INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

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Newsletter January 2017

In This Issue

Portable Devices to Predict An Illness: Will The Apps Today Keep The Doctor Away?

The introduction of mobile computing devices such as smartphones and tablet computers has greatly impacted many fields, including medicine. Health care professionals now use smartphone or tablet computers for functions they used to need a pager, cellphone, and PDA to accomplish.

The use of mobile devices by health care professionals has transformed many aspects of clinical practice. Mobile devices have become commonplace in health care settings, leading to rapid growth in the development of medical software applications for these platforms.

Mobile devices and apps provide many benefits for health care professionals, perhaps most significantly increased access to point-of-care tools, which has been shown to support better clinical decision-making and improved patient outcomes. Let's look further into this!

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And The Result Is...

Reading a scientific article could be very tiring and confusing, especially because of the complicated language, structure, and excessive information given. So, how do we attract more people to read our paper? Find out more about it here!

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Save The Date

Important Events, Meetings, & Holidays

1 January	New Year's Day 2017
11 January	AFIRE Protocol Core Team Meeting
28 January	*Chinese New Year*

January Birthday

7 Jan	Ms. Wiwik Lestari	Lab Tech Site 560
10 Jan	dr. Umi Solekhah Intansari	Co-PI SEA050 Site 43
24 Jan	Mr. M. Alfian	Lab Tech Site 530
25 Jan	dr. I Made Gede Dwi Lingga Utama	Co-PI INA101 Site 520
27 Jan	dr. Ida Safitri	Co-PI INA101 Site 580

Announcement

New Year is always so magnificent. It is when we celebrate the new upcoming year and say good bye to the previous *year, 2016*. Let us all welcome the coming New Year 2017 with open hearts and remember all the moments in our lives that were memorable from the previous year.

This January 2017, in addition to the usual Gregorian calendar's New Year, we also celebrate the Lunar New Year, the year of Rooster!

We wish you a very Happy New Year with the hope that you will have many blessings in the year to come.

INA-RESPOND Study Updates

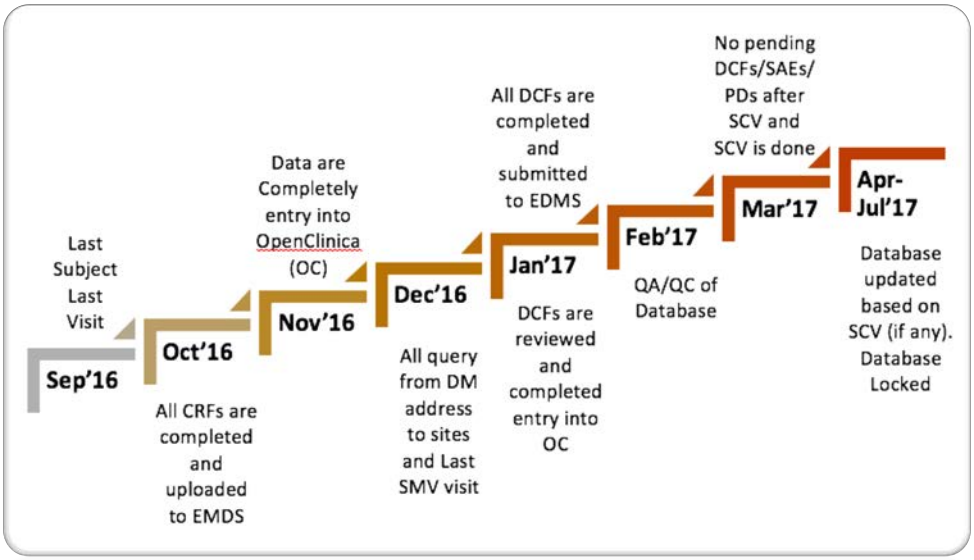
By:

Dr. Nurhayati

INA101 (AFIRE) Study Updates

A Protocol Core PIs meeting took place on 11 January 2017. The meeting was attended by dr M. Karyana M.Kes, Prof dr Emiliana Tjitra MSc, PhD, Dr dr Bachti Alisjahbana, SpPD-KPTI, PhD, Prof dr M Hussein Gasem, SpPD-KPTI, PhD, dr Dewi Lokida, Sp.PK, and Secretariat staffs. The progress of the AFIRE study's lab tests and manuscript preparation were discussed. A timeline for manuscript writing was set and agreed by the protocol PIs. At least 6 manuscripts will be drafted, finalized, and published this year.

Data management section set a timeline for CRFs and database so the data will be ready to be used by the Protocol PIs to draft the manuscript. The timeline can be seen in the chart below.



