INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

March 2018

INA-RESPOND ACTIVITIES

OpenClinica Users Training

Risk-Based Monitoring in Clinical Trials

Vitamin D for Respiratory Infections ?

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
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INA-RESPOND newsletter

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Anandika Pawitri, Dona Arlinda, Dedy Hidayat, Herman Kosasih, Lois E. Bang, Louis Grue, Maria Intan, Neneng Aini, Nurhayati

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INA-RESPOND Network and Partners

INA-RESPOND Secretariat

Badan Penelitian dan Pengembangan Kesehatan, RI
Gedung 4, Lantai 5

Jl. Percetakan Negara no.29, Jakarta, 10560

www.ina-respond.net

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BY: ANANDIKA PAWITRI, CALEB L. HALIM, LOIS E. BANG, MARIA INTAN, M. IKHSAN JUFRI

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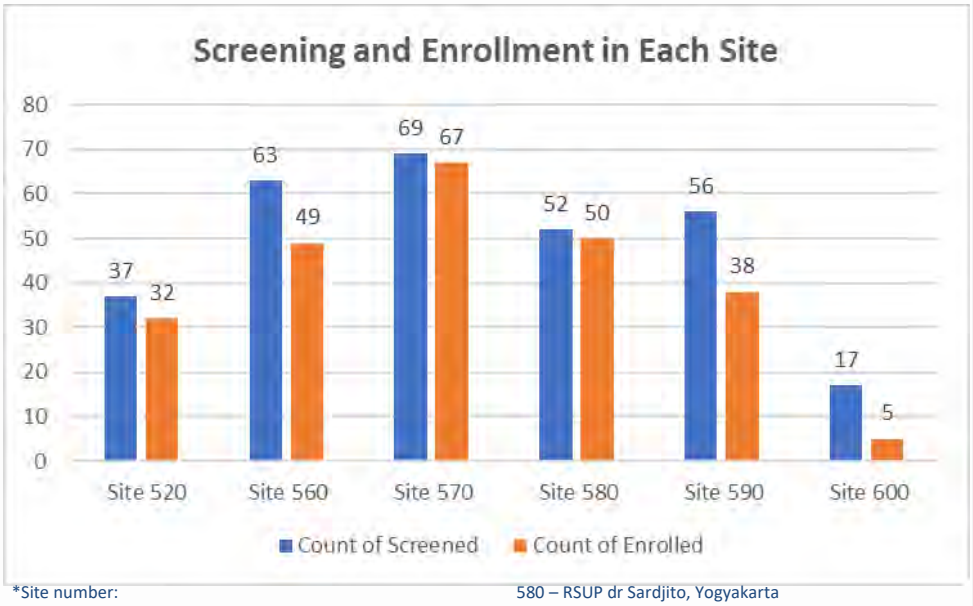
Screening and Enrolment



Up to 7 March 2018, sites have enrolled 231 subjects. Site 570, RSUD dr Soetomo, is still the top recruiter with 67 subjects. Enrolment by site 520, RSUP Sanglah, is temporarily stopped until the study permission is cleared. Interim analysis will be held on 3 April 2018 in Jakarta to clarify site data for initial analysis. Research Assistants and Principal Investigator/Co-PI from each site will attend this meeting. Enrolment progress until the end of January 2018 can be seen in the graphic above.

*Site number:

520 – RSUP Sanglah, Denpasar
560 – RSUP dr Kariadi, Semarang
570 – RSUD dr Soetomo, Surabaya
580 – RSUP dr Sardjito, Yogyakarta
590 – RSUP Persahabatan, Jakarta
600 – RSUP H Adam Malik, Medan

NIH/Leidos Visit to INA-RESPOND Secretariat

On 19—23 Feb, Ms Lori Dodd, Mr Michael Duvenhage, and Ms Wang Jing from NIAID/Leidos visited INA-RESPOND Secretariat to meet with INA-RESPOND's Data Managers, Statistician, and Protocol Specialists from TRIPOD, PRO-ACTIVE, and Schistosomiasis studies. That week, the discussions were focused on finalizing Data Management-related SOPs, reviewing the critical data elements in TRIPOD and PRO-ACTIVE studies, and developing table shells for TRIPOD study's automated reporting program.

