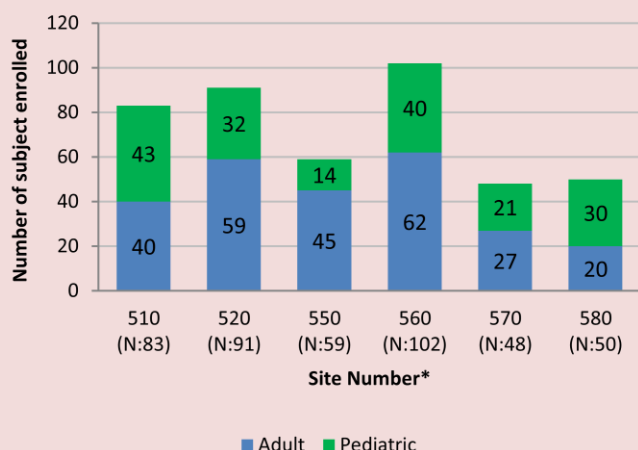


AFIRE STUDY

Good news from AFIRE Study's update! Two sites from Jakarta (RSUPN Dr Cipto Mangunkusumo and RS Penyakit Infeksi Sulianti Saroso) will be enrolling subjects for AFIRE in the near future. Currently the Sekretariat is preparing the sites so they can be activated by July.

From 6 active sites, a total of 433 subjects has been enrolled, consisting of 253 adults and 180 pediatric subjects. Enrollment progress up to May 25, 2014 can be seen in the graphic below:



*510 – RSUP dr Hasan Sadikin, Bandung 520 – RSUP Sanglah, Denpasar
550 – RSUP dr Wahidin, Makassar 560 – RSUP dr Kariadi, Semarang
570 – RSUP dr Soetomo, Surabaya 580 – RSUP dr Sardjito, Yogyakarta

Detailed screening and enrollment progress is available in portal folder: Studies\INA101\Screening progress.pdf or go to the following link: <https://ina-respond.s-3.com/EdmFile/getfile/797233>

-UN-

TRIPOD STUDY

Across April 29 – May 10, 2014, three meetings were held to discuss the TB protocol and Case Report Form (CRF). Based on the inputs from National TB Program (NTP), NIAID and TB Core Team, the protocol draft was revised once again to accommodate 2 changes.

The first change is on the sample size, which is modified from 940 to 1,357 presumptive TB patients. The increase of subject number is due to the changes in the estimated percentage of bacteriologically confirmed cases. The second major change is on the study procedure. The revised procedure is simple and applicable to all subjects no matter what is the treatment they get.

The CRF was also revised based on the latest version of the protocol. The latest CRF is more streamlined with the module design in order to accommodate future changes.

We are excited to share the most current study design in the next TB meeting in June 11-12 which will be attended by TB core team, NTP, NIAID, USAID, CDC, and NIHRD.

-NHS-

SEPSIS STUDY

Sepsis study preparation is underway after Indonesia confirmed her commitment in this study. SEAICRN will amend some sections of the current Manual of Procedures (MOP) as there were lessons learned after the study was up and running in Thailand and Vietnam.

The Sekretariat is adopting the MOP and other study documents hoping that we can soon follow the other 2 countries that have started recruiting subjects.

We are looking forward to the SEAICRN Annual Meeting in Bangkok on June 15 – 18 to hear more about other sites' experiences in this study.

-SK-

HIV MEETING

A HIV/AIDS meeting was held on April 25 at NIHRD, Jakarta to brainstorm for the HIV/AIDS research concept. Dr Siswanto and Dr Cliff Lane, serving as the Governing Board, as well as several experts from various HIV-related institutions such as HIV/AIDS Sub Directorate, Directorate General of Disease Control and Environmental Health (P2PL), National AIDS Commission (KPAN), NIHRD Centre 1 and Centre 2, Statistics Indonesia (BPS), Epidemiology and Microbiology department, CDC, and USAID came and made positive contribution towards the success of the study. In this meeting, Dr. Lane conveyed his contentment and high hopes knowing that the Ministry of Health and NIAID support this study.

The panel discussion led by Dr. Trihono conclusively settled the research question, which is to determine whether early administration of ART can decrease the number of new HIV infection/transmission in community. The HIV/AIDS study is expected to begin in 2015.

-AP-



SCIENTIFIC Corner

MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS: EPIDEMIC POTENTIAL OR A STORM IN A TEACUP?

Alimuiddin I. Zumla and Ziad A. Memish. An excerpt from European Respiratory Journal.



