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UPM UNIVERSITI PUTRA MALAYSIA BERILMU BERBAKTI

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FROM THE EDITOR'S DESK

CRU welcomes its Associate Members (CRAMs) Clinician Scientist Coterie (CSC) members for the coming years of 2022 to 2023. CRAMS are representatives of every department in HPUPM. They will bridge the communication between CRU and their respective departments, as well as between other departments in sharing of research experience, activities and culture that may be unique in every respective department. CRAMs have access to all the CRU's facilities and privileges to attend research activities organised by CRU. They also have greater exposure to updates on meta-research and opportunity to lead research initiatives for and in HPUPM. These are shared by CSC members who are academic staff with a PhD degree. CSC Members are think-tank of CRU in providing ideas and opinions towards higher quality research, relevant areas, impactful measures, and forging or reconnecting to research-intensive centres of excellence. They are also coaches to all other staff including CRU's research officers. All these members are like a big family to grow and to strive together scaling new heights of clinical/biomedical research for HPUPM, country and the world.

This issue presents to you at least 2 interesting articles, the available insurance policy for clinical trials and some key points of randomisation. The former has progressed to a master policy with a more competitive premium to CRU (ie clinical trials in HPUPM) with the Great Eastern. Do find out more details from us about the other insurance companies and the procedures to obtain for your clinical trials or even non-experimental clinical research (from CHUBB). Randomisation is now an available service from CRU. The charges are being formalised but consultation is for free for now. Key points in sample size determination are summaries from the recently concluded workshop that could refresh some important memory about it. Hopefully it would transform the newly gained knowledge into a more firmly long-term memory.

As usual, the appraisals in written is published for the Meta-Journal Hour (MJH) Series 6 on The impact of Movement Control Order during the COVID-19 pandemic on lifestyle behaviors and body weight changes from the MyNutriLifeCOVID-19 online survey. MJH 7 follows tomorrow when we will look into the Malaysian Ivermectin I-TECH randomised controlled trial whether it was a well-designed study and with fair conclusions, and is Ivermectin not effective in treating people with mild to moderate COVID-19. CRU has put up MJH 8 to appraise a randomised clinical trial on the Effects of a Lifestyle Intervention to Prevent Deterioration in Glycemic Status Among South Asian Women With Recent Gestational Diabetes. The questions are What has gone wrong in this trial? Why did the dietary and physical activity interventions not seem to work? It was a very relevant trial in a high-risk population but the 'proven' interventions did not perform as expected.

In this issue 13, RECRUS publishes a new content for Current Evidence section. It shares the results from the project between the Springer Nature and The Association of Universities in the Netherlands (VSNU) on the societal impact through open research. The subprojects include Project 1on SDG relevancy mapping, Project 2 on Assessing non-academic usage and Project 3 on Helping researchers maximise societal impact.

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BREAKING NEWS

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CLINICAL TRIALS INSURANCE SERVICES

By: Nurfaizah Saibul

What is clinical trial insurance?

Insurance is a system under individual or business entity or organization, where in exchange for payment (premium) guarantees compensation for losses resulting from certain perils under specified conditions in a contract or policy. Clinical trial insurance is an important section of liability insurance. This insurance plan offers protection against legal liabilities which result from clinical trials. In principle, clinical trial insurance covers the design risk of the protocol.

Requirements of Clinical Trial Insurance

The requirement for trial insurance was initially featured in the ethical guidelines for biomedical research on human subjects published by the Indian Council of Medical Research in 2000. These guidelines in the "principles of nonexploitation" state that *"Each research shall include an in-built mechanism for compensation for the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary."*

According to the **Section 5.8.1 in the Malaysian Guideline for Good Clinical Practice** (NPRA, 2018)[2], *"If required by the applicable regulatory requirement(s), the sponsor should provide insurance or should indemnify (legal and financial coverage) the investigator/ the institution against claims arising from the trial except for claims that arise from malpractice and/or negligence."*

There are many insurance companies offering a broad range of coverage, each with its own terms and conditions. This can be confusing and as a result, the process of acquiring coverage can be time-consuming. Whilst Malaysia has no legal act governing clinical trial activities (including clinical trial indemnification and insurance), the Malaysian GCP guideline states that such indemnification and insurance should be provided if required by applicable regulatory requirements.

It is a requirement by the Independent Ethics Committee (IEC)/ Medical Research & Ethics Committee (MREC), Ministry of Health Malaysia that all ethics submissions for clinical trials must include proof of trial indemnification either by insurance certificate or letter of indemnity. These documents should indicate the protocol title and number, period of coverage and list of coverage for Malaysia sites among others. Insurance certificates that are renewed should be duly submitted to the ethics committee on an on-going basis[3].

Any institution/ center or investigator involved in clinical trial should be indemnified or insured for claims arising from:

i. Use of investigational medicinal product (IMP)
ii. Procedures/ activities performed for clinical trial
iii. Malpractice/ negligence.

Having the appropriate insurance coverage is part of the clinical trial and the needs should be addressed as early as possible. A sponsor/ contract research organization (CRO) needs to consider the product liability, geographical coverage and cost of clinical trial insurance (among others) when choosing insurance providers for a multi-center trial involving various countries. On the other hand, site and investigators must consider coverage for all their clinical trials and negligence activities when choosing insurance providers.

Clinical Trial Insurance Coverage

The service of providing insurance by insurers in Malaysia is governed by the Financial Service Act 2013. Under this act, the insurers can be a Malaysia company or an international company with license to operate in Malaysia[3].

Some examples of insurance companies that provide clinical trial insurance in Malaysia are:

i. Great Eastern (GE)
ii. Allianz (Az)
iii. Chubb Malaysia (CM)

*The summary of clinical trial insurance services provided by these companies is in **Table 1**. The main differences are that GE allows a no-cost master policy under CRU to cover for all future clinical trials. This is not available to CRU from the other 2 companies. Both GE and AZ have a high deductible before a claim is payable from the company. CM has the extra coverage that others do not have.

The common clinical trial insurance policy coverage is:

i. **Agreed Compensation Cover:**
Compensation to patients follows the agreed amount under the applicable clinical trial compensation clauses in the policy. It covers all the team members within the same institution or partner (which can be included with extra payment) including error or omission.

ii. **Legal Liability Cover:**
It covers damages, defense and claimant's costs that are legally liable to be paid.

Coverage by Endorsement is another type of clinical trial insurance. Some product liability policy provides clinical trial extension coverage by an endorsement to this policy. It is not covered if a particular trial is not specified and scheduled on the endorsement. Hence, it is important for the investigator to check the policy clause for this rider or extension. This form of insurance premium is usually cheaper. Be careful when an investigator is conducting an out-of-label claim clinical trial/ new indication trial, as this type of policy will be null and void.

Other liability insurance that site/ investigators overlook is equipment/ material/ public liability damage coverage. This insurance must be purchased separately to cover the equipment loaned from the sponsor. For example, spoilt by any human or natural disaster, stolen, or not returned by the patient.

How to choose a clinical trial insurance provider?

The decision to choose an insurance provider or a policy should be made after considering factors including:

i. How much insurance/ limit of indemnity to provide (per claim/ per patient/ per occurrence; per aggregate/ all claim) with retention/ deductible/ out of pocket for each claim by investigator/ sponsor?
ii. At what cost or premium?
iii. How long to cover the indemnity after the expiration of the insurance or any exclusion of pre-existing disease that will not be covered?

What information is needed for a clinical trial insurance application?

The required documents are subject to the requirements of the insurers and depend on the type of coverage to be applied for. As part of the clinical trial insurance application process, the applicant must provide an estimate of the number of subjects/ patients participating in the clinical trial to be covered, and the insurers are using this as a basis of premium.

As a general guideline, the compulsory documents needed are the **investigator's names, trial protocol, patient consent form,** and **approval letter by IEC.**

Claim handling

Potential claims include the following[3]:

i. A subject/ patient reports on injuries that is claimed to be caused by participation in clinical trials, for which cost is not covered within the clinical trial budget and with no other means of cost coverage, especially when the claim amount is more than the access or deductible in the policy.
ii. A serious side effect or any event that causes bodily injuries during a clinical trial.
iii. A technical operational staff realizes that he/she has committed some error or missed some step which would cause adverse event/effect.

Steps to abide by when the above scenario arise[3]:

i. To inform the following personnel when such a scenario arises as soon as possible. This shall include the CEO of institution (CRC or CRO), principal investigator, sponsor (depending on SOP of site).
ii. The person in-charge or any other person involved should not at any point of time, admit liability or settle any claim or incur any costs or expenses in connection therewith.
iii. The personnel should immediately contact insurance agent within a time limit not exceeding three (3) days. It is advisable to use multiple forms of communications to ensure the agent is informed.

References:

1. Gooi RB and Divekar D (2014). Insurance in clinical research. Perspectives in Clinical Research.5(4),145-150.
2. Society of Clinical Research Professionals Malaysia (SCRPM) (2016). A guide to conducting clinical trials in Malaysia. First Edition 2016.
3. National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia (2018). Malaysian Guideline for Good Clinical Practice, 4th Edition.

TABLE 1: SUMMARY OF CLINICAL TRIALS INSURANCE SERVICES IN MALAYSIA

No.	Description	Great Eastern A member of the OCBC Group	Allianz	CHUBB®
1.	**Policy Coverage**	➢ Compensates the research subject for bodily injury arising from the use of any pharmaceutical or medical devices in human clinical trials. ➢ The claim must be first notified to the insurers in writing during the period of insurance. ➢ The cover is on both "No Fault Compensation" and "Legal Liability" forms (dependent upon local licensing and regulatory requirements).	➢ The legal liability imposed by law to pay damages in respect of injury to any research subject caused by or arising out of participation by the research subject in any clinical trial. ➢ Claims-made basis i.e. claims first made against an insured and notified to the company during the period of insurance or within an agreed extended reporting period following the expiration date of the policy. ➢ The application will be reviewed and evaluated by the regional office.	**Clinical Trials Liability** ✓ Legal Liability Claims ✓ No Fault Compensation Claims (where applicable). ***Human Clinical Trial Insurance*** ✓ Indemnifies the insureds (Sponsor, CMO, CRO, investigators) against claims in respect of 3rd party bodily injury arising out of or in connecting with the insured trial. **Clinical Trials Extras** ✓ Clinical trial product recall expenses. ✓ Crisis response expenses. ✓ Medical expenses. ✓ Medical monitoring expenses etc.
2.	**Major Exclusions**	The policy does **not cover: -** ✓ Any liability for injury to employee unless such employee is a research subject in the clinical trial. ✓ Penalties, liquidated and punitive damages. ✓ Deductible amount specified in the policy. ✓ A clinical trial which was not approved by the ethics committee, all required authorization, licensing authority including the Ministry of Health Malaysia. ✓ Intended or expected injury. ✓ Pre-existing medical conditions.	The policy does **not cover**: ✓ Any injury to any employee unless the employee is a research subject. ✓ Any liability in respect of fines, penalties, punitive or exemplary damages. ✓ Any liability for clinical trials that have not received approval from authorities. ✓ Any liability arising from the departure from the agreed protocol. ✓ Any liability arising from the failure to obtain informed consent from the patient.	The policy is **not suitable** for: ✓ Hospital's roles as both sponsor and investigator involve surgery procedures in the clinical trial.