Besides that, a discussion on data management issues related to the Schistosomiasis study was also conducted. NIAD/Leidos team also gave a demonstration about REDCap and talked about the possibility of using it for our Schistosomiasis study. NIAID/Leidos and INA-RESPOND team also decided to develop automated reporting program for TRIPOD study. Hopefully, in the next 3—4 months the program can be finalized and used for TRIPOD reporting. From the meetings, it is expected that the Data Management and Statistics of INA-RESPOND Secretariat will become more comprehensive and robust.

Research Assistant Gathering @Ancol, Jakarta

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Screening and Enrolment

So far, site 610 (Tangerang Hospital) has enrolled 16 participants for INA-PROACTIVE study and site 600 (Adam Malik Hospital) has enrolled one participant, so in total, 17 participants have been enrolled for INA-PROACTIVE Study.

Currently, six study sites have signed the contract and agreement. Site 570 (Soetomo Hospital) has agreed to sign the IRB Reliance and is collecting signature from Hospital Director and Head of Local IRB before any site visits may be conducted. Site 560 (Kariadi Hospital) is still conducting intern meeting to decide whether to use the Local Ethical Committee or rely on NIHRD IRB.

We are preparing a collaboration invitation letter for Jayapura Hospital to join our study. This collaboration invitation is opened for any hospitals in Indonesia. We hope after the SIV for Cipto Hospital the activation for the sites will follow soon and increase the number of subject enrolled for INA-PROACTIVE study.

Operational Call and Training Updates

Because the study enrolment has started, operational call is conducted to share experiences, evaluate, report, and discuss any strategies related to the study. So far, three weekly operational calls have been held (on 21 February, 28 February, and 7 March 2018).

In addition, a training on Clinical Research Form Completion Guideline (CRFCG) was held on 5 and 8 March to give information for all study site members on how to complete the CRF.

Site	SPV	SIV	Activation	Enrolled Subjects
Site 610 (Tangerang Hospital)	19-20 Dec 2017	22 & 27 Dec 2017	09 Jan 2018	16
Site 600 (Adam Malik Hospital)	7-8 Feb 2018	12-13 Feb 2018	12 Mar 2018	1
Site 550 (Wahidin Hospital)	13-14 Feb 2018	19-20 Feb 2018	13 Mar 2018	-
Site 530 (Cipto Hospital)	21-22 Feb 2018	13-14 Mar 2018	Early April	-
Site 570 (Soetomo Hospital)	20-21 Mar 2018	4th week of March	April	-

OPEN CLINICA SUPER USER & SITE USER TRAINING INCREASING THE NETWORK'S CAPACITY FOR DATA MANAGEMENT AND PROCESSING

INA-RESPOND Newsletter

OPEN CLINICA TRAINING WEEK

BY: SILVERA ERARI & KANTI LARAS

OpenClinica is an open source software for Electronic Data Capture (EDC) and Clinical Data Management (CDM) used by INA-RESPOND to manage study data collected from INA-RESPOND study sites. The purpose of using OpenClinica on clinical research studies is to reduce data entry errors, to better manage clinical data, to foster good communication among study team members, and to schedule/set reminders for study participants' scheduled visits. OpenClinica provides an online data entry feature. Moreover, it also stores its data in an online server data storage.

Since INA-RESPOND have been conducting studies using OpenClinica as a data capture tool, it is crucial for INA-RESPOND staffs as well as study sites' staffs to understand how OpenClinica works and how to use it. Therefore, INA-RESPOND Secretariat took the initiative to hold the OpenClinica training. This effort was part of the capacity building for study sites (hospitals) and staff who are participating in INA-RESPOND studies.

The OpenClinica (OC) training was held on 26 February 2018 to 2 March 2018 at Double Tree Hotel in Cikini, Jakarta. it was divided into 2 sessions: Super User Training for 4 days (from 26 February 2018) and Site User Training for one day (2 March 2018). Participants were divided into groups consisting of two to three people. One of the group members was responsible as a group leader (main trainee) while the other two

acted as observers. This training had 24 participants who come from a wide range of organizational and professional background. Participants were from INA -RESPOND Secretariat, INA-RESPOND study sites (Research Assistants), National Institute of Health Research and Development, Indonesian Ministry of Health (data center's staffs), and National Institute of Health, USA (Mr. Michael Duvenhage).