CRF and Database Timeline

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

For further information about this study please go to: http://www.ina-respond.net/afire-study/

INA102 (Tripod) Study Updates

The cohort observational study title "Tuberculosis Research of INA-RESPOND on Drug Resistance" (INA102-TRIPOD) will start to screen and enroll subjects in the near future. Preparation activities such as Site Preparation Visit (SPV), Site Initiation Visit (SIV) were conducted at 4 out of 7 sites. The site research teams are completing the outstanding document. We expect that in January, two sites will be activated and start to enroll subjects.

For further information about this study please go to: http://www.ina-respond.net/tripod-study/

Antibiotics Can Increase Risk of Childhood Obesity. How Does This Happen?

By:

Dr. Anandika Pawitri

A publication in *Gastroenterology*, the official journal of the American Gastroenterological Association, discovered that administration of certain frequency of antibiotics before a child reaches the age of 2 is associated with an increased risk of childhood obesity. The study mentions three or more courses of antibiotics can be a risk to the condition.

For decades, antibiotics have been used in livestock as treatment when they are ill, and to gain weight. It seems that it has the same effect in human. Research done in University of Colorado and University of Pennsylvania confirms this. Doctors and parents should pay attention regarding antibiotic use in infants in the absence of well-established indications.

The theory behind this is that antibiotics may progressively alter the composition and function of the gut microbiome.

The result of a population-representative cohort study in United Kingdom in assessing the association between antibiotic exposure before the age of 2 and obesity at the age of 4 showed that children with antibiotic exposure had a 1.2 percent absolute and 25 percent relative risk of early childhood obesity. Risk is strongest when considering repeat exposure to antibiotic with three or more courses.

Further research is required to assess whether these findings remain into adolescence and young adulthood, as well as to determine if early antibiotic use leads to later-onset obesity. Research should also examine whether specific classes of antibiotics are more strongly associated with subsequent obesity.

Reference:

Frank I. Scott, Daniel B. Horton, Ronac Mamtani, Kevin Haynes, David S. Goldberg, Dale Y. Lee, James D. Lewis. Administration of Antibiotics to Children Before Age 2 Years Increases Risk for Childhood Obesity. *Gastroenterology*, 2016; DOI: 10.1053/j.gastro.2016.03.006

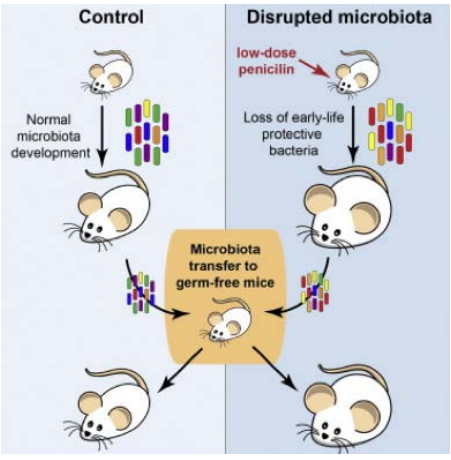
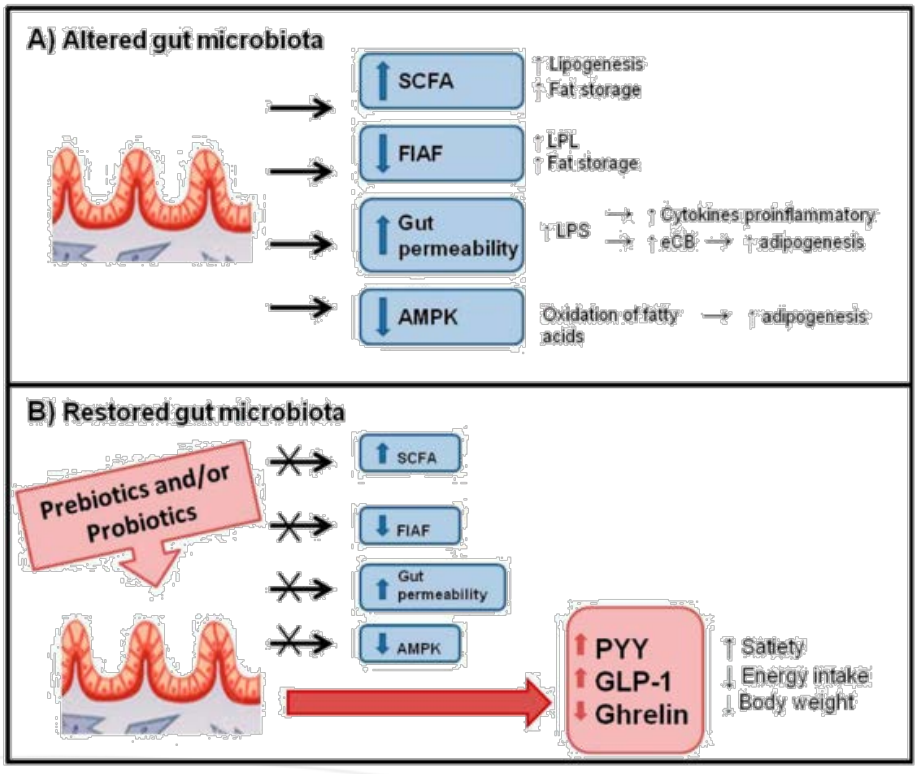