The Middle East respiratory syndrome (MERS) is a new killer respiratory disease caused by MERS coronavirus (CoV), first reported from the Kingdom of Saudi Arabia (KSA) in September 2012 after identification of a novel beta coronavirus from a Saudi Arabian patient who died from a severe respiratory illness. The appearance of any new fatal infectious disease and uncertainty about its origin and mode of transmission invariably threatens global health security, and its detection in western countries rapidly focuses political and scientific attention. Unfortunately, at the same time, it evokes unnecessary and unwarranted fierce scientific competition and discourse.

6 months after MERS-CoV was discovered, at the end of March 2013, there were only 17 MERS-CoV cases reported globally, nine of which were from KSA and four of these from one family cluster. This small number of MERS-CoV cases would not have attracted much global attention had it not been for the high mortality rate in persons who contracted the disease, all of whom had medical comorbidities.

Urgent research conducted after the Al-Hasa outbreak suggested that aerosol transmission appeared to be the likely route of human-to-human transmission of MERS-CoV in hospitals and that those with medical comorbidities suffered a higher death rate. The presenting clinical symptoms include chills, malaise, rigor, headache, myalgia, and malaise. While respiratory failure is a major clinical feature of MERS-CoV infection, atypical presentation with diarrhea has been reported in both MERS and SARS. There is no specific treatment yet, although several treatment options used in SARS epidemic are recommended and other therapies are under development.

A critical question which remains unanswered is the source and mode of transmission to humans of MERS-CoV. While careful monitoring of MERS-CoV genome evolution will continue, the likelihood of an impending global epidemic based on current genomic data appears unlikely. As of December 27, 2013, worldwide, 20 months since the first discovery of MERS-CoV in Jeddah, KSA, there have been a total of 171 cases of MERS-CoV infection with 73 deaths (42.6% mortality) reported to the WHO. The trend in case detection rate does not suggest that an impending epidemic is inevitable.

As prevention measures WHO has published guidance and updates accessible at:
http://www.who.int/csr/disease/coronavirus_infections/en/

–SK–

Source:

Eur Respir J 2014; 43: 1243-1248

TABLE 1 Epidemiological, clinical and laboratory features of Middle East respiratory syndrome (MERS)

History	April 2012: Jordan; first case diagnosed retrospectively in November 2012 June 2012: KSA; first Saudi case reported in September 2012 September 2012: first UK case (Qatar referral) October 2012: KSA family case cluster January 2013: UK family cluster Feb 2013: first German case April–May 2013: KSA; Al-Hasa hospital outbreak of 21 cases May 2013: Italy; first case
Source of MERS-CoV and mode of transmission	Zoonotic reservoir: MERS-CoV RNA identified in bats and camels Mode of transmission from animals to humans unknown Human-to-human transmission occurs via aerosol from index case to secondary cases
Geographical distribution	Middle East: KSA; UAE; Qatar; Oman; Jordan; Kuwait Case reports from UK, France, Germany, Italy, Tunisia of returning travellers from Middle East, secondary cases from these have occurred
Incubation days	Mean (95%CI) Range
Serial interval days	7.6
Clinical spectrum of disease	Asymptomatic Mild, moderate-to-severe pneumonia Acute respiratory distress syndrome to fulminant multiorgan failure Gastrointestinal symptoms occur in 20–33% Affects all ages but predominantly adults
Age group	Adults % Children %
Age	Range 14 months to 94 years; mean 56 years, median 50 years
Sex	Male % Female % Male:female ratio
Mortality	Overall case fatality rate Time from symptom onset to death mean (range) days
Diagnostic test	Confirmatory test Serological tests
Treatment	No specific treatment Supportive therapy for organ failure and antimicrobial therapy for secondary infections Ribavirin and interferon- α under trial.

KSA: Kingdom of Saudi Arabia; CoV: coronavirus; UAE: United Arab Emirates; ALT: alanine aminotransferase; AST: aspartate transaminase. #: 56% dry cough and 44% productive cough. Data from [2, 3, 12, 14–21, 24].

GCP Forum

Subject Lost To Follow-Up

We often hear the words “lost to follow-up” in clinical research, what does it actually mean? Lost to follow-up refers to subjects who at one point were actively participating in a clinical research trial, but have become lost at the point of follow-up in the trial. There are many reasons a subject can become lost. The subject may move away from the particular research site or become ill and unable to communicate. After a certain number of failed attempts, the subject may be considered lost-to-follow-up with no plan or requirement for continued attempts at contact.

Several unfavorable effects were observed as a result of lost-to-follow-up subjects. The negative effects are on trial outcome and on institution sponsoring the clinical research trial. Subjects who are lost-to-follow-up lead to incomplete study results, which can put a bias on the result of the study. Besides partial study data and regulatory issues, a serial event of lost-to-follow-up subject can lead to slow progression of the clinical research study. These may bring many side effects, including longer clinical trial periods and more monetary expenditure because extra resource may be required to recruit targeted amount of subject.