Super User Training refers to data managers, project managers, CRAs, biostatisticians, and users who do not essentially work in a study site. Topics covered on this training were about creating a clinical study, creating CRFs, creating event definitions, creating subject group classes, creating rules, creating sites, assigning users, entering clinical data, importing clinical data, exporting clinical data, and managing queries. Besides OpenClinica, additional tasks to support the use of OpenClinica such as creating advanced eCRF layouts as well as designing rules and validations were given and practiced. Advanced eCRF layouts were created and built in MS Excel. On the other hand, rules and validations were created in XML form using Notepad+++ for Windows or BBedit for Mac. Additionally, other than learning from materials provided by the instructor, best practices were also part of the training in order to better understand the use of OpenClinica and other supporting tools. Furthermore, even though the main focus of this training was for data managers, playing other roles related to a clinical study in using OpenClinica provided some knowledge and understanding about how clinical data flows in a clinical study. Therefore, participants of this training performed several roles during the training practice. Participants started with creating several users and assigning their roles that were then used in different situations. The roles were as data manager, study director, data specialist, monitor, and data entry person.

The other session, the Site User training, focused on OpenClinica users at study sites. This training topics included viewing study subjects, adding study subjects, adding a new study event, viewing study events, creating notes and discrepancies, and importing clinical data. There were approximately participants of this training including from INA-RESPOND Secretariat, INA-RESPOND study sites, and National Institute of Health Research and Development, Indonesian Ministry of Health.

These two sessions of OpenClinica training were conducted and instructed by Ms. Laura Keita (Director of Training & Compliance, OpenClinica LLC). The OpenClinica training was an excellent opportunity because besides gaining knowledge directly from OpenClinica developer itself, participants also had a chance to meet and exchange ideas with other OpenClinica's users. Being trained directly by Ms. Laura Keita offered an opportunity to ask as many questions as possible related to OpenClinica. Ms. Laura Keita was very helpful and knowledgeable with all her answers and examples.

Overall impression of this training was that the instructor of the training was very professional, full of knowledge, and excellent with OpenClinica. Therefore, despite of lack of experience from some of the participants, many materials were well-absorbed and participants were very excited to play their role as different study positions. However, constant use of OpenClinica software would give more improvement on OpenClinica skills especially for data managers. OpenClinica training was a decent starting point for better data managerial system in all INA-RESPOND studies. It is also important to all study personnel to understand the benefit of good-quality clinical data because the quality of clinical data is an essential component of study quality. Finally, as participants gained some knowledge through this OpenClinica training, INA-RESPOND Secretariat, especially Data Management, expects to become more comprehensive, robust, and independent in managing its clinical data. Furthermore, hopefully, in the future all INA-RESPOND study sites would be able to use OpenClinica not only for INA_RESPOND related studies but also for their independent studies (if they are willing to use OpenClinica). Therefore, this training directly creates mutual benefit.

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CLINICAL BRIEF: VITAMIN D FOR RESPIRATORY INFECTION?

BY: HENING TIRTA KUSUMAWARDANI, M. HELMI AZIZ

1,25-dihidroxyvitamin D_3 [1,25$(OH)_2D_3$], the sunshine vitamin, is the active form of vitamin D, produced in large amount within the skin exposed to ultra-violet B (UVB) [1]. Despite the well-known function in bone mineralization and calcium homeostasis, vitamin D has recently been proven to regulate more than 200 genes including cell proliferation differentiation, apoptosis, and interaction with the immune system (Figure 1) [1]. Researchers have been studying the new role of vitamin D and found that vitamin D deficiency is associated with diseases such as cancer and some infectious diseases [1]. This article will focus on the unfamiliar role of vitamin D in respiratory infection, especially in Tuberculosis (TB) and influenza infection.

The discovery of the expression of nuclear vitamin D receptor (VDR) in immune cells leads to the considerable amount of research on vitamin D potency in maintaining immune homeostasis. Vitamin D has been proven to directly suppress the cell-mediated immune responses by inhibiting inflammatory cytokine expression. This inhibition is due to the reduction in transcription of Th1 cytokines (IL-2, GM-CSF, IFN-γ) and the increase in expression of Th2 cytokines (IL-4, IL-5, IL-10) [1]. Another immunomodulator effect of vitamin D is to prevent the activation of peripheral autoreactive T cells by regulating the regulatory T cells (T_{regs}) [1]. Therefore, low vitamin D status is often associated with an increased risk of developing autoimmune diseases, such as multiple sclerosis and type 1 Diabetes [1].

