar GS, Hutchinson DS, Piette JD. Integrating physical activity into mental health services for persons with serious mental illness. Psychiatric services (Washington, DC). 2005;56(3):324-31.

2. Callaghan P. Exercise: a neglected intervention in mental health care? Journal of psychiatric and mental health nursing. 2004;11 (4):476-83.

3. Guszkowska M. [Effects of exercise on anxiety, depression and mood]. Psychiatria polska. 2004;38(4):611-20.

4. Rimes RR, de Souza Moura AM, Lamego MK, de Sa Filho AS, Manochio J, Paes F, et al. Effects of Exercise on Physical and Mental Health, and Cognitive and Brain Functions in Schizophrenia: Clinical and Experimental Evidence. CNS & neurological disorders drug targets. 2015;14(10):1244-54.

5. Firth J, Stubbs B, Vancampfort D, Schuch F, Lagopoulos J, Rosenbaum S, et al. Effect of aerobic exercise on hippocampal volume in humans: A systematic review and meta-analysis. NeuroImage. 2018;166:230-8.

6. Viana RB, Gentil P, Naves JPA, Rebelo ACS, Santos DAT, Braga MAO, et al. Interval Training Improves Depressive Symptoms But Not Anxious Symptoms in Healthy Women. Frontiers in psychiatry. 2019;10:661.

7. Chekroud SR, Gueorguieva R, Zheutlin AB, Paulus M, Krumholz HM, Krystal JH, et al. Association between physical exercise and mental health in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study. The Lancet Psychiatry. 2018;5(9):739-46.

8. Alexandratos K, Barnett F, Thomas Y. The Impact of Exercise on the Mental Health and Quality of Life of People with Severe Mental Illness: A Critical Review. British Journal of Occupational Therapy. 2012;75:48-60.

9. Samuel B. Harvey, F.R.A.N.Z.C.P., Ph.D. ,, Simon Øverland, Ph.D. ,, Stephani L. Hatch, Ph.D. ,, Simon Wessely, F.R.C.Psych., M.D. ,, Arnstein Mykletun, Ph.D. ,, Matthew Hotopf, F.R.C.Psych., Ph.D. Exercise and the Prevention of Depression: Results of the HUNT Cohort Study. American Journal of Psychiatry. 2018;175(1):28-36.

10. Tahmassian K, Jalali Moghadam N. Relationship between self-efficacy and symptoms of anxiety, depression, worry and social avoidance in a normal sample of students. Iran J Psychiatry Behav Sci. 2011;5(2):91-8.

11. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety. Frontiers in psychiatry. 2013;4:27-.

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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.

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