No.	Description	Great Eastern A member of the OCBC Group	Allianz	CHUBB
2.	**Major Exclusions**	The policy does **not cover**: ✓ War. ✓ Nuclear, radioactive contamination. ✓ Any claim arising from Hepatitis, Human T-Cell Lymphotropic Virus Type iii (HTLV iii) or Lymphadenopathy Associated Virus (LAV) or the mutants derivatives or variations thereof, related to Acquired Immune Deficiency Syndrome. ✓ Transmissible Spongiform Encephalopathy (TSE) Creutzfeldt-Jakob Disease (CJD), variant Creutzfeldt-Jakob Disease (vCJD) or new variant Creutzfeldt-Jakob Disease (nvCJD). ✓ Liability arising from any Occurrence happening prior to the retroactive date. ✓ Known circumstances by Insured prior to the inception of the policy. ✓ Cyber liability exclusion. Communicable disease exclusion.	The policy does **not cover**: ✓ Any liability arising from the deterioration of existing health conditions, which would have occurred whether the patient had participated in the study or otherwise. ✓ Any liability arising from the failure of any Medicinal Product to have its intended medicinal purpose. ✓ Any liability arising from an injury that was intended or expected by the Insured.	
3.	**Required information to get indication/ quotation**	1. A copy of duly completed of clinical trial insurance proposal form. 2. A copy of protocol. 3. Patient's consent form. 4. Confirmation of no serious adverse events being reported. 5. Past experience from similar trials.	1. Trial protocol. 2. Informed consent form. 3. Clinical trial proposal form.	1. Clinical trial protocol (full version or synopsis or draft). 2. ICF (Informed Consent Form) or PIS (Patient Information Sheet)-prefer draft. 3. Chubb HCT application form.

No.	Description	Great Eastern A member of the OCBC Group	Allianz	CHUBB
4.	**Product information /contact information**	www.greateasterngeneral.com. **Contact info:** Great Eastern General Insurance (Malaysia) Berhad Level 18, Menara Great Eastern 303 Jalan Ampang 50450 Kuala Lumpur Tel: 1300-1300 88 ***Important Note:*** *This information is issued as a matter of information only and please refer to the policy wording for more comprehensive terms and conditions.*	https://www.allianz.com.my/corporate/liabilities-operations-and-asset-protections/liabilities/clinical-trial-insurance.html **For product disclosure sheet:** https://www.allianz.com.my/content/dam/onemarketing/azmb/wwwallianzcommy/corporate/liabilities-operations-and-asset-protection/liabilities/clinical-trial-insurance/ClinicalTrialInsuranceDisclosureSheet_EN.pdf **Contact info:** Allianz Malaysia Berhad Allianz Arena, Ground Floor, Block 2A, Plaza Sentral, Jalan Stesen Sentral 5, Kuala Lumpur Sentral, 50470 Kuala Lumpur. Tel: 1-300-22-5542 customer.service@allianz.com.my	https://www.chubb.com/sg-en/business/clinical-trials-liability-insurance.html https://www.chubb.com/content/dam/chubb-sites/chubb-com/pl-pl/products/life-science/OWU-LIFE-SCIENCE-ENG-III-2020.pdf **Clinical Trials Fact Sheet:** https://www.chubb.com/content/dam/chubb-sites/chubb-com/sg-en/business/clinical-trials-liability-insurance/documents/pdf/chubb-clinical-trials-factsheet--sg.pdf **Clinical Trials Liability Policy Case Study Infographic:** https://www.chubb.com/content/dam/chubb-sites/chubb-com/sg-en/business/clinical-trials-liability-insurance/documents/pdf/clinical-trials-liability-policy-case-study-infographic--sg.pdf **Contact info:** Chubb Insurance Malaysia Berhad Wisma Chubb Jalan Sultan Ismail 50250 Kuala Lumpur Tel: 03 2058 3000 Fax: 03 2058 3333 www.chubb.com/my
5.	**How to apply?**	Contact CRU, HPUPM at 03-97699763 or email to cru_hpupm@upm.edu.my for further information.		

APPRAISALS IN META-JOURNAL HOUR 6

By: Salwana Ahmad, Nurul Iman Hafizah and BH Chew

The paper:

The impact of Movement Control Order during the COVID-19 pandemic on lifestyle behaviors and body weight changes: Findings from the MyNutriLifeCOVID-19 online survey. DOI: https://doi.org/10.1371/journal.pone.0262332

Watch the video recording on:

YouTube

Click [HERE] and don't forget to subscribe to our channel!

Why was this study conducted?

The COVID-19 pandemic was declared as a global pandemic on March 11, 2020, by the World Health Organization (WHO). Due to the persistent increase in COVID-19 cases in Malaysia, the government officially announced a national lockdown (Movement Control Order) on March 18, 2020 to prevent the further spread of the disease. However, early studies in a few countries found that prolonged home confinement during a disease outbreak could lead to dramatic changes in lifestyle behaviors of the population and subsequent changes in body weight(1-3). Therefore, the MyNutriLifeCOVID-19 study was conducted in Malaysia to determine the lifestyle behaviors during the lockdown and to assess whether these lifestyle behaviors are associated with bodyweight changes.

How was it done?

Study design and respondents

A cross-sectional online survey was conducted between April 21 – June 7, 2020 among 1319 Malaysian adult volunteers aged 18 years and above. Sampling was done using non-probability sampling (convenience sampling method) since it was an online survey. Information on study background, objectives and the scope of questions was provided before the study was conducted. Participants were also informed their participation was voluntary, which they may withdraw anytime without penalty or loss of benefit to which the participant is entitled before the participants agreed and gave their written consent and continue with the online survey. Before taking the online survey, participants were also informed that all data collected would be used solely for research purposes, and their permission for data sharing and publication was obtained.

Questionnaire administration

The online survey was disseminated through emails and social media (Facebook, Instagram, WhatsApp, and personal networks of respondents) using Google online survey platform. It was made available in 3 languages: English, Malay, and Chinese. Before the study commenced, the questionnaire was compared for consistency in usage for different languages and was pre-tested before data collection to ensure clarity and ease of understanding among respondents.

Questionnaires

The self-administered questionnaire consisted of five sections that assessed socio-demographic characteristics, body weight status, disease history, and lifestyle habits that include eating patterns, physical activity, and sleep quality.

Sections	Tool/Assessment	Validity and Reliability of Measurements.
Characteristics of the respondents	• Age • Ethnicity • Sex • Educational level • Marital status • Occupation • Monthly household income • Number of family members • Current living condition **Assessment:** • Self-reported diseases history • Type of diseases • Adoption of weight management strategies.	-

Anthropometric Information	• Height • Bodyweight • BMI • Bodyweight changes (weight decreased, no difference, weight increased)	-
Physical Activity	**Assessment:** • Performing any physical activities or exercise for at least 30 minutes per day during MCO. • Changes in the pattern of exercise or physical activity they performed during MCO as compared to pre-MCO	*Both translated and back-translated were compared for consistency and pre-tested before data collection for clarity and understanding.*
Sleep Pattern	**Assessment** of sleep pattern was measured using the Pittsburgh Sleep Quality Index (PSQI): • Sleep duration, sleep latency, and overall sleep quality	▪ *A useful tool for the assessment of subjective sleep quality in non-clinical and clinical settings.* ▪ *Validated questionnaire in Malay, with acceptable internal consistency (Cronbach's α coefficient= 0.74), fair test-retest reliability (intra-class correlation coefficient (ICC) = 0.58), and adequate convergent validity with comparison with Epworth sleepiness scale (ESS-M) score (Pearson's correlation coefficient, r=0.37)* (*Farah et al, 2019 (9)*)
Eating pattern	**A series of self-developed questions to identify changes in eating patterns during MCO:** **(1)** Perceived eating behaviors changes during MCO in comparison to pre-MCO. **(2)** Dietary habits including consuming homecooked meals, consuming foods or drinks from restaurants/hawker centers/coffee shops/other food stalls, consuming foods or drinks from western fast-food restaurants, going out to pack foods/drinks, ordering foods/drinks through Food Delivery Apps, obtaining free/donated foods/drinks, obtaining free foods/drinks, baking and preparing desserts at home, practicing healthier cooking methods, and practicing healthy eating concept "Quarter-Quarter-Half" **(3)** Food group consumption including rice/noodles/bread/cereals/cereal products/tubers, egg/fish/chicken, meat and meat products, legumes and nuts, milk and dairy products, fruits, vegetables, sugar-sweetened beverages, fried foods/high-fat foods, sweet foods/high sugary foods, dietary supplements, probiotic drinks. **(4)** Main meal consumption including breakfast, lunch, and dinner as well as snacking between main meal consumption	*Both translated and back-translated were compared for consistency and pre-tested before data collection for clarity and understanding.*

Data analysis

Descriptive statistics were presented as frequency and percentage for categorical variables and mean and standard deviation for continuous variables. Chi-square test of independence was used to determine the bivariate associations between the lifestyle behaviors and body weight changes; followed by generalized linear mixed model (GLMM) for variables with p-value <0.05 in the preceding statistical tests of association between lifestyle and body weight changes during MCO. Study sites and respondents were entered as random effects. Multivariable models are adjusted for potential confounding (age, sex, ethnicity, and BMI categories before MCO). Data were presented as odds ratio (OR) and 95% confident interval (CI), while all statistical significance level was set at $p<0.05$.

What was the finding?

Characteristics of the respondents

A total of 1319 Malaysian adults participated in the present study with a mean age of 36.3 ± 11.2 years. The majority of them were females (76.3%), attained tertiary education (90.9%), had a moderate to high monthly household income (84.5%), and lived with their family members during MCO (79.2%). A quarter of them were Malays (44.4%), 51.9% were married, and more than half of them began working from home during MCO (54.3%). Less than one-quarter of the respondents had chronic diseases (21.4%), with hypertension (8.5%), diabetes (5.2%), and hyperlipidemia (2.3%) as the top three common chronic diseases. Changes in body weight and BMI category during MCO.

Table 1 shows the overall changes in body weight and BMI category during MCO. Before MCO, about half of the respondents had a normal weight (54.7%), 7.8% were underweight, 25.5% were overweight, and 12.1% were obese. About one-third of the respondents gained weight during MCO (30.7%) with an average weight gain of 2.1 kg, while 32.2% lose weight with an average weight loss of 2.3 kg. About 11.0% of the respondents who were underweight before MCO had a further reduction in their body weight, while 46.3% gained weight, respectively. In terms of BMI category changes, 14.8% of the respondents who were underweight and 9.5% who were overweight attained normal BMI during MCO. For respondents who were normal weight before MCO, 1.5% and 4.5% of them became underweight and overweight, respectively.