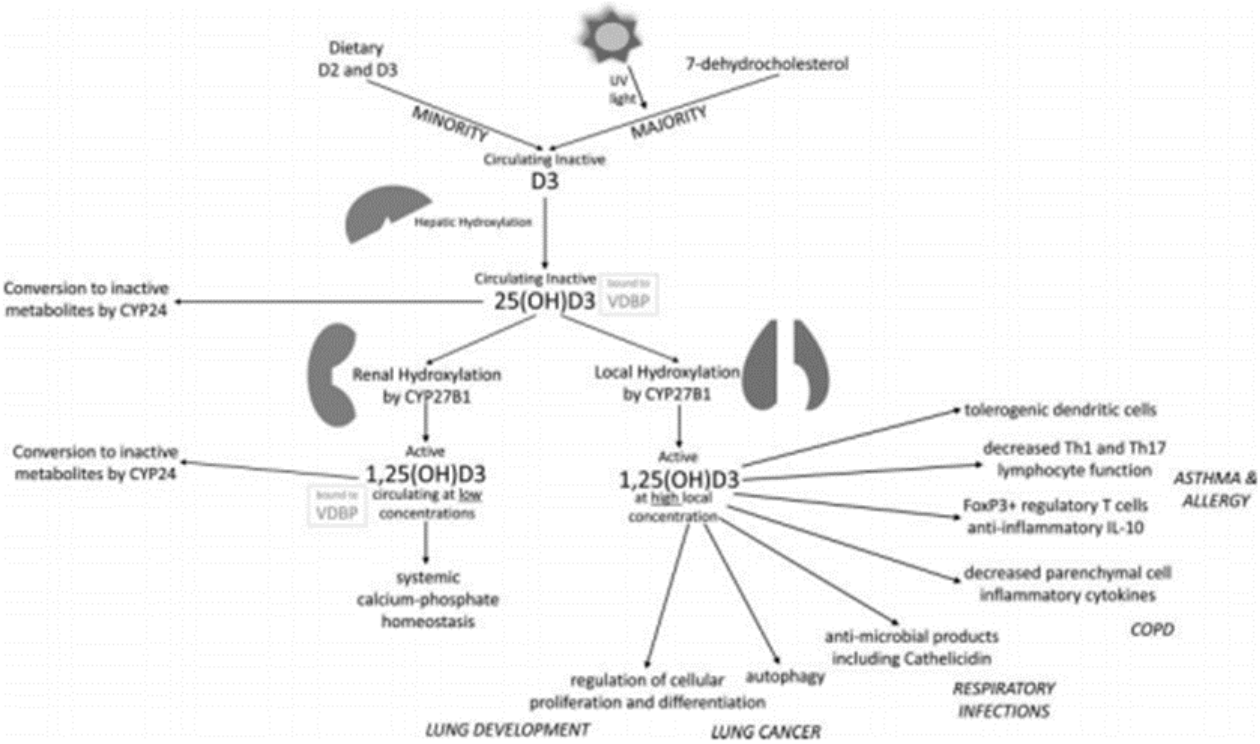

Figure1. Schematic of vitamin D metabolism and example of functions in the lungs [2].

Exposure to sunlight and dietary sources of vitamin D (cod liver oil, eggs, and liver) has been known as treatments for TB since 1840 [1, 3]. However, after the discovery of anti-TB drugs in 1940, the interest of vitamin D as a TB treatment modality decreased. Surprisingly, in the last three decades, studies have demonstrated that vitamin D deficiency is a risk factor for active TB and impaired antimycobacterial activity. In the 1980s, adding vitamin D in monocytes and macrophages infected with *M. tuberculosis in vitro* was able to reduce the bacterial load by boosting phagocytosis and increase the production of antimycobacterial activity [2, 3]. This effect was the result of a complex process involving TLR2/1 signaling pathway in monocyte/macrophages, *CAMP* gene on respiratory epithelial cells, and secretions of human cathelicidin (LL-37), which in the end improves the innate immunity (Figure 2) [1, 3, 4]. LL-37 has been proven to be able to disrupt the integrity of the bacterial cell membrane, resulting the death of the gram-negative and gram-positive organism [1, 3, 4].