Fig. 1 When normal microbiota in mouse gut is disrupted, it can cause obesity



Comic Corner

And The Results Is ...

By:

dr. Aly Diana

Complicated information can really waste our time and be the source of our stress. Imagine the stress when we are reading a scientific article in a peer-reviewed journal and have to re-read the result section 3-5 times just to grab the essence of the study. Often when we encounter something like this, we give up halfway. In addition, complicated information/presentation may also lead us to wrong interpretation. Although experts have more skills in digesting new knowledge, a straightforward result or message is always preferable. Therefore, as we are craving for easy-to-read materials, we have to present our results in a simpler, clearer, and more concise way (without any errors) – just to be fair.

General suggestion is to display the data in tables (which present the exact values) and figures (which provide an overall assessment of the data, such as trend or differences in proportion). Then, decide the primary outcome and secondary outcomes that we want to report. Temptation to report everything that we have usually is the main culprit that makes our result section looks more complex than it should be. Stick to the order/the structure of the importance of findings, the most important goes first - keeping the best for last is simply not applicable in journal writing. Using sub-headings can be very helpful to prompt us and the readers with the flow of our results. Do not repeat all data in tables into the text, try our best to extract the information that we want to share.

Most of the result section in a quantitative study involves statistical analysis, and this part is usually the most complicated component to deal with. Although some of more complex/advanced statistical procedures produced reporting errors, unexpectedly, more errors come from basic statistical methods. Straightforward suggestion to avoid this: please look at the "Instruction for Authors" of the related journal. If we do not find any recommendations about how to report our results, we can follow the general rules or guidelines; for example: "The Statistical Analyses and Methods in the Published Literature (SAMPL) Guidelines". This example guidelines cover most common statistical analyses, to prevent some general reporting errors by focusing attention on key points in the analyses.

In this opportunity, I will highlight several useful suggestions. Firstly, present your findings with appropriate indicators of measurement error, such as: mean (standard deviation (SD)) for normally distributed data, median (IQR and/or range) for not normally distributed data, proportion/risks/rates/ratios (95% confidence interval (CI)), etc. Avoiding solely dependency on reporting result of hypothesis testing, such as p-value; as p-value does not convey any information on effect size. Secondly, report the descriptive statistics which become the basic sources of other analyses, such as sample size, the enumerators, and denominators of percentages. Having the first and second points provided will bring opportunity to incorporate our results into other analyses (re-analyses).

For primary outcomes, please report the numbers (for example: differences between groups, diagnostic sensitivity, and slopes of regression lines), as well as the measure of precision (such as the 95% CI). If desired, p-value should be reported to two decimal places, as equalities as possible (for example: p-value = 0.04 or 0.34 and NOT p-value <0.05); with the exception if the p-value < 0.001 (it is the smallest number that should be reported). In addition, do not report p-value as not significant (NS), but still give the actual p-value.

Asking our friends to read our draft for their honest comments is usually very helpful. By reading their facial expression while they are reading our results, we can tell whether we have to fix the draft or give it a go to be checked by other co-authors. Best wishes for 2017; hoping this year will also be fun and productive (with lots of published papers)!

References:

Lang T, Altman D. Basic statistical reporting for articles published in clinical medical journals: the SAMPL Guidelines. In: Smart P, Maisonneuve H, Polderman A (eds). *Science Editors' Handbook,* European Association of Science Editors, 2013.

Portable Devices to Predict An Illness: Will The Apps Today Keep The Doctor Away?

By

dr. Venty

Do you know that there are around 200 million portable wearable devices currently distributed in our market (one of them being our smart watches)? And that there are various portable wearable devices in the market that can be used to help us monitor our health?

By using a user-friendly applications compatible for the device, these devices can be easily used to monitor our physiological parameters. Unfortunately, we have not been using the data from these devices in the best way.