Variables	Total (n = 1319)	BMI before MCO, n (%)				
		Underweight (n = 108)	Normal (n = 717)	Overweight (n = 328)	Obesity (n = 166)	*p*-value
Body weight changes during MCO (kg) [a]	-0.1 ± 2.1	0.6 ± 1.3	0.0 ± 1.8	-0.3 ± 2.3	-0.9 ± 3.1	< 0.001
Decreased	425 (32.2)	12 (11.1)	211 (29.4)	118 (36.1)	84 (50.3)	< 0.001
No change	489 (37.1)	46 (42.6)	290 (40.4)	113 (34.6)	40 (24.0)	
Increased	405 (30.7)	50 (46.3)	216 (30.1)	96 (29.4)	43 (25.7)	
BMI during MCO						
Underweight	103 (7.8)	92 (85.2)	11 (1.5)	0	0	< 0.001
Normal weight	721 (54.7)	16 (14.8)	674 (94.0)	31 (9.5)	0	
Overweight	336 (25.5)	0	32 (4.5)	281 (85.9)	23 (13.8)	
Obesity	159 (12.1)	0	0	15 (4.6)	144 (86.2)	

[a] Data are presented as mean ± standard deviation (SD).

https://doi.org/10.1371/journal.pone.0262332.t002

Table 1: Changes in body weight of the respondents during MCO

Lifestyle behavioral changes during MCO

More than half of the respondents reported managing their weight during MCO (84.4%). More than two-fifth of them practiced a healthier eating pattern (41.2%), 36.3% reduced their physical activities, and 25.7% had a poorer sleep quality during MCO. Amongst respondents who reported having lost weight during MCO, 68.1% claimed they managed their weight, 38.4% practiced healthier eating patterns, 41.0% performed more physical activities, and 37.0% had a better sleep quality as compared to before MCO. About 29.1% of respondents who have gained weight did not manage their weight during MCO, 49.0% practiced less healthy eating patterns, 38.6% performed lesser physical activities, and 38.9% had poorer sleep quality as compared to before MCO.

Eating pattern of the respondents during MCO.

Overall, respondents who gained weight reported ordering foods or drinks through food delivery apps (43.4% vs. 18.9%), consuming foods or drinks from restaurants, hawker centers, coffee shops, or other food stalls (41.7% vs. 26.2%), drinking sugar-sweetened beverages (41.1% vs. 26.2), consumed fried or high-fat foods (39.0% vs. 29.1%), consumed sweet or high sugary foods (39.6% vs. 29.5%), and snacking (36.3% vs. 26.5%) more frequently as compared to those who lose weight during MCO. On the other hand, respondents who lose weight tend to practice healthier cooking methods (36.5% vs. 24.3%) and comply with the healthy eating concept "Quarter-Quarter-Half" (36.1% vs. 24.9%), as well as consumed lunch (31.6% vs. 30.1%) more frequently compared to those who gained weight during MCO. No significant associations were found between consumption of home-cooked meals, going out to pack foods or drinks, obtaining free foods or drinks, consumption of foods or drinks from western fast-food restaurants, baking and preparing desserts at home, consumption of rice, noodles, bread, cereals, cereal products, and tubers, consumption of egg, fish, chicken, meat and meat products, consumption of legumes and nuts, consumption of milk and dairy products, consumption of fruits, consumption of vegetables, consumption of dietary supplements, consumption of probiotic drinks, as well as consumption of breakfast and dinner with body weight changes during MCO (data not shown).

In terms of **physical activity**, a total of 76.0% of respondents performed physical activities at least 30 minutes per day at less than five days per week during MCO. Respondents who lose weight performed physical activities at least 30 minutes per day more frequently as compared to those who gained weight (42.6% vs. 18.3%).

In terms of **sleep pattern**, more respondents had 6 to 7 hours of actual sleep at night (53.7%), with average sleep latency (32.3%), and fairly good sleep quality (58.7%) during MCO. More respondents who lose weight reported having a very poor sleep latency (34.0% vs. 33.3%) as compared to those who gained weight. There were no significant associations between duration of actual sleep at night and overall sleep quality with body weight changes during MCO (data not shown).

Associations between lifestyle behaviors and body weight changes during MCO

Results of the multivariable generalized linear model of associations between lifestyle behaviors and body weight changes during MCO are shown in the paper. After adjustment for confounding variables namely age, sex, ethnicity, and BMI category before MCO, practicing the healthy eating concept "Quarter-Quarter-Half", skipped lunch, and more frequent physical activities were factors that accounted for significant weight loss. Meanwhile, respondents who never consumed lunch were more likely to lose weight as compared to those with daily consumption (OR = 3.87, 95% CI = 1.27–11.73). Performing any physical activities at least 30 minutes/day for at least 5 days/week was associated with 1.4 times higher odds of weight loss among the respondents (OR = 1.44, 95% CI = 1.05–1.97).
After adjustment for confounding variables, respondents who practiced healthy cooking methods (OR = 1.61, 95% CI = 1.08–2.40) and consumed lunch (OR = 2.39, 95% CI = 1.25–4.60) less frequently were associated with higher odds of weight gain as compared to their counterparts. In contrast, respondents who consume fried/high-fat foods (OR = 0.64, 95% CI = 0.41–0.99) less frequently were less likely to gain weight as compared to those with daily consumption. Performing physical activities at least 30 minutes/day for at least 5 days/week reduced the odds of weight gain by 45% (OR = 0.55, 95% CI = 0.38–0.79). In terms of sleep patterns, respondents with good sleep latency were less likely to gain weight as compared to those with average sleep latency (OR = 0.62, 95% CI = 0.43–0.90).
The associations between lifestyle behaviors and body weight changes during MCO were further analyzed by adding BMI before MCO as an interaction term to the adjusted multivariable models. Among the overweight respondents, never (OR = 4.16, 95% CI = 1.13–15.26) or less frequent practice of healthy cooking methods (OR = 2.45, 95% CI = 1.05–5.68) were associated with weight gain, omit of high-fat foods were associated with higher odds of weight loss (OR = 14.98, 95% CI = 0.28–79.53), while not practicing healthy eating concept was associated with lower odds of weight loss. On the other hand, obese respondents who never practiced the healthy eating concept (OR = 6.32, 95% CI = 1.26–31.68) were more likely to gain weight, while those who performed physical activity more frequently were more likely to lose weight (OR = 3.35, 95% CI = 1.11–10.12). Among the normal weight respondents, those who consumed high-fat foods less frequently performed physical activity more frequently (OR = 0.53, 95% CI = 0.32–0.85), and had good sleep latency (OR = 0.52, 95% CI = 0.31–0.85) were less likely to gain weight, while those who skipped lunch were more likely to lose weight (OR = 4.76, 95% CI = 1.11–20.36). No significant associations were found between lifestyle behaviors and body weight changes during MCO among underweight respondents.

How much can we take out from this research/paper?

This study is considered a success in terms of the online recruitment of respondents. Another remarkable achievement is being relevant to the situation of the nation to know the people's health behaviors amid MCO and their lifestyle effect on body weight. The ability of a research group to garner support and to harness effort to complete a relevant study is always recommendable. Additionally, MyNutriLifeCOVID-19 uses many important and validated measures to capture lifestyles. Although inherent to an online survey to base on self-reporting of these measures including body weight and height, and other challenges of data quality, complete and comprehensive reporting are indispensable to make clear the study to others to have a wide impact.

Online surveys are more commonly completed by those who have access to the internet or those who are sufficiently biased to be interested in the subject [4]. The sociodemographic characteristics of the participants in this online survey are the middle-to-high income earners with 90% of them having at least tertiary education which presumably indicates that they might be more "health-cautious" as compared to the whole Malaysian population [6]. It would be more educational to have a note in the paper on how the recruitment was conducted, how wide it reached the Malaysian people, was reminder used, what token was given, was there any inquiry from prospective participants, response pattern according to the social media and states. This information would be helpful for future researchers who want to conduct online surveys. This learning point is more important than the results of the study because the MCO is unlikely to be repeated in any near future for the current socio-political reasons. This lacking of details is also quite substantial in other parts of the study, especially the analysis strategy and results sharing. In future similar studies where probability sampling is not possible or the need to correct non-representativeness in the study samples, statistical analysis techniques such as weighting [5], bootstrapping or propensity score matching could be done to improve the generalizability and representativeness of the data, or to make a fairer comparison between two groups of the primary exposure on the outcomes [6,7].

It was not explained how the collected samples were handled and the quality control applied to the data. Although the excluded number of respondents from the final analysis was small (about 20) but it is a good reporting practice to disclose this including handling of missing or extreme value data. The findings from pre-testing of the survey questionnaire and approaches could also be reported of any changes made.

The choice of GLMM and the modeling were not justified and elaborated, respectively. The statistical assumptions of the final GLMM model were not reported. The decision to estimate predictors/determinants on weight changes both on the Decreased and Increased could be made clear in the text. The number of samples included in each of the modelings should appear on the respective tables will increase readability.

Baseline characteristics and the lifestyles of the respondents were very illustrative of the 'who' and 'what' they behaved during the MCO. The findings right from the descriptive statistics to the inferential GLMM should bear in mind the characteristics of the respondents. These were mostly below 40-year-old of age, had tertiary education, were female, and were over-represented by Chinese in terms of ethnicity proportion in the larger population. Tables 2 and 3 are very informative as they describe weight changes and lifestyles. The former shows that at the most about 15% of the respondent reported a weight change. This information could be discussed by comparing to the people's behaviors before the COVID-19 pandemic, and I believe much we could learn from this alone.

The inferential statistics from GLMM provided many expected determinants of the weight changes but also some 'unexpected' factors. It is uncertain whether this observation was purely due to chance or multiple testing in the analysis that was not adjusted for with a reduced alpha value such as by the Bonferonni method where 0.05 is divided by the additional number of testings. There are some inconsistencies within and between the 2 outcome variables of Decreased and Increased weight.

Discussion and the limitations suggested were fair and rightly cautioned when interpreting and applying the results from the study. Future studies using online surveys should take to heart disseminating the survey invitation to different social media populated by different groups of people. This could improve the representativeness of the study samples to the population at large.

References

1. Sidor A, Rzymski P. Dietary choices and habits during COVID-19 lockdown: Experience from Poland. *Nutrients*. 2020; 12(6):1657. https://doi.org/10.3390/nu12061657 PMID: 32503173
2. Ammar A, Brach M, Trabelsi K, Chtourou H, Boukhris O, Masmoudi L, et al. Effects of COVID-19 home confinement on eating behaviour and physical activity: Results of the ECLB-COVID19 International Online Survey. *Nutrients*. 2020; 12(6):1583. https://doi.org/10.3390/nu12061583 PMID: 32481594
3. 14. Rodrı´guez-Pe´rez C, Molina-Montes E, Verardo V, Artacho R, Garcı´a-Villanova B, Guerra-Herna´ndez EJ, et al. Changes in dietary hehaviours during the COVID-19 outbreak confinement in the Spanish COVIDiet Study. *Nutrients*. 2020; 12(6): 1730. https://doi.org/10.3390/nu12061730 PMID: 32531892
4. Andrade, C. The Limitations of Online Surveys. *Indian J Psychol Med*. 2020;42(6):575-576.
5. Lavrakas, P. J. (2008). Encyclopedia of survey research methods (Vols. 1-0). Thousand Oaks, CA: Sage Publications, Inc. doi: 10.4135/9781412963947. https://methods.sagepub.com/reference/encyclopedia-of-survey-research-methods/n632.xml
6. MyCensus 2020 Recorded Population (2022). Department of Statistics Malaysia. Accessed via: https://www.dosm.gov.my/v1/index.php?r=column/cthemeByCat&cat=117&bul_id=akliVWdIa2g3Y2VubTVSMkxmYXp1UT09&menu_id=L0pheU43NWJwRWVSZklWdzQ4TlhUUT09
7. Austin, P.C. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res*. (2011);46(3):399-424.
8. De Bin, R., Janitza, S., Sauerbrei, W., Boulesteix, A-L. Subsampling versus bootstrapping in resampling-based model selection for multivariable regression. (2014) Department of Statistics, University of Munich, 171.
9. Farah, N. M., Saw Yee, T., & Mohd Rasdi, H. F. (2019). Self-Reported Sleep Quality Using the Malay Version of the Pittsburgh Sleep Quality Index (PSQI-M) In Malaysian Adults. *International journal of environmental research and public health*, *16*(23), 4750. https://doi.org/10.3390/ijerph16234750.