Based on the interaction of vitamin D and LL-37, several trials were conducted to identify vitamin D as an adjunctive therapy for TB or latent TB. Sputum clearance of *M. tuberculosis*, clinical, and radiological improvement was observed in some studies, while some studies observed no response related to vitamin D supplementation [1, 5]. This conflicting result could be explained by the *Fok1* and *Taq1* VDR gene polymorphism. Studies from Lima, Peru, showed that patients who had *Fok1* FF and *Taq1* Tt genotype had faster sputum conversion than patient who does not have those genotypes [5]. Despite the potential as adjuvant therapy, the side effect of vitamin D supplementation should be kept in mind especially for patients who previously had renal disease [5].

It has been thought that vitamin D elicits innate immune mechanism which is critical to the response of influenza infection [6]. The innate responses including cytokines, chemokines, cellular responses (neutrophils, macrophages, and NK cells), and other soluble factor within airway surface (defensins and collectins) assisting containment and clearance of initial influenza infection [7]. The important component of early innate immune response is cationic-host defense peptides (CHDP) which demonstrated not only antibacterial properties but also antiviral activity. Two major families of CHDP in humans are cathelicidin (LL-37) and defensins and as previously described cathelicidin expression related to vitamin D presence [7]. Evidence of LL-

37 antiviral functions have been demonstrated by the inhibition of HIV-1 replication and reduced vaccinia plaque formation *in vitro* [7].

Related to influenza infection, in mice infected with influenza A, nebulized LL-37 have been showed to reduce disease severity and viral replication to a similar extent of zanamivir, antiviral influenza-specific drug [7]. Moreover, in bronchoalveolar lavage (BAL) of LL-37 treated mice the secretion of inflammatory cytokines diminished on day three after infection, which protects the mice's lungs from potentially harmful inflammatory cytokines [7]. A prospective study showed that maintaining levels of vitamin D serum of 38 ng/mL or higher had proven to reduce the incidence of acute viral respiratory tract infections and the burden of illness [6]. Another study in 334 Japanese schoolchildren who were given cholecalciferol 1200 IU/day for 4 months showed reduced risk of seasonal influenza A infection [4]. A meta-analysis reviewing randomized controlled trials of vitamin D supplementation showed that daily or weekly vitamin D supplementation without additional bolus doses protected subjects against acute respiratory tract infection, whereas single regimen containing large bolus doses did not [8]. This protective effect was observed higher in people who had vitamin D deficiency at baseline [8].

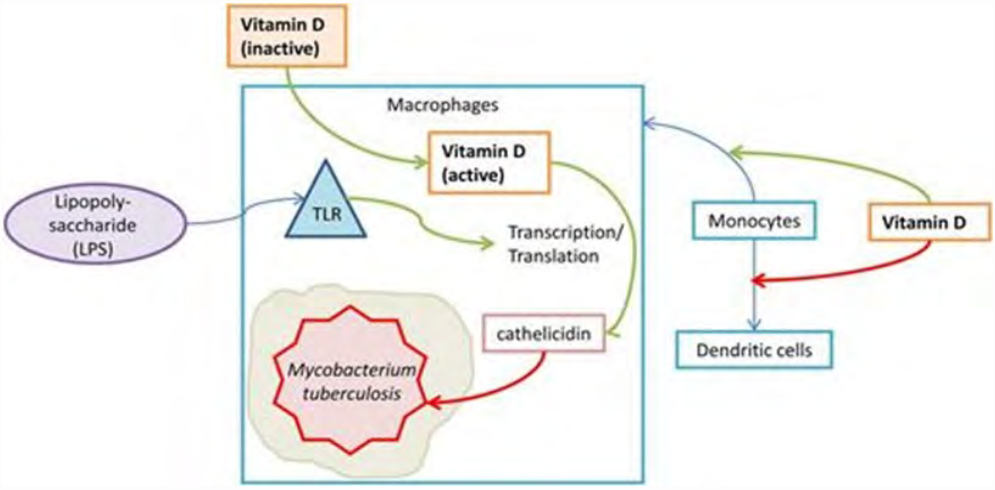

Figure2. Vitamin D promotes differentiation of monocytes into macrophages and transcription of cathelicidin, an antimicrobial peptide that could kill *Mycobacterium tuberculosis* [4].