We normally use our portable devices for counting steps and measuring other physiological parameters individually. However, a Research team from Stanford University, California have found that it is possible to use the information gathered from our portable wearable devices to predict an illness. *"We want to tell when people are healthy and also catch illnesses at their earliest stages," said Michael Snyder, PhD, Professor and Chair of Genetics at Stanford University and senior author of the study.*

Physiological parameters such as heart rate (HR), blood pressure (BP), oxygen saturation, and skin temperature can provide information about the physical health status of a person. Any change, either elevation or a decrease of these parameters can indicate an alteration in health condition. Portable devices are capable of routine recording and delivery of multiple types of measurements in real time to the wearer or physician. Since the devices continuously follow the measures, they potentially provide rapid means to detect the early onset of a disease where it starts to change your physiology.

For this study, the researcher used seven devices and mobile apps, selected by 4 criteria: (1) ability to access data; (2) cost; (3) ability to measure more than one parameters; and (4) ease of use. They used a mobile apps called MOVES, which can continuously measure the activity status, and a smart watch called Basis, which is able to measure activity, steps, heart rate, and skin temperature in real time. Three portable devices, Scanadu Scout, iHealth-finger and Masimo, which have ability to measure heart rate and $Sp0_2$ are also used, as well as RadTarge to measure X-ray radiation exposure and Withings to predict weight and count calorie intake. (fig.1, column 1). In order to ensure the quality of the devices, they performed an extensive testing to assess the accuracy of the different devices against gold standard measurement and/or their instruments at clinical laboratory services, Stanford University.

To fulfill their study objective, two

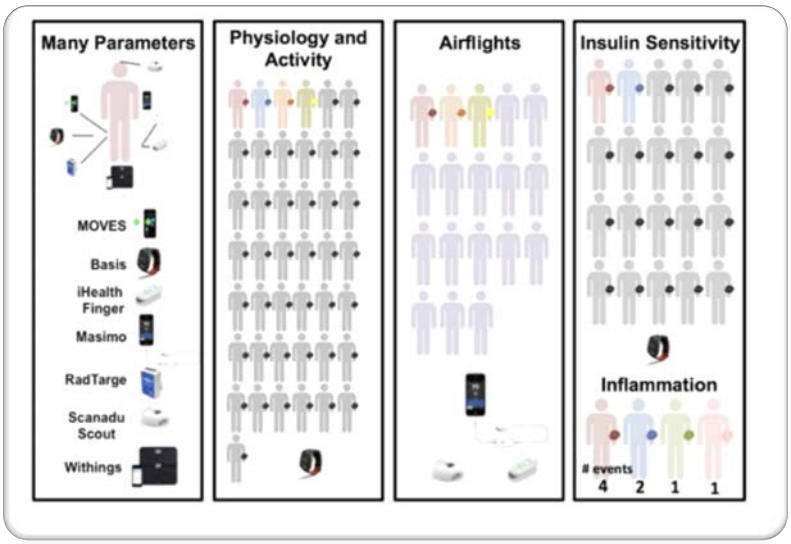


Fig 1. Overview of the project. Column 1: Wearable devices used in this study. **Column 2-4**: the 4 sub studies. The different colors for the human figures indicate the specific studies in which each individual participated (i.e., red participated in all five studies, grey in two studies [Physiology/Activity and Insulin Sensitivity], blue in three studies [Physiology/Activity, Insulin Sensitivity, and Inflammation], orange and yellow in two studies [Physiology/Activity and Airflights], and green and pink in one study [Inflammation] and purple in one study [Airflights]).

approaches were used. First, to intensely study one participant with many devices. The aim is to determine the ease of collecting different data types and identify interesting pattern during over 24 months monitoring period (Participant #1). The next step is to follow 60 participants in total which were divided in 4 sub studies: (1) Physiology and Activity; (2) Air flights; (3) Insulin sensitivity; (4) Inflammation. (fig.1, column 2-4).

Analysis of physiology and activity baseline included 43 individuals (including Participant #1) ages 35-70 years old using Basis smart watch for 11 months. The result is that there are highly varied baseline physiological differences among individuals that relate to clinically relevant parameters, suggesting that each of us have personal physiome and activity patterns that can be tracked using wearable technologies.

During monitoring of participant #1, the researchers identified several days of abnormal HR and skin temperature pattern, which interestingly coincided with the time when participant was sick. On days 470-474, when researcher detected abnormally elevated HR and skin temperature, participant #1 was suffering from Lyme disease (diagnosed on day 487 by a positive antibody test). Lyme disease is a bacterial infection (*Borrelia burgdoferi)* from an infected tick. On day 474, he went to a doctor and was treated by doxycycline. The symptoms and abnormal vital signs then disappeared on the following days. (Fig. 2)

Previously, on days 455-456, they also found elevated HR and skin temperature when participant #1 had Human rhinovirus infection (diagnosed by GeneMark test); as well as elevated hs-CRP levels and inflammatory cell counts).