There is no specific guidance regarding lost-to-follow-up subject matter. Section 4.3.4 of the ICH E-6 Good Clinical Practice: Consolidated Guidance states, “Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.” So if a subject is constantly absent for appointments, the study team should try to contact him/her by all means. If attempts to pursue the subject fails to convince the subject to report for scheduled appointments, the subject must be withdrawn from the study. The dates the subject was contacted and the type of contact used should be recorded in the study documentation. (CRC handbook)

To sum up, it is important for subject to receive appropriate information about the study in order to retain them in the trial voluntarily. Failure to do this will contribute to the increase of lost-to-follow-up, which in return will affect the study.

–AP–

Sources:

- Cleland J et al. A method to reduce loss to follow-up in clinical trials: informed, withdrawal of consent. 2004
- Elie A et al. LOST to follow-up Information in Trials (LOST-IT): a protocol on the potential impact. 2009
- Norris D. Clinical Research Coordinator Handbook. 2009.

UPCOMING
EVENTS
IN JUNE

- 9 June : Sepsis Meeting, Jakarta
- 10 June : Lecture on The Role of Monitoring in Clinical Research
Lecture on The Role of Protocol Development
- 11 – 12 June : TB Meeting, Jakarta
- 15 June : SEAICRN Governing Board Meeting, Bangkok
- 16 – 17 June : SEAICRN Annual Meeting, Bangkok
- 18 June : SEAICRN Executive Committee Meeting, Bangkok

Job
Openings

Secretariat INA-RESPOND is seeking for a Data Manager and a Clinical Research Associate.

Detailed requirements and job description can be seen at www.ina-respond.net/join-us/
To apply, please email your Resume/CV to Meity Siahaan at MSiahaan@s-3.com
Please write down the position that you'd like to apply in the subject line of your email.
Application closing date: 15 June 2014.

Best Wishes for INA101 team members celebrating their birthday in June:

- 06 Jun – dr. Fatmawati, MPH (NSC Member)
- 13 Jun – dr. Dewi Lokida, Sp.PK (Protocol Core Team)
- 17 Jun – dr. Anggraini Alam, Sp.A(K) (Co-PI Site 510)
- 21 Jun – dr. I Made Susila Utama, Sp.PD-KPTI (PI Site 520)
- 27 Jun – dr. Ni Made Tyas Dwi Arsanti (RA Site 520)



Site 560 – RSUP dr. Kariadi, Semarang

Site 560 RSUP dr. Kariadi, Semarang is the current top recruiter in AFIRE study. Its research team consists of wonderful people. Let's meet them!



From left to right: dr. M.H. Gasem, dr. Hapsari, dr. Endang, dr. Indri, Wiwik, Rina, dr. Annisa, dr. Venty, Dr. Annisa (In action ☺)

dr. Hussein is a very busy and active doctor. He loves cycling and reading. His interest is vastly ranging from economics to architecture. You can almost be sure to find him reading his Bloomberg magazine in this leisure time. His particular interest and passion in architecture inspired him to design his own house, and it was featured in an architecture magazine.

dr. Hapsari is an adorable pediatrician and famous for her patience and hospitality. That's why her clinic is always packed with parents and their children eagerly waiting to see her. Besides her love as a clinician, this fashionable pediatrician is also crazy about research with quite the same fervor.

dr. Endang is a PhD in Microbiology, who also plays an important role as the site financial advisor. Besides her busy activities, she still sets aside some of her time for research. Currently, she is pursuing her desire to become an entrepreneur.

dr. Indri, is passionate about research and tropical medicine, and her passion has brought her to become a research assistant in this study. She used to be an active backpacker. However, she has to take a breather as she is now pregnant with her first child.

dr. Annisa is a very motivated research assistant who always has the energy and charm to enroll patients. During long weekends, she is often away on family visits, so you will have little luck trying to find her in Semarang.

dr. Venty is a newly-wed who has just finished her master degree in Genetic Counseling. She will be replacing dr. Indri while she is taking her maternity leave. We are all looking forward to sharing the excitement of recruiting subjects into the AFIRE study.

Ms. Wiwik is a lovely mother of two children and a meticulous analyst in genetic laboratory. You can easily recognize this perfectly dressed woman with an air of chic that is unmistakably Indonesian in special events.

Ms. Rina is a modest woman. She has been working at RSUP Dr. Kariadi laboratory for almost 20 years and knows how to deal with any laboratory issues in the lab well. This diligent laboratory technician is particularly very helpful in making the AFIRE study a success.



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PhD, SpPD- KPTI

Co-PI
dr. MMDEAH Hapsari,
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PhD

Research Assistant
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Rina Sirait, S. Kom

-UN-

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