KEY POINTS IN SAMPLE SIZE WORKSHOP

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Justification of sample size calculation is a vital part of any clinical research. However, estimating the number of participants required to give a valid result is not always easy. Studies that have a sample size that is too small will be underpowered and may lead to inconclusive results, while too large of sample size will lead to waste of resources and expose more participants than necessary to any related risk related to the study. Important components that are required in the calculation of sample size include study design, an estimated important effect size, type 1 error, type 2 error, desired power, also sometime number of variables and precision are relevant considerations. A brief discussion of the important components of sample size calculation had been discussed in a previous article on Determination of Sample Size (CLICK HERE).

This article will briefly describe important steps in sample size calculation for clinical trials followed with observational studies. In addition, this article will introduce the methods to calculate sample size required for studies using common statistical analysis in multivariable modelling. There are various ways to estimate sample size required for a proposed study.

Sample size calculation can be done manually using specific formula or sample size software can be used to ease the calculation. Common free software to calculate sample size is available at Software & Calculator | HOSPITAL PENGAJAR UNIVERSITI PUTRA MALAYSIA (upm.edu.my). Nowadays, scholars have tabulated sample size table from various statistical test and these are also available in the literatures. Some scholars presented their sample size estimation using nomograms."

Study Design 1: Randomised Controlled Trial

Randomised controlled trials (RCT) are prospective studies that commonly used to measure the effectiveness of a new intervention or treatment. Many clinical trials that do not carefully consider the sample size requirement turn out to lack the statistical power or the ability to detect intervention effects of magnitude that has clinical importance (45,46). The numerous designs of RCT such as parallel RCT, cluster RCT, and factorial will require slightly different sample size estimation approaches. This article will demonstrate an example for parallel RCT which is the most common RCT. The method to calculate sample size for other design of RCT will be discussed in future articles.

Generally, there are **two types of formula to calculate sample size in RCT** which are **two proportion** which be used in **dichotomous data** (the outcome) and **two means** which being used for **continuous variable** (the outcome) with the assumption that the sample are recruited and assigned randomly to the groups.

Using the recently published study on JAMA, the ITECH trial with the aim to determine the efficacy of ivermectin in preventing progression to severe disease among high-risk patients with COVID-19.

Let's go through the statement in study on the section of sample size.

The sample size was calculated based on a superiority trial design and primary outcome measure. The expected rate of primary outcome was **17.5%** in the control group, according to a previous local data of high-risk patients who presented with mild to moderate disease. **A 50% reduction of primary outcome**, or a 9% rate difference between intervention and control groups, was considered clinically important. This trial required 462 patients to be adequately powered. This sample size provided a **level of significance at 5% with 80% power for 2-sided tests**. Considering potential dropouts, a total of 500 patients (250 patients for each group) were recruited.

1) Using two proportion formula (Pocok's formula)

$n = [(p_1 (1-p_1) + p_2 (1-p_2)] x (Z_\alpha + Z_\beta)^2 / (p_1-p_2)^2$

$n = \frac{[0.175(1-0.175)+0.087(1-0.087)] x (0.84+0.05)^2}{(0.175-0.087)^2}$

= 228 per arm, so there are two arms in the trial

Total sample size required: 457 with 10% drop up, round up to nearest number total 500 participants needed.

where :

n = required sample size
α = level of statistical significance
1-β = power of study
$z\alpha$ = value of the standard normal distribution cutting off probability α in one tail for a one –sided alternative or $\alpha/2$ in each tail for a twosided alternative
$z\beta$ = value of the standard normal distribution cutting off probability β

2) Using G-power software using exact test

Exact – Proportions: Inequality, two independent groups (Fisher's exact test)

Options:	Exact distribution		
Analysis:	A priori: Compute required sample size		
Input:	Tail(s)	=	Two
	Proportion p1	=	0.1750000
	Proportion p2	=	0.08699999999999999
	α err prob	=	0.05
	Power (1-β err prob)	=	0.8
	Allocation ratio N2/N1	=	1
Output:	Sample size group 1	=	247
	Sample size group 2	=	247
	Total sample size	=	**494**
	Actual power	=	0.8011141
	Actual α	=	0.0352500

	Z_α	
α	One-sided test	Two-sided test
0.10	1.282	1.645
0.05	1.645	1.960
0.025	1.960	2.240
0.01	2.326	2.576

$1-\beta$	Z_β
0.50	0.00
0.60	0.25
0.70	0.53
0.80	0.84
0.85	1.036
0.90	1.282
0.95	1.645
0.975	1.960
0.99	2.326

The concept of sample proportion as shown above is relevant, however, modification is needed to calculate sample size for **continuous variable**. Below is the formula for continuous outcome variable:

$N = \frac{2\sigma^2 (Z\alpha+Z\beta)^2}{\Delta^2}$

Where:
σ = standard deviation of either group
Δ = expected detectable difference between two groups
$z\alpha$ = value of the standard normal distribution cutting off probability α in one tail for a one –sided alternative or $\alpha/2$ in each tail for a two-sided alternative

Below is an example of sample size calculation for continuous outcome variable which is blood pressure.

A new antihypertensive drug is to be tested against current treatment practice in people with systolic blood pressure > 160 mmHg and/or diastolic blood pressure > 95mmHg. It is felt that if the new drug can achieve blood pressure levels that are on the average **10 mmHg** than those achieve using current treatment then it would be accepted by the medical community. The investigators would like at **least 90% power** and have chosen **α = 0.01 (two-sided)** as the current therapy is quite acceptable and they want to be sure that the new therapy is superior before switching over. Blood pressure measurement has a standard deviation of **20 mmHg.**

α= 0.01 Δ=10 Z α=2.58 β= 0.1 σ=20 Z β=1.28

Substitute the value into the formula

$N = \frac{2\sigma^2 (Z\alpha+Z\beta)^2}{\Delta^2}$

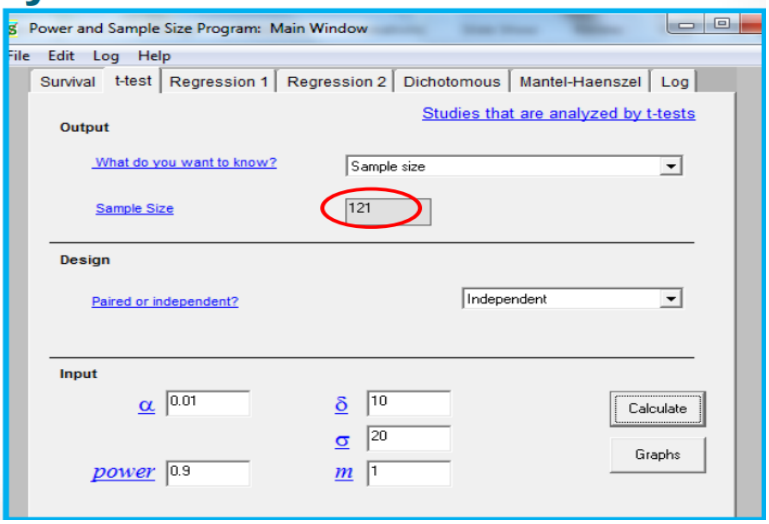
n = 119.2

Required sample size is **120** per group (240 hypertensive in all)
It is recommended to consider 10 -20% drop out rates in the sample size calculation.

The number of sample size calculated using the software also yielded almost similar value which is **121** subjects per group.

On the other hand, the figure below showed the calculation of sample size using the software Power and Sample Size.

By software



Study Design 2: Observational Study

Cohort, cross sectional, and case-control studies are examples of data collection designs in observational studies. Often, these studies are the only practicable method of studying various problems related to a disease of interest, for example, studies of aetiology are one of the instances where a randomised controlled trial might be unethical, or if the condition to be studied is rare.

Researchers can utilise similar formula to calculate sample size. However, little modification is needed for calculation sample descriptive studies which mainly aimed to determine the prevalence of diseases size. One proportion sample size formula can be used to calculate sample size in descriptive studies. The main difference between one proportion and two proportion formulae is the calculation in one proportion formula do not involve hypothesis testing thus power is not included in the formula.

One proportion sample size formula:

$$n = \left(\frac{z}{\Delta}\right)^2 p(1-p)$$

Where:

p : expected proportion of individuals in the sample with the characteristic of interest at the determined 100(1-α)% confidence interval. It can be obtained from literature or a pilot study or preliminary work

Δ = precision (generally at 0.05, however it can be adjustable to achieve affordable, feasible and statistically meaningful sample size

Below is an example of sample size calculation using one proportion formula:

A local health department wishes to estimate the prevalence of dental carries among children under 12 years of age in its locality. How many children should be included in the sample so that it may be estimated to within **5 percentage points of the true value with 95% confidence**? It has been estimated that the prevalence of dental carries among children was **20%** from previous literature

Solution :
Anticipated population proportion (p) = 20% (0.2)
Level of significance = 5% (0.05)
Absolute precision (Δ) = $\pm$ 5%
n = 246

The sample of 246 children required at the analysis stage.

3) Calculation Based on Statistical Analysis:

Multivariate analysis deals with simultaneously predicting **multiple** outcomes while multivariable analysis is a tool for determining the relative contributions of different factors to a **single** event.

Observational study that is causal in nature will has many confounding factors that can be controlled using multivariable analyses. Generally, the number of sample size required for observational studies with planned multivariable analysis is higher compared to univariate and bivariate analysis. The number of sample size is heavily depended on the number of independent variables in the final model.

Different types of statistical test require different method of sample size calculation.

Table 1 shows the published articles related to sample size determination for various statistical tests.

Statistical test	Published articles
a/ To estimate parameters for population	Krejcie and Morgan (1), Lachin (2), Campbell et al. (3), Bartlett et al. (4), Israel (6), Naing et al. (7)
b/To infer the results for larger population	
Correlation	Cohen (8), Algina and Olejnik (9), Bujang and Nurakmal (10)
Intra-class correlation	Fleiss and Cohen (11), Bonett (12), Zou (13), Bujang and Baharum (14)
Kappa agreement test	Cicchetti (15), Flack et al. (16), Cantor (17), Sim and Wright (18), Bujang and Baharum (19)
Independent sample t-test and paired t-test	Lachin (2), Cohen (8), Dupont and Plummer (20).
One-way ANOVA	Cohen (8), Jan and Shieh (21)
Pearson's chi-square	Lachin (2), Cohen (8), Dupont and Plummer (20)
Cronbach's alpha	Bonett (22), Bonett (23), Bonett and Wright (24), Bujang et al.(25)
Sensitivity and specificity	Buderer (26), Malhotra and Indrayan (27), Bujang and Adnan (28)
Linear regression or Multiple linear regression	Cohen (8), Dupont and Plummer (20), Hsieh et al. (29), Knofczynski and Mundfrom (30), Tabachnick and Fidell (31), Bujang et al. (32).
Analysis of covariance	Borm et al. (33), Bujang et al. (34)
Logistic regression	Peduzzi et al. (35), Hsieh et al. (29), Bujang et al. (34)
Survival analysis	Lachin (2), Lachin and Foulkes (36), Dupont and Plummer (20).
Cox regression	Peduzzi et al. (37), Hsieh and Lavori (38), Schmoor et al. (39).
Exploratory factor analysis	Barrett and Kline (40), Osborne and Costello (41), Bujang et al. (42),Bujang et al. (43).