In order to look further regarding the findings in Participant #1, the researchers investigated 3 other participants (Participant #39, #58 and #59 who reported themselves ill (all of them experienced a high CRP levels as evidenced by the inflammation during their illness period), and they were grouped with participant #1 in an inflammation study (see Fig. 1).

The researcher aimed to investigate the association between unusual physiological signals with disease status or disease markers. They analyzed skin temperature and HR change of the participants that were recorded during monitoring period. During their ill period, Stanford researchers found that only one participant had elevated skin temperature, whereas elevated HR was consistently observed for all individuals. This finding suggests that monitoring of HR using portable device can detect the inflammatory periods.

For further research at which illness might be confidently identified, the study team developed a software program called "Change of Heart" or COH for processing data from a smart watch. This software is able to recognize periods with abnormal HR patterns. The researchers focused on deviations in resting HRs and applied them into a peak-finding-based algorithm to the continuous HR signals. This peak-finding method is the best way to identify the shift time from healthy to sick status and thus detecting the disease in its early periods.

Another interesting finding were revealed during monitoring period. When some of their participants have a flight schedule, the researchers found that on long flights greater than 7 hours, SpO_2 – blood oxygenation levels were significantly higher toward than those at the beginning, measured

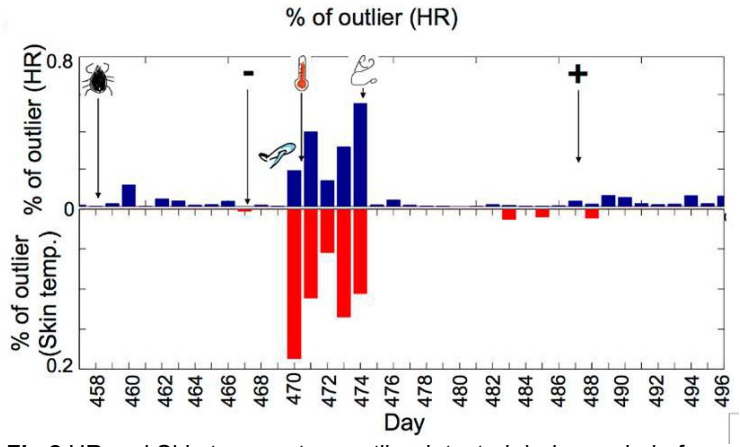


Fig.2 HR and Skin temperature outlier detected during period of Lyme disease.

at the same altitude level. This observation was not detected on short flights. The participants were tested by a psychomotor vigilance test to quantified a fatigue after landing. They observed that the decrease of SpO2 level is positively correlated with the fatigue status. This finding explains the adaptation on long flights and strong correlation between fatigue levels and decreased SpO_2 after flight.

After the study was over, the researchers also examined the relationship between blood glucose (BG) level and HR, as well as the relationship between activities and BMI because many of their participants were at risk for type 2 diabetes (T2D).

Firstly, they started to examine 20 individuals for Insulin sensitivity study (see Fig.1) in order to find out the association between daytime, nighttime and delta (daytime minus nighttime) HR and BG levels. Then they assessed a relationship between daily activity, BMI and BG levels. They found that an elevated HR have a strong positive association with BG level, independently with the effect of activity and BMI. In the future, a wearable portable device could potentially be developed into a simple test for those at risk for T2D by detecting variations in HR patterns.

In conclusion, the data presented by portable devices that are collected on a long-term basis can be used to measure, monitor, and analyze health-related physiology and also predict an illness

"It is likely in the future that these devices will be used by physicians to help assess health states and guide recommendations and treatments" said Snyder

References:

- Xiao Li, Jessilyn Dunn, Denis Salins, Gao Zhou, Wenyu Zhou, Sophia Miryam Schüssler-Fiorenza Rose, Dalia Perelman, Elizabeth Colbert, Ryan Runge, Shannon Rego, Ria Sonecha, Somalee Datta, Tracey McLaughlin, Michael P. Snyder. Digital Health: Tracking Physiomes and Activity Using Wearable Biosensors Reveals Useful Health-Related Information. *PLOS Biology*, 2017; 15 (1): e2001402 DOI: 10.1371/journal.pbio.2001402
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- PLOS. "Wearable biosensors can flag illness, Lyme disease, risk for diabetes; low airplane oxygen." ScienceDaily. ScienceDaily, 12 January 2017. <www.sciencedaily.com/releases/2017/01/170112141153.htm>

INA-RESPOND Newsletter

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