Systematic Review of Palm Oil and Its Implications on Diet Related NCDs

Presented by: Terence Tan

Palm International Nutra-Cosmesceutical Conference (PINC) 2017
31st July - 2nd August 2017

OUTLINE

1) Introduction
2) Objectives & Research Question
3) Methodology
4) Outcomes
5) Results
6) Quality of Evidence Assessment
7) Conclusion

1

INTRODUCTION

INTRODUCTION

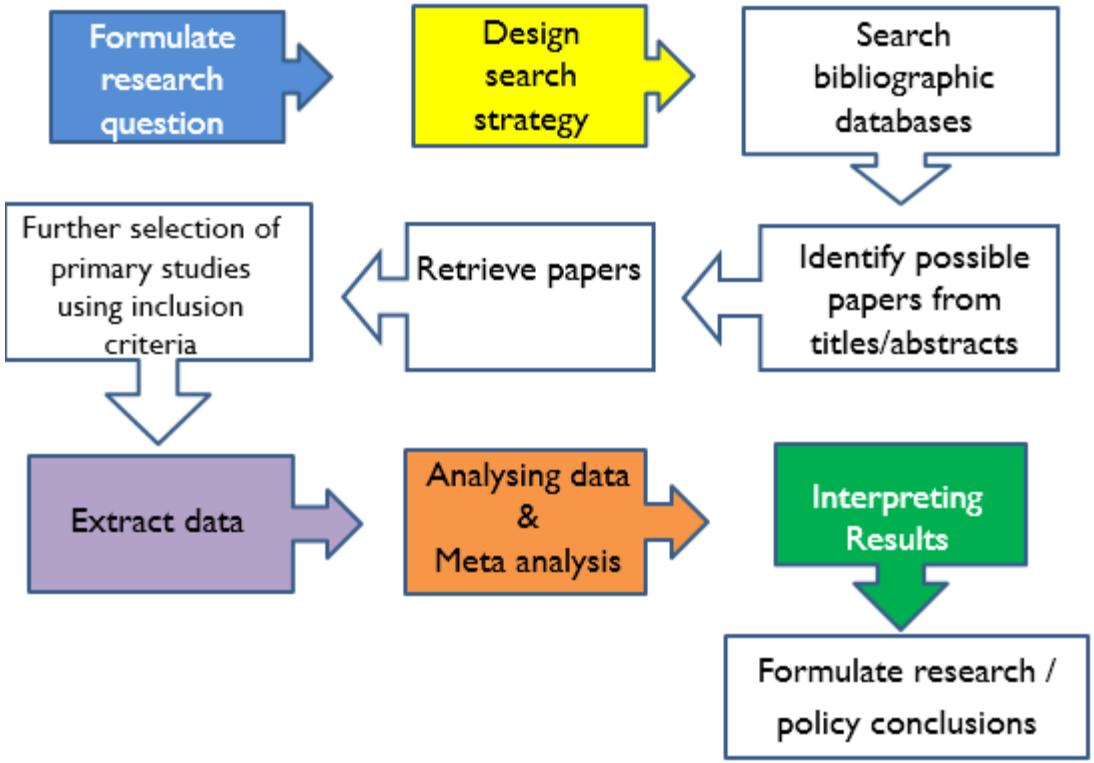