Table adapted from Bujang MA. A step-by-step process on sample size determination for medical research Malays J Med Sci. 2021;28(2):15–27. https://doi.org/10.21315/mjms2021.28.2.2.

Next, this article will discuss on the rule of thumb for common statistical test used in medical and clinical research which include logistic regression, cox regression, multiple linear regression and analysis of covariance (ANCOVA).

i) Logistic regression and cox regression:

The similarities between logistic regression and cox regression are both have binary outcome. Therefore, similar formula can be applied to calculate sample size. Previous study by Peduzzini et al (1996) suggested to used EPV 10 (event per variable = 10) where the rule of thumb depends on a few parameters which are:
1/ Prevalence of the outcome of interest
2/ Number of participants to be recruited
3/ Number of independent risk factor on final model

However, the rule received some critics and recommended to used EPV20 instead of EPV50. In a latest publication by Bujang et al (2018), the author recommend a simplified version of formula which is : **n = 100 + 5i** where i refers to number of independent variables in the final regression model.

ii) Multiple linear regression (MLR) and analysis of covariance (ANCOVA)

MLR and ANCOVA share a common assumption however usually applied in different scenario. The proposed formula to be used in multiple linear regression (MLR) and general linear model (ANCOVA) is **N> 50 + 8M** as proposed by Tabachanick et al (2013).

Where :
N = sample size required
M= no of predictors or risk factor

Although sample size estimation based on a rule of thumb may considered as a weak method compare to the proper sample size calculation, but scholars have proposed rule of thumbs to ease researchers. The idea is researchers to be able to come out with sufficient sample size that will likely prevent the study from underpowered and at the same time prevent them from wasting resources. In addition, it is not practical to calculate sample when the minimally important effect sizes are unknown and unpredictable.

In a nutshell, there is no one-size-fits-all formula for sample size calculation that will be able to fit all study designs and statistical analyses. Sample size must be calculation properly to ensure the study have enough power to justified the aim of the study.

References :

1. Krejcie RV, Morgan DW. Determining sample size for research activities. Educ Psychol Meas. 1970;30:607–610. https://doi.org/10.1177/001316447003000308
2. Lachin JM. Introduction to sample size determination and power analysis for clinical trials. Controlled Clin Trials. 1981;2(2):93–113. https://doi.org/10.1016/0197-2456(81)90001-5
3. Campbell MJ, Julious SA, Altman DG. Estimating sample sizes for binary, ordered categorical, and continuous outcomes in two group comparisons. BMJ. 1995;311:1145–1148. https://doi. org/10.1136/bmj.311.7013.1145
4. Bartlett JE, Kotrlik JW, Higgins C. Organizational research: determining appropriate sample size for survey research. Inf Technol Learn Perform J. 2001;19:43–50
5. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther. 2005;85:257–268. https://doi.org/10.1093/ptj/85.3.257
6. Israel GD. Determining sample size (Tech. Rep. No. PEOD-6). Florida: University of Florida, Institute of Food and Agricultural Sciences; 2003
7. Naing L, Winn T, Rusli BN. Practical issues in calculating the sample size for prevalence studies. Archives of Orofacial Sciences. 2006;1:9–14.
8. Cohen J. A power primer. Psychol Bull. 1992;112:155–159. https://doi.org/10.1037/0033- 2909.112.1.155
9. Algina J, Olejnik S. Sample size tables for correlation analysis with applications in partial correlation and multiple regression analysis. Multivar Behav Res. 2003;38:309–323. https:// doi.org/10.1207/S15327906MBR3803_02
10. Bujang MA, Nurakmal B. Sample size guideline for correlation analysis. World Journal of Social Science Research. 2016;3(1):37–46. https://doi. org/10.22158/wjssr.v3n1p37

11. Fleiss J, Cohen J. The equivalence of weighted kappa and the intraclass correlation coefficient as measures of reliability. Edu Psychol Meas. 1973;33:613–619. https://doi. org/10.1177/001316447303300309
12. Bonett DG. Sample size requirements for estimating intraclass correlations with desired precision. Stat Med. 2002;21:1331–1335. https:// doi.org/10.1002/sim.1108 25.
13. Zou GY. Sample size formulas for estimating intraclass correlation coefficients with precision and assurance. Stat Med. 2012;31(29):3972– 3981. https://doi.org/10.1002/sim.5466 .
14. Bujang MA, Baharum N. A simplified guide to determination of sample size requirements for estimating the value of intraclass correlation coefficient: a review. Arch Orofac Sci. 2017;12:1– 11.
15. Cicchetti DV. Testing the normal approximation and minimal sample size requirements of weighted kappa when the number of categories is large. Appl Psychol Meas. 1981;5(1):101–104. https://doi.org/10.1177/014662168100500114
16. Flack V, Afifi A, Lachenbruch P. Sample size determinations for the two rater kappa statistic. Psychometrika. 1988;53:321–325. https://doi. org/10.1007/BF02294215
17. Cantor AB. Sample-size calculations for Cohen's kappa. Psychol Methods. 1996;1(2):150–153. https://doi.org/10.1037/1082-989X.1.2.150
18. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther. 2005;85:257–268. https://doi.org/10.1093/ptj/85.3.257
19. Bujang MA, Baharum N. Guidelines of the minimum sample size requirements for Kappa agreement test. Epidemiology, Biostatistics, and Public Health. 2017;14(2);e12267-1. https://doi. org/10.2427/12267
20. Dupont WD, Plummer WD. Power and sample size calculations for studies involving linear regression. Control Clin Trials. 1998;19:589–601. https://doi.org/10.1016/S0197-2456(98)00037-3
21. Jan SL, Shieh G. Sample size determinations for Welch's test in one-way heteroscedastic ANOVA. Br J Math Psychol. 2014;67:72–93. https://doi. org/10.1111/bmsp.12006
22. Bonett DG. Sample size requirements for testing and estimating coefficient alpha. J Educ Behav Stat. 2002;27:335–340. https://doi. org/10.3102/10769986027004335
23. Bonett DG. Sample size requirements for comparing two alpha coefficients. Appl Psychol Meas. 2003;27(1):72–74. https://doi. org/10.1177/0146621602239477 35.
24. Bonett DG, Wright TA. Cronbach's alpha reliability: interval estimation, hypothesis testing, and sample size planning. J Organ Behav. 2015;36(1):3–15. https://doi.org/10.1002/ job.1960 36.
25. Bujang MA, Omar ED, Baharum NA. A review on sample size determination for Cronbach's alpha test: a simple guide for researchers. Malays J Med Sci, 2018;25(6):85–99. https://doi.org/10.21315/ mjms2018.25.6.9
26. Buderer NM. Statistical methodology: incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Acad Emerg Med. 1996;3:895– 900. https://doi.org/10.1111/j.1553-2712.1996. tb03538.x 38.
27. Malhotra RK, Indrayan A. Simple nomogram for estimating sample size for sensitivity and specificity of medical tests. Indian J Ophthalmol. 2010;58:519–522. https://doi.org/10.4103/0301- 4738.71699
28. Bujang MA, Adnan TH. Requirements for minimum sample size for sensitivity and specificity analysis. J Clin Diagn Res. 2016;10(10):YE01–YE06. https://doi.org/10 .7860/JCDR/2016/18129.8744
29. Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. Stat Med. 1998;17(14):1623– 1634. https://doi.org/10.1002/(SICI)1097- 0258(19980730)17:14%3C1623::AID-SIM871%3E 3.0.CO;2-S
30. Knofczynski GT, Mundfrom D. Sample sizes when using multiple linear regression for prediction. Educ Psychol Meas. 2008;68(3):431–442. https://doi.org/10.1177/0013164407310131
31. Tabachnick BG, Fidell LS. Using multivariate statistics. 6th ed. Boston: Pearson Education; 2013.
32. Bujang MA, Sa'at N, Tg Abu Bakar Sidik TMI. Determination of minimum sample size requirement for multiple linear regression and analysis of covariance based on experimental and non-experimental studies. Epidemiology Biostatistics and Public Health. 2017;14(3):e12117-1. https://doi. org/10.2427/1211
33. Borm GF, Fransen J, Lemmens WA. A simple sample size formula for analysis of covariance in randomized clinical trials. J Clin Epidemiol. 2007;60:1234–1238. https://doi.org/10.1016/j. jclinepi.2007.02.006
34. Bujang MA, Sa'at N, Tg Abu Bakar Sidik TMI, Lim CH. Sample size guidelines for logistic regression from observational studies with large population: emphasis on the accuracy between statistics and parameters based on real life clinical data. Malays J Med Sci. 2018;25(4):122–130. https://doi. org/10.21315/mjms2018.25.4.12
35. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996:49;1373–1379. https:// doi.org/10.1016/S0895-4356(96)00236-3
36. Lachin JM, Foulkes MA. Evaluation of sample size and power for analyses of survival with allowance for nonuniform patient entry, losses to follow-up, noncompliance, and stratification. Biometrics. 1986;42:507–519. https://doi. org/10.2307/2531201
37. Peduzzi P, Concato J, Feinstein AR, Holford TR. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. J Clin Epidemiol. 1995;48:1503–1510. https://doi. org/10.1016/0895-4356(95)00048-8
38. Hsieh FY, Lavori PW. Sample-size calculations for the Cox proportional hazards regression model with nonbinary covariates. Control Clin Trials. 2000;21:552–560. https://doi.org/10.1016/ S0197-2456(00)00104-5
39. Schmoor C, Sauerbrei W, Schumacher M. Sample size considerations for the evaluation of prognostic factors in survival analysis. Stat Med. 2000;19:441–452. https://doi.org/10.1002/ (SICI)1097-0258(20000229)19:4%3C441::AIDSIM349%3E3.0.CO;2-N
40. Barrett PT, Kline P. The observation to variable ratio in factor analysis. Personality Study in Group Behavior. 1981;1:23–33.
41. Osborne J, Costello A. Sample size and subject to item ratio in principal components analysis. Practical Assessment, Research & Evaluation. 2004;9(11):Article 11. https://doi.org/10.7275/ ktzq-jq66
42. Bujang MA, Ab Ghani P, Soelar SA, Zulkifli NA. Sample size guideline for exploratory factor analysis when using small sample: taking into considerations of different measurement scales. Statistics in Science, Business, and Engineering (ICSSBE) 2012, Langkawi, Malaysia, 10–12 September 2012. https://doi.org/10.1109/ ICSSBE.2012.6396605
43. Bujang MA, Ghani PA, Soelar SA, Zulkifli NA, Omar ED. Invalid skewed responses contributes to invalid factor solution in exploratory factor analysis: a validation approach using real-life data. J Behav Health. 2019;8(4):152–160. https://doi.org/10.5455/jbh.20190628084939
44. Naing et al Determination of Sample size: Concept and Application, Determination of Sample Size in Interventional Study, Determination of Sample size in Analytical Study, Determination of Sample size in descriptive study Sample Size Workshop Lecture Notes Feb 2022
45. Freiman JA, Chalmers TC, Smith H, Jr., Kuebler RR. The importance of beta, the type II error and sample size in the design and interpretation of the randomized control trial. Survey of 71 "negative" trials. N Engl J Med 1978;299:690–694.
46. Moher D, Dulberg CS, Wells GA. Statistical power, sample size, and their reporting in randomized controlled trials. JAMA 1994;272:122–124

RANDOMISATION IN CLINICAL TRIALS

By: Salwana Ahmad

Background

Randomization is a procedure in experimental studies when assigning participants to treatment groups before a clinical trial start. Randomization ensures that each subject has an equal chance of receiving any of the interventions under the study. It produces study groups that are comparable in terms of both known and unknown risk variables, eliminates investigator bias in participant allocation (i.e., allocation concealment), minimizes the variability of the evaluation, provides an unbiased evaluation of the intervention, and ensures that statistical tests have valid false positive error rates (Friedman, Furberg, & Demets, 2010).