The evidence of association between vitamin D and respiratory tract infection does exist. Several *in vitro* studies have been able to demonstrate the role of vitamin D related to immune system, and some observational human studies correlate lower vitamin D levels with an increasing risk of respiratory tract infection. Moreover, vitamin D supplementation have mixed results but is promising to try since vitamin D side effects are dose-dependent. More thorough studies involving large populations are needed to elucidate the possible relationship between vitamin D supplementation and respiratory tract infection.

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INA-RESPOND Newsletter

RISK-BASED MONITORING IN CLINICAL TRIALS

BY: MILA ERASTUTI, NENENG AINI

Extent and Nature of Monitoring

As on the ICH-GCP requirement, the sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. The flexibility in the extent and nature of monitoring described in this section is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring. The sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring. The sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan).

On-site monitoring is performed at the sites at which the clinical trial is being conducted. Centralized monitoring is a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons (e.g., data managers, biostatisticians).

Centralized monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data.

Why is risk-based monitoring on the rise?

Over the last decade, the complexity and cost of clinical trials has increased dramatically. Current operational practices used in clinical trials are expensive and do not guarantee data quality. Through modernization, including use of technology enablers, efficiencies can be gained without impacting subject safety by implementing quality risk management approaches to clinical trial oversight. Risk-based monitoring (RBM), a proven approach utilizing centralized monitoring as the core for executing integrated clinical operations, clinical monitoring, data management, and site and patient-level medical review plans, continues to gain ground

The pharmaceutical industry has traditionally relied heavily on On-site Monitoring approaches, including significant amounts of Source Data Verification (SDV) to help ensure subject safety and generate quality data. It is a reactive approach, limited in its ability to quickly identify issues and prevent them from recurring. Further, this resource-intensive approach is applied uniformly throughout a trial rather than proportionate to risks. Since intense On-site Monitoring does not guarantee identification of all subject safety or

Figure 1. Risk-based Monitoring as part of Quality Management System Approach

data quality issues, the associated high costs are disproportionate with the value gained. Therefore, there is movement within the industry driven by health authorities to transition to Risk-Based Monitoring.

What is risk-based monitoring?

Risk-based monitoring is the process of ensuring the quality of clinical trials by identifying, assessing, monitoring and mitigating the risks that could affect the quality or safety of a study. Guidance from the US Food and Drug Administration (FDA) outlines three steps in a risk-based approach to monitoring:

1. Identify critical data and processes.

To accurately monitor the quality of a study and the safety of its participants, the sponsor must know which elements are most important for each particular study, from informed consent to eligibility, screening, serious adverse events, and study endpoints.

2. Perform a risk assessment.

A risk assessment involves determining specific sources of risk and the effect of study errors on those risks. Perform and document a risk assessment to identify risks to these critical data and processes. The identified risks should be assessed and prioritized by considering the following:

- the likelihood of errors occurring
- the impact of such errors on human subject protection and trial integrity
- the extent to which such errors would be detectable

3. Develop a monitoring plan.

According to FDA's guidance, a monitoring plan should "describe the monitoring methods, responsibilities, and requirements of the trial." The plan is responsible for communicating risks and monitoring procedures to everyone involved in monitoring the trial.

A monitoring plan ordinarily should focus on preventing or mitigating important and likely risks, identified by the risk assessment, to critical data and processes. The types (e.g., on-site, centralized), frequency (e.g., early, for initial assessment and training versus throughout the study), and extent (e.g., comprehensive (100% data verification) versus targeted or random review of certain data (less than 100% data verification)) of monitoring activities will depend to some degree on a range of factors, considered during the risk assessment.

Why is it better?