The important roles of randomization are as follows:

i. It eliminates the possibility of allocation/selection bias in study sampling involving a selection of participants who may not represent the study population. Such allocation/selection bias can easily occur when a researcher or participant influences group selection spontaneously or involuntarily which may lead to imbalance of prognostic factors at baseline. The direction of the allocation/selection bias can be positive or negative, which can invalidate comparisons between groups. The researcher would have to control for covariates in the analysis to obtain an unbiased outcome caused by the indistinguishable between treatment effects due to the influence of risk imbalance (Friedman et al., 2010).

ii. Effective randomization produces comparable groups in term of a balance in the known and unknown confounding or unmeasured prognostic variables/factors. Although some of the baseline variables or covariates may not be a perfect balance, the overall magnitude and direction of the differences will tend to be equally divided between the two groups. In relatively small study and in the present of strong risk factors, randomization with balanced groups can be achieved using stratified randomization (Friedman et al., 2010).

iii. Randomization provides a basis for the statistical methods to be used when analyzing the data. If randomizations are not used, additional assumptions about group comparability and the appropriateness of statistical models must be made before the comparison are valid. Although group comparison is never perfectly balanced for all covariates in any single experiment, the randomization process allows us to assign a probability distribution to the difference in outcome between treatment groups. Another benefit of randomization is fulfilling the statistical tests assumption (Byar et al., 2009).

What needs to be avoided when dealing with randomization?

During a randomization process, a researcher should avoid two types of biases:

Selection bias might occur when the researcher questions on what types of intervention that participants should receive if the allocation is predictable or known (Altman & Doré, 1990, Williams & Davis, 1994). Randomization procedures should be done in an unpredictable situation where the best is to blind the researchers. (i.e., allocation concealment). According to Schulz & Grimes, 2002, trials with insufficient or unclear randomization procedures tend to exaggerate treatment effects by up to 40% when compared to trials with proper randomization. This insufficient randomization may harm the research's outcome.

Accidental bias can occur if the randomization procedure does not achieve balance on risk factors or prognostic covariates, particularly in a small study (Lachin, 1988). Accidental bias is associated with covariates imbalances when comparing the treatment groups. However, larger sample size and using right randomization procedure can avoid accidental bias.

METHODS OF RANDOMIZATION

Many procedures can be used for the random assignment of participants in treatment groups depending on scientific arguments reflecting the special aspects of the trial setting (Hilgers et al., 2017). The common randomizations method used to generate the random allocation sequence is Fixed Allocation Randomization, in which allocation to intervention and control groups should be in equal probability and is not altered as the study progresses (Lachin, 1988). It includes main types of randomizations but is not limited to simple, mixed blocks and stratified. There are researchers such as Peto, 1978 that used unequal allocation ratios such as 2:1,

for intervention and control groups to gain more information about participants' responses towards new interventions, such as toxicity and side effects, but the study may loss some power. However, the topic will not be discussed here.

Type of Randomisation	Usage and technique
Simple Randomization	▪ Known as complete randomization, it is based on a single sequence of random assignments (Altman & Bland, 1999). ▪ Simple and easy approach and works well for a large sample size in clinical trials (n>100) in which it can generate similar numbers of subjects among groups. ▪ In a small sample size clinical trial, simple randomization may be resulting in an unequal number of participants among groups (Lachin, 1988). For example, using a coin toss with a small sample size (n = 10) may result in an imbalance such that 7 participants are assigned to the control group and 3 to the treatment group. ***Technique used:*** - Flipping a coin is the most common and basic method of simple randomization. With two treatment groups (control versus treatment), for example, the side of the coin (heads – control, tails - treatment) determines each subject's assignment. - Using a shuffled deck of cards (e.g., even - control, odd - treatment) or throwing dice are two other options (e.g., below, and equal to 3 - control, over 3 - treatment). - A random number table found in a statistics book or computer-generated random numbers can be used. - Advanced random strategies to allocate participants in more than two groups where algorithms and online statistical computing web programs were used.
Block Randomization	• Block randomization is designed to randomly allocate subjects into groups with equal sample sizes. • Each block is small in size and has balanced predetermined group assignments, which each block has the same number of subjects at all times during the trials. • Block randomization procedure produces a balanced study arm in small to moderate clinical trials (n<100) without covariates. • If certain covariates happen to be in the groups at different quantity, they need to be controlled to avoid bias in the statistical analysis. ***Technique used:*** • The researcher will determine the size of the blocks in a multiple of the number of groups (i.e., with two treatment groups, block size of either 4, 6, or 8) and all possible balanced combinations of assignment within the block (i.e., an equal number for all groups within the block) will be calculated. The patients are then assigned to groups based on a random selection of blocks. (Altman & Bland, 1999)
Stratified Randomization	▪ The stratified randomization method addresses the need to control and balance the possible influence of covariates that would jeopardize the conclusions of the clinical trial. The stratified randomizations are performed by creating a separate block for each combination of covariates and all subjects are assigned to the appropriate block of covariates. Simple randomizations are applied within each block to assign participants to one of the groups. ▪ This type of randomization is useful in a smaller clinical trial but can be complicated when dealing with many covariates (Weir & Lees, 2003). ▪ The researchers need to identify all subjects at baseline before group allocation is done which each influence of identified covariate has on the dependent variable. ***Technique used:*** ▪ For an example, 2 groups involving 40 participants, with the covariates of sex (2 levels: male, female) and body mass index (3 levels: underweight, normal, overweight) between study arms. With these 2 covariates, possible block combinations total 6 (eg, male, underweight). A simple randomization procedure, such as flipping a coin, is used to assign the participants within each block to one of the treatment groups (Weir & Lees, 2003).

Recommendation of the methodology for randomization.

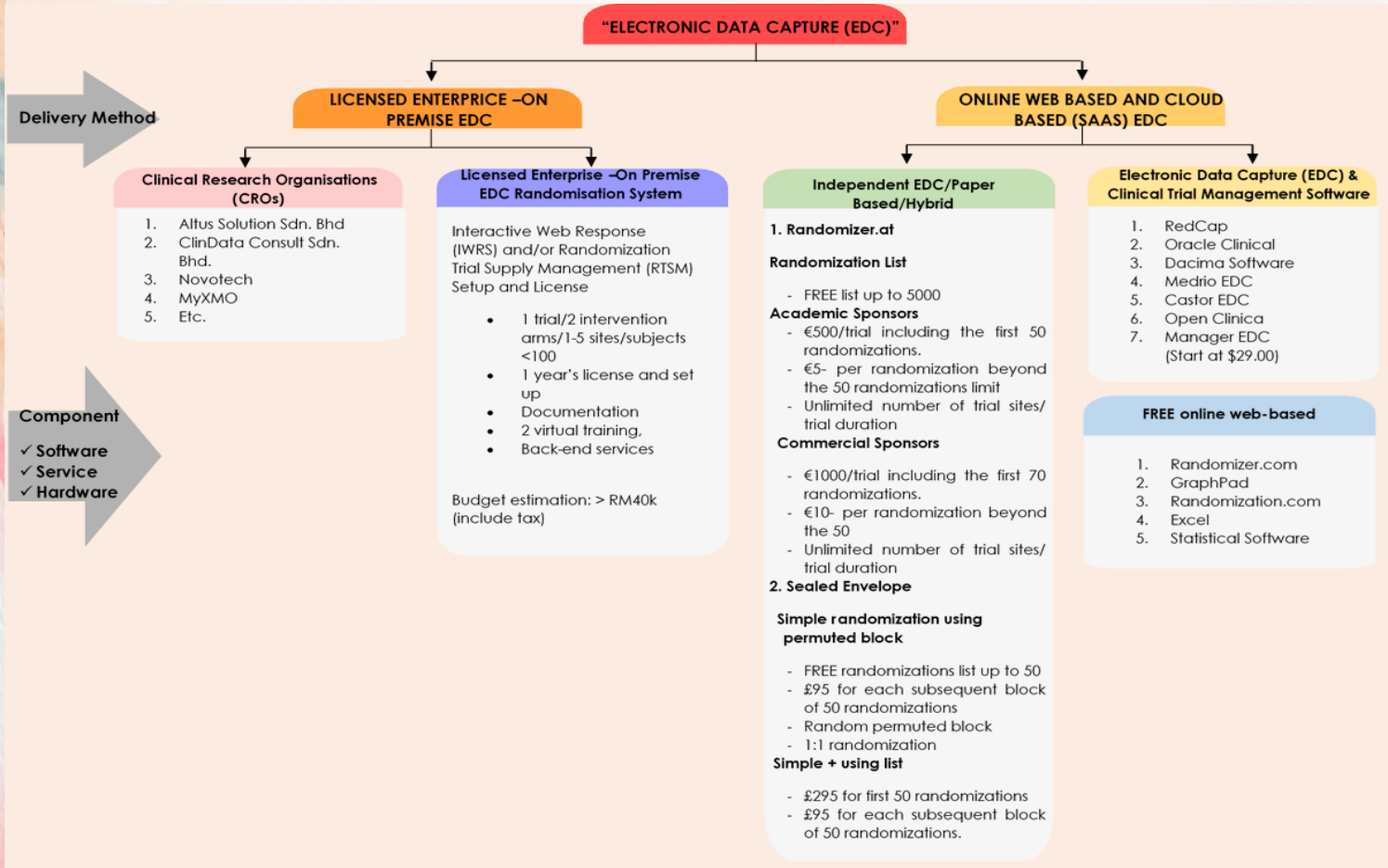
It is critical to consider how the randomization procedure is applied (Pocock S.J. & Simon, 1975). It is advised that an independent unit/body be responsible for establishing the randomization procedure and assigning participants to the appropriate group to achieve reliable randomization. In the independent unit/body, there could be a statistician or physician, or knowledgeable research personnel who is not involved in the research or participants' treatment. In the larger clinical trial scale that involved multicenter trials, the coordinating center is normally in charge of the randomization process. They are usually known as Clinical Research Organization (CRO).

In a normal situation where fixed proportion randomization is used, the randomization is done before the study begins. The researcher will call the independent unit/body to get the treatment assigned for the next subjects, where for the situation not available, the sequenced and sealed envelope containing information about the treatment will be provided to the researchers beforehand. In several double-blind drug studies, medication bottles labeled with small, perforated tabs have been used to identify the treatment to the subjects. In the multicenter trial, a central randomization operations process might be used. The systems, referred to as Interactive Voice Response Systems (IVRS) or Interactive Web Response Systems (IWRS) are effective and can be used to not only assign intervention but can also capture basic eligibility data. The use of IWRS becoming common due to its ease of use where the researchers need to log in to a central computer via the internet or dial into a central computer and enter data via touchtone, with a voice response (Krischer et al., 1991).

What is available in Malaysia? What is your option? Should you try do-it-yourself randomization, or should you use a professional clinical trials unit?

- You could do it yourself if you have:
  - a small trial
  - AND it is under personal control
  - AND you have the skills
- You should use an independant unit if you have:
  - a large trial
  - OR a multicenter trial
  - OR more than one person recruiting participants
  - OR you need experienced support

Randomization Service below summarizes options for what is available in Malaysia.



RANDOMISATION SERVICES as used by Clinical Research Organizations (CROs), Hospital, Clinics and Academic Research Centre

FREE ONLINE WEB-BASED AND CLOUD

Services	Types of Services	Fee	Requirement	Owner/ Country of Origin	Establishment	Features and extra applications added	Limitation
Randomizer.org https://randomizer.org/	Simple	Free	Standard web browser connected to the Internet (e.g., Chrome, Safari, Firefox, Internet Explorer) No specialized software, plugins, or extensions	Wesleyan Uni, Connecticut, England	Science.org American Psychological Association Web of Science Cited >500 publications	Very simple and easy to implement	Only run Simple Random number
GraphPad https://www.graphpad.com/quickcalcs/index.cfm	Simple Block	Free	Standard web browser connected to the Internet (e.g., Chrome, Safari, Firefox, Internet Explorer)		1. Widely used in the scientific community 2. Cited more than >100 citations	Very simple and easy to implement	• Once the randomization plan is generated, the same randomization plan cannot be generated as this uses the seed point of the local computer clock and is not displayed for further use. • A maximum of only 10 treatments can be assigned to patients.
Randomization.com http://www.jerrydallal.com/random/randomize.htm	Simple Block	Free	Standard web browser connected to the Internet (e.g., Chrome, Safari, Firefox, Internet Explorer)		Cited more than >100 citations	Up to 20 treatments can be specified	Available only for simple and block randomization.

PAID ONLINE WEB-BASED AND CLOUD

Services	Types of Services	Fee	Requirement	Owner	Establishment	Features and extra applications added	Limitation
Randomizer.at https://randomizer.at	Permuted blocks, minimization, biased coin, urn randomization, other algorithms, etc.	**Randomization List** FREE list up to 5000 **Academic Sponsors** €500/trial including the first 50 randomizations. €5- per randomization beyond the 50 randomizations limit Unlimited number of trial sites Unlimited trial duration **Commercial Sponsors** €1000/trial including the first 70 randomizations. €10- per randomization beyond the 50 Unlimited number of trial sites Unlimited trial duration	Online web-based	Medical University of Graz Institute for Medical Informatics, Statistics, and Documentation (IMI)	Most cited in medical and health sciences journal	Within six months after trial activation - no more than 10 subjects have been randomized into a trial and the trial coordinator confirms trial termination, the full basic fee will be refunded.	Randomization is limited to 10 randomizations per trial for FREE randomization list
Sealed Envelope **https://www.sealedenvelope.com/**		**Simple randomization using permuted block** FREE randomizations list up to 50 £95 for each subsequent block of 50 randomizations Random permuted block	Online web-based		Most cited in medical and health sciences journal	• Web-based online • Randomization by text message. • Code Breaking Costume: blinding, rescue medication, maintenance therapy and dose	

		1:1 randomization **Simple + using list** **£295 for first 50 randomizations** £95 for each subsequent block of 50 randomizations. Random permuted block 2:1 or other unequal allocations Randomize by text message Stratification Named randomization groups Eligibility criteria checks **Fully Featured Randomisation for blinded and unblinded trials** From £1,800 Set-up Unblinded trial for public sector/academic/non-profit customers From £60 per month - **Up to 100 randomizations. et-up by Sealed Envelope Minimization Expert technical support Customized randomization form Role-based user accounts Reports Comprehensive audit log Code list management Maintenance and rescue codes Unblinding Change request process Validation documentation Price exclude Value Added Tax (VAT)				calculations as appropriate, Eligibility criteria, randomization protocol, and patient characteristics	

References:

1. Altman, D. G., & Bland, M. J. (1999). Statistics notes: Treatment allocation in controlled trials: why randomise? *BMJ: British Medical Journal*, *318*(7192), 1209. https://doi.org/10.1136/BMJ.318.7192.1209
2. Altman, D. G., & Doré, C. J. (1990). Randomisation and baseline comparisons in clinical trials. *The Lancet*, *335*(8682), 149–153. https://doi.org/10.1016/0140-6736(90)90014-V
3. Amberson JB, M. B. P. M. (n.d.). *A Clinical Trial of Sanocrysin in Pulmonary Tuberculosis | American Review of Tuberculosis*. Retrieved March 14, 2022, from https://www.atsjournals.org/doi/abs/10.1164/art.1931.24.4.401
4. Armitage, P. (1982). The role of randomization in clinical trials. *Statistics in Medicine*, *1*(4), 345–352. https://doi.org/10.1002/SIM.4780010412
5. Byar, D. P., Simon, R. M., Friedewald, W. T., Schlesselman, J. J., DeMets, D. L., Ellenberg, J. H., Gail, M. H., & Ware, J. H. (2009). Randomized Clinical Trials. *Http://Dx.Doi.Org/10.1056/NEJM197607082950204*, *295*(2), 74–80.
6. Friedman, L. M., Furberg, C. D., & Demets, D. L. (2010). Fundamentals of clinical trials. *Fundamentals of Clinical Trials*, 1–445. https://doi.org/10.1007/978-1-4419-1586-3
7. Friedman, L. M., Furberg, C. D., & DeMets, D. L. (2010). The Randomization Process. *Fundamentals of Clinical Trials*, 97–117. https://doi.org/10.1007/978-1-4419-1586-3_6
8. Hilgers, R.-D., Uschner, D., Rosenberger, W. F., & Heussen, N. (2017). ERDO-a framework to select an appropriate randomization procedure for clinical trials. *BMC Medical Research Methodology*, *17*, 159. https://doi.org/10.1186/s12874-017-0428-z
9. I., J. O. (1936). The Design of Experiments. *Nature 1936 137:3459*, *137*(3459), 252–254. https://doi.org/10.1038/137252a0
10. Krischer, J. P., Hurley, C., Pillalamarri, M., Pant, S., Bleichfeld, C., Opel, M., & Shuster, J. J. (1991). An automated patient registration and treatment randomization system for multicenter clinical trials. *Controlled Clinical Trials*, *12*(3), 367–377. https://doi.org/10.1016/0197-2456(91)90017-G
11. Lachin, J. M. (1988). Properties of simple randomization in clinical trials. *Controlled Clinical Trials*, *9*(4), 312–326. https://doi.org/10.1016/0197-2456(88)90046-3
12. Peto, R. (1978). CLINICAL TRIAL METHODOLOGY. In *Biomedicine Special Issue* (Vol. 28).
13. Pocock S.J., & Simon, R. (1975). Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. *Biometrics*, *31*, 103–115.
14. Schulz, K. F., & Grimes, D. A. (2002). Allocation concealment in randomised trials: defending against deciphering. *The Lancet*, *359*(9306), 614–618. https://doi.org/10.1016/S0140-6736(02)07750-4
15. Weir, C. J., & Lees, K. R. (2003). Comparison of stratification and adaptive methods for treatment allocation in an acute stroke clinical trial. *Statistics in Medicine*, *22*(5), 705–726. https://doi.org/10.1002/SIM.1366
16. Williams, D. H., & Davis, C. E. (1994). Reporting of assignment methods in clinical trials. *Controlled Clinical Trials*, *15*(4), 294–298. https://doi.org/10.1016/0197-2456(94)90045-0

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CURRENT EVIDENCE

TOWARDS SOCIETAL IMPACT THROUGH OPEN RESEARCH

New and dynamic open practices are increasing the findability, accessibility and reusability of results. Is open research accelerating progress on global societal challenges? Check out a project from a strategic partnership between the Springer Nature and the Association of Universities in the Netherlands (VSNU).

https://www.springernature.com/gp/researchers/sdg-impact

PROJECT 1: SDG relevancy mapping

How much of scholarly research addresses the sustainable development goals? What are the publication trends and gaps around the world?

This project surveys and categorises scholarly research outputs such as articles and chapters into select UN Sustainable Development Goals.

For further reading on this project: Click this **[LINK]**

PROJECT 2: Assessing non-academic usage

How much of SDG-relevant research is openly available? And further, how successful are scholarly publications in reaching their target audience, whether scientists, policy makers, or practitioners in the field?

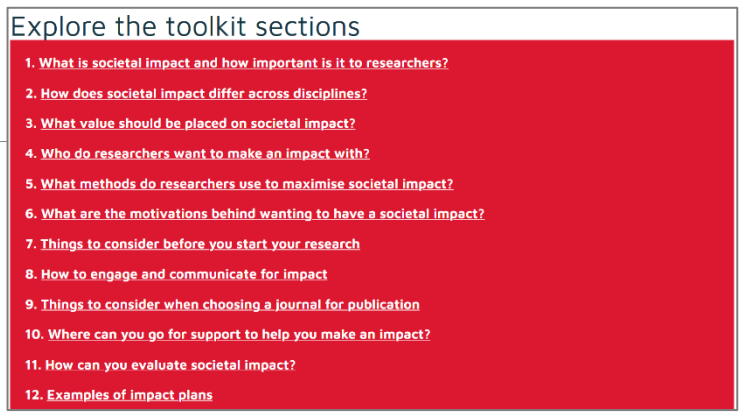
This project sets out to "dig deeper" and assess the exact nature and scope of impact that research outputs in selective SDGs have on non-academic actors. These stakeholders include: business, politics, industry, interest groups – all drawing on research for critical decision making.

Find out the details of this project: Click this **[LINK]**

PROJECT 3: Helping researchers maximise societal impact

What are researchers' motivations and attitudes towards societal impact? And further, what tools and services exist to help early career researchers devise a societal impact strategy to maximize dissemination and reach?

Hear from researchers about societal impact: Click this **[LINK]**



ANNOUNCEMENT

- MJH series 7: 25th March 2022
- MJH series 8: 15th April 2022
- International Clinical Trials Day, 19th May 2022. First Announcement.
- Research Development Workshop, 25-26 August 2022. Early announcement and calling for registration.
- Statistical tests assumptions. What are they and how to check for them? Early announcement.
- The 6th International Clinical Trials Methodology Conference 2022.
- 7th World Conference on Research Integrity. Cape Town, South Africa, 29 May-1 June 2022.
- ABSTRACT SUBMISSION CLOSED. 9th International Congress on Peer Review and Scientific Publication. September 8-10, 2022 Chicago, IL

CLINICAL RESEARCH UNIT PRESENTS

META-JOURNAL HOUR

IS IVERMECTIN EFFECTIVE IN TREATING COVID-19: A WELL-DESIGNED STUDY AND WITH FAIR CONCLUSIONS?