As opposed to on-site monitoring based on 100% source data verification, centralized monitoring promises a number of benefits:

- Fewer errors. On-site monitoring methods, like any manual effort, are limited in scope and prone to error. Risk-based, centralized monitoring uses more automated reviews to determine the need for manual intervention and is more likely to uncover errors.
- Lower cost. With centralized monitoring, activities like on-site audits can be limited to study sites where problems are most likely occurring, which can dramatically reduce the cost of monitoring.
- Better analysis. With all data flowing into a central risk dashboard, statistical and graphical checks can much more easily be used to determine the presence of outliers or unusual patterns in the data.
- Cross-site comparison. Centralized monitoring also allows us to compare data between sites to assess performance, identify potentially fraudulent data, or locate faulty or mis-calibrated equipment.

- More timely results. A dashboard also makes it possible to identify and resolve issues while the trial is ongoing.

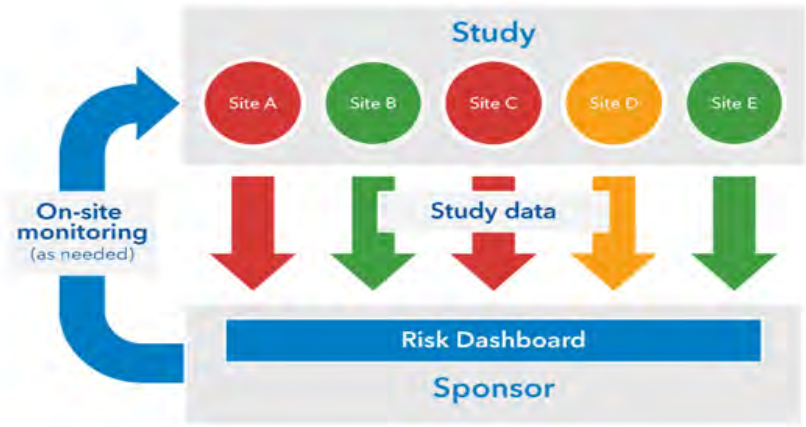

Figure 3. A risk-based monitoring process feeds data from study sites into a dashboard, alerts the sponsor to situations that need further investigation.

There is a growing consensus that risk-based approaches to monitoring, focused on risks to the most critical data elements and processes necessary to achieve study objectives, are more likely than routine visits to all clinical sites and 100% data verification to ensure subject protection and overall study quality. For example, incorporation of centralized monitoring practices, where appropriate, should improve a sponsor's ability to ensure the quality of clinical trial data.

Several publications suggest that certain data anomalies (e.g., fraud, including fabrication of data, and other non-random data distributions) may be more readily detected by centralized monitoring techniques than by on-site monitoring. It has been suggested that a statistical approach to central monitoring can "help improve the effectiveness of on-site monitoring by prioritizing site visits and by guiding site visits with central statistical data checks," an approach that is supported by illustrative examples using actual trial datasets.

A recent review of on-site monitoring findings collected during a multi-center international trial also suggests that centralized monitoring can identify the great majority of on-site monitoring findings. The review determined that centralized monitoring activities could have identified more than 90% of the findings identified during on-site monitoring visits.

<u>The monitoring processes in the RBM</u>

As discussed above, the FDA has provided some detailed guidance on how to prepare a monitoring plan, but once the plan is in place, it's the sponsor's responsibility (or the sponsor's delegate, like a CRO) to execute the plan. While specifics will differ widely between studies, a risk-oriented monitoring program will typically contain the following activities, which all flow through a comprehensive risk dashboard built for particular study:

Data collection and submission. A centralized approach requires a steady and reliable flow of data from each study site to the central monitoring system. This may occur either through manual entry and transfer of relevant data, or through an automated connection between the data entry system and the central dashboard.

Figure 2. The traditional monitoring process relies on 100% source data verification, which is time-consuming and costly.

(https://www.jmp.com/content/jmp/en_nl/software/clinical-data-analysis-software/risk-based-monitoring)

Dashboard monitoring. The function of the dashboard is to provide, at a glance, information about the status of each study site relative to the specific risk factors in our trial. When a site shows a high risk level, the monitoring plan should help us decide whether further investigation is appropriate, from in-depth statistical analysis to on-site data verification.

Statistical analysis. In addition to monitoring risk dashboard, it can also be useful to perform supplementary statistical analyses to help identify problems.

Targeted on-site investigation. Dashboard monitoring and further analysis will sometimes signal strongly that in-person investigation is needed at a particular site. In these cases, it may be appropriate to visit and perform a more traditional source data verification activity, depending on the nature of the study. The key is that once a centralized system in place, on-site investigation should be the exception, not the norm.