FULL ARTICLE

Efficacy of Ivermectin Treatment on Disease Progression Among Adults With Mild to Moderate COVID-19 and Comorbidities: The I-TECH Randomized Clinical Trial

Click to access full article:
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2789362

25th MARCH 2022 (FRIDAY) | 10.30 – 11.45AM | WEBEX

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Speaker

Ms. Salwana Ahmad
Research Officer, CRU

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CLINICAL RESEARCH UNIT PRESENTS

META-JOURNAL HOUR

A very relevant trial in a high-risk population but the 'proven' interventions did not perform as expected. What has gone wrong in this trial?

FULL ARTICLE

Effects of a Lifestyle Intervention to Prevent Deterioration in Glycemic Status Among South Asian Women With Recent Gestational Diabetes: A Randomized Clinical Trial

Click to access full article:
https://jamanetwork.com/journals/jamanetworkopen/articlepdf/2789570/tandon_2022_oi_220047_1645625918.56331.pdf

15th APRIL 2022 (FRIDAY) | 10.30 – 11.45AM | WEBEX

Speaker

Ms. Nurfaizah Saibul
Research Officer, CRU

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LIVE WEBINAR

Cisco webex

In conjunction with

INTERNATIONAL CLINICAL TRIALS DAY (ICTD) 2022

CRU, HPUPM will organize a webinar, covering on clinical trials topics

19th May 2022 | 9.00 am - 5.00 pm

Theme: *"Good Science in Clinical Trials"*

Registration fees:

UPM Student / Staff : RM50
Non-UPM Student : RM50
Non-UPM Staff : RM100

Method: Bank Transfer (EFT / CDM)
Beneficiary Name: Hospital Pengajar UPM
Bank Name: Bank Islam Malaysia Berhad
Account Number : 14014010156683
Payment Reference: Participant's full name & 'ICTD 2022'

REGISTRATION

For any inquiries, please contact:
Dr. Nur Aazifah Ilham | 03-9769 9761 | aazifah@upm.edu.my
Ms. Faridzatul Syuhada Abdul Rashid | 03-9769 9763 | faridzatul@upm.edu.my

3 GOOD HEALTH AND WELL-BEING

TENTATIVE PROGRAM

Time	Topic	Speaker/Panelist
0900-1000	What is a clinical trial? Q and A	Dr. Yew Sheng Qian (CRU, HPUPM)
1000-1100	How to conduct clinical trials? Q and A	YBhg. Prof. Dato' Dr. Nik Hisamuddin Nik Ab Rahman (Universiti Sains Malaysia)
1115-1215	What is the difference between ITT, PPA, as treated analysis? Q and A	Dr. Najib Majdi bin Yaacob (Universiti Sains Malaysia)
1215-1230	What is the procedure to apply to conduct clinical trials at HPUPM?	Ms. Faridzatul Syuhada Abdul Rashid (CRU, HPUPM)
1230-1400 (Lunch Break / Prayer)	Sharing session: CRO -Parexel, Iqvia, Across global, Icon, Info Kinetics, Labcorp, PPD	TBC
1400-1530	Forum: • Experience by researcher conducting Clinical Trial • How to be a successful researcher in Malaysia?	1. YBhg. Dato' Prof. Dr. Adeeba bt. Kamarulzaman, (University of Malaya) 2. YBhg. Datuk Prof. Dr. Looi Lai Meng (University of Malaya) 3. YBhg. Prof. Dato' Dr. Nik Hisamuddin Nik Ab Rahman (Universiti Sains Malaysia)
1600-1630	Sharing session: Clinical Research Malaysia (CRM) – experience in Phase 1 Clinical Trial	Ms. Nurul Haniza binti Zaini (CRM)

Note: The Organiser reserves the right to cancel or change the topic or trainer of the program, if for whatever reasons beyond its control.

FIRST ANNOUNCEMENT

CLINICAL RESEARCH UNIT (CRU), HPUPM PRESENTS

RESEARCH DEVELOPMENT WORKSHOP

A hybrid workshop to learn and conduct a proper and high-quality clinical, biomedical and health sciences research.

25 – 26 AUGUST 2022 | 8.00 AM – 4.30 PM

BOOK YOUR PREFERRED SLOT

Venue: Hospital Pengajar UPM, Serdang

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1. GO-NOW Hands-on Physical Sessions Participants*

LIMITED TO 10 SEATS ONLY!

OR

2. Attendees* (Physical / Online)

Categories of participants	
GO-NOW Participants	To attend with output*
Attendees	Without output

*Output:
Research proposal/ mini review/ peer-review

GO-NOW Participants are required to submit 500 words essay to introduce and argue on a topic of own professional interest or areas to pursue; at least one month before workshop to CRU.

Category	Fees
HPUPM/ FPSK staff/ students	RM 200
Other UPM faculties	RM 300
Non-UPM (Malaysians)	RM 500
Non-Malaysians	USD 500

For pre-registration, scan QR code below
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Register Now PAY LATER

***An email will be sent for registration and payment confirmation near to the workshop date.

For further information, please email: cru_hpupm@upm.edu.my or contact: 03-9769 9763/ 9759/ 9761

FIRST ANNOUNCEMENT

TENTATIVE OF THE WORKSHOP

Hour	Talk/ Topic	Tentative speaker
	DAY 1 (25 AUGUST 2022)	
0800 - 0815	***REGISTRATION***	
0815 - 0830	Introduction : Quality healthcare, research, KPI & career advancement	CBH & TDPA
0830 - 0845	**Testimony I :** Personal sharing by an outstanding researcher	TBD
0845 - 0915	***Interactive talk 1***: Understanding the whole research process	CBH
0915 - 1015	***Interactive talk 2:*** Fundamental concepts of clinical epidemiology	CBH
1015 - 1030	***Interactive talk 3:*** Classification of epidemiologic research	CBH
	BREAK	
1045 - 1115	***Interactive talk 4:*** An introduction to qualitative study & designs	Invited speaker
1115 - 1145	***Interactive talk 5:*** Research question, literature review & conceptual framework	CBH
1145 - 1215	***Interactive talk 6:*** An introduction to databases & search strategies	CBH & an invited speaker
1215 - 1245	***Interactive talk 7:*** Theoretical design	CBH
1245 - 1315	***Interactive talk 8:*** Data collection design	CBH
	LUNCH	
1400 - 1430	***Interactive talk 9:*** Sample size estimation	CBH
1430 - 1500	***Interactive talk 10:*** Statistical design	CBH
1500 - 1515	***Interactive talk 11:*** Summary: clinical epidemiology & research methodology	CBH
1515 - 1545	***Interactive talk 12:*** Writing up a study proposal	CBH
1545 - 1615	***Interactive talk 13:*** Ethics clearance for a clinical study	Invited speaker
1615 - 1645	***Interactive talk 14:*** Funding opportunities	Invited speaker
	DAY 2 (26 AUGUST 2022)	
0800 - 0815	***REGISTRATION***	
0815 - 0915	***Interactive talk 15:*** Statistical analysis	CBH
0915 - 1000	***Interactive talk 16:*** Comprehensive reporting, quality writing	CBH
1000 - 1030	***Interactive talk 17:*** Publication process	CBH
	BREAK	
1045 - 1245	***Interactive talk 18:*** Intellectual Property. UPM IP Putra Science Park and the Sistem PRiMS (Putra Research & Innovation Management System)	Invited speaker
	LUNCH	
1400 - 1500	***Interactive talk 19:*** What is evidence-based practice? Appraise the evidence: primary research and systematic reviews & meta-analysis	CBH
1500 - 1530	***Interactive talk 20:*** Summary: a suggested roadmap for clinicians to higher quality in research and publication	CBH
1530 - 1545	**Testimony II :** Personal sharing by an outstanding researcher	TBD
1545 - 1630	**Closure :** Summary & What have you learned? **Q&A**	CBH
	Break & dismissed	
	DAY 3 (AFTER 2-3 MONTHS POST-WORKSHOP) ****For GO-NOW Participants only***	**Facilitator**
0800 - 0830	***REGISTRATION & Intro***	
0830 - 1630	Study proposal presentation	CBH

*CBH: Associate Prof. Dr. Chew Boon How

ORGANIZED BY
CLINICAL RESEARCH UNIT, HPUPM

Organised by: Clinical Research Unit, HPUPM

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PROVIDING EXTRAORDINARY CARE TOGETHER

LIVE WEBINAR

Cisco webex

First Announcement

Webinar on

STATISTICAL TESTS ASSUMPTIONS

What Are They & How To Check For Them?

July 28th, 2022 (Thursday)

8.30 am – 1.00 pm

GUEST SPEAKER

REGISTRATION OPENING SOON!

FEES

RM100
FOR UPM STAFF / STUDENT

RM200
FOR NON-UPM STAFF / STUDENT

3 GOOD HEALTH AND WELL-BEING

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Tentative Program

Opening speech

TOPIC

What it is and why need to be checked?

Parametric Test: T-test, Pearson Correlation
Non-parametric test: Spearman Correlation, Chi-Square, Wilcoxon Rank sum Test, Mann-Whitney U Test

Multivariable linear regression statistical test assumptions

Multivariable logistic regression, Poisson regression and Survival analysis statistical test assumptions

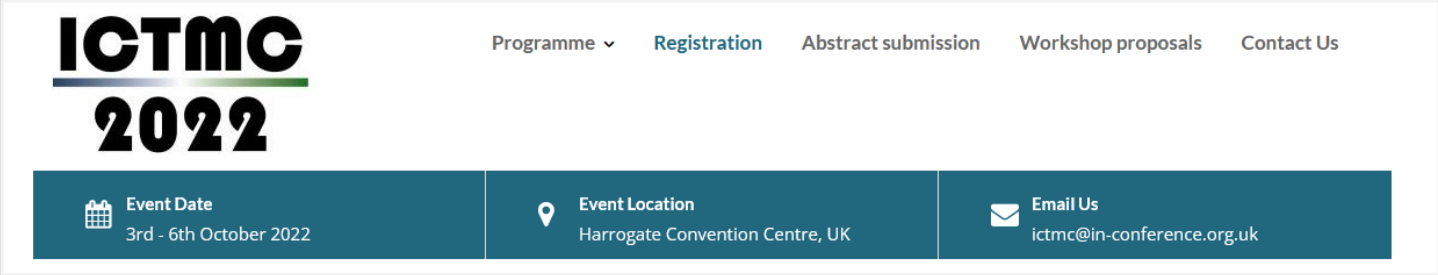
Generalised linear model and Random / Mixed effect model statistical test assumptions

Q&A session

Organised by: Clinical Research Unit, HPUPM

Upcoming Conference & Congress

1. The 6th International Clinical Trials Methodology Conference 2022. https://ictmc.org/



2. 7th World Conference on Research Integrity 2022. https://wcri2022.org/

3. UPDATE: ABSTRACT SUBMISSION CLOSED. 9th International Congress on Peer Review and Scientific Publication (Abstract Submission Extended)
https://peerreviewcongress.org/

- Editorial on September 20, 2021. John P. A. Ioannidis et al. Ninth International Congress on Peer Review and Scientific Publication Call for Abstracts. JAMA. 2021;326(13):1265-1267. doi: 10.1001/jama.2021.16596.
- Editorials published 20 September 2021. John P. A. Ioannidis et al. Ninth international congress on peer review and scientific publication—call for abstracts. BMJ 2021;374:n2252. doi: 10.1136/bmj.n2252.