Implementation Considerations

1. Measures

Collectively, measure changes in quality, timeliness of data collection and issue resolution, and efficiency of trial operations affected by Risk-Based Monitoring, on an ongoing basis or after the closure of a study.

2. Technology

Technology, data integration, and analytics are all key enablers for efficient implementation of the proposed methodology. A significant but achievable challenge to enable efficient remote monitoring is the effective integration of disparate data sources and formats. Looking ahead, the continued digitization of clinical research data will enable further expansion of Off-site and Central Monitoring Activities. As all clinical trial data, including Informed Consent becomes digital, a major shift to Off-site and Central Monitoring is possible.

3. Capabilities and Organizational Change Management

It is important to consider resourcing capabilities, as well as the organizational change management required to implement risk-based methodology. Training, coaching, and ongoing communication will be necessary at all levels of the sponsor organization, associated third-party providers, and at the investigational sites.

Looking Ahead

As previously mentioned, clinical research data is becoming increasingly digitized. As this trend continues and data standardization is realized, a transition to centralized, analytics-enabled monitoring will become a reality.

INA-RESPOND will start to implement the centralized monitoring as part as implementation of risk-based monitoring for INA104 INA-PROACTIVE study for any site based on the dashboard monitoring such as status of each study site relative to the specific risk factors.

INA-RESPOND will also possible to implement the centralized monitoring to all studies depend on several considerations such as the risk-based monitoring approach, objective, purpose, design, complexity, blinding, size and endpoints of the trial. To ensure the quality of monitoring process, the monitor will follow the applicable SOPs, ICH-GCP and applicable regulatory requirement when performing monitoring activities.

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COLIN KEPT A NOTEBOOK BY HIS BED TO RECORD ANY IDEAS HE HAD DURING THE NIGHT

INA-RESPOND Newsletter

NOTE MAKING—KEEPING A PART OF YOUR BRAIN OUTSIDE

BY: ALY DIANA

Nowadays, the world is filled with information overload, from the facts, the fictions, and our own ideas about a certain topic. The danger of it is that we can be lost in space and just wonder around without reaching a conclusion about what we want to do with all the information we have. In addition, sometimes we might mix our own ideas with other people's ideas and then claim everything as ours authentically. Therefore, making notes efficiently can be very beneficial to keep our sanity while facing the wealth of information, especially in the long run, when our brain can no longer remember everything accurately. It would not be a problem if you have an eidetic memory, though!

An important part of a research and planning process is making notes of the information and ideas. Good notes can help us to organize our ideas, keep our focus while reading, better understand what we read, think critically, draw links with other studies, and separate our ideas from others. However, we still need a good note-taking strategy to make this whole idea to work for our benefit.

Firstly, we need to know what kind of ideas that we need to record. The initial step of note making is creating an outline. We need to decide the topic, preliminary list of subtopics that we may find from the reading process, and then formulate the initial objectives/research questions. At this step, changing and refining our outline is a thing to be expected; It is not a blue print that we must follow very strictly.

Secondly, don't write down too much. A research article should be an expression of our own thinking/ideas, supported by previous research and theories, but should not be a patchwork or borrowed ideas. Compress the theories or results from other articles in our own words instead of paraphrasing word by word. Reading the whole article before making notes usually helps us to avoid copying words. In case the words from others are memorably phrased or surprisingly expressed, we can copy them word by word but don't forget to put those words in quote. It is important to differentiate an exact copy/quote and our own words, but in both cases, please always keep tract of the authors.

Thirdly, label your notes intelligently. We can make a separate sub-topic on separate sheets/cards. For example, prepare one sheet of paper for every single idea that we have in the outline, and write a note under the proper label/sheet. We can let the ideas grow there without overlapping them with others, so it will be easier for us to keep our note taking focused for when we synthesize our ideas later. As mentioned before, keep track of the authors/sources and the important pages and paragraphs, so it will be faster for us to go back and check the source of information of our notes in the future.

Closing remarks: Note making is an art, and like every art in this world it needs a lot of practice to make it excellent. And yes, making notes during the night or from your dream is a part of the art. Happy note making!

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INA-RESPOND Newsletter

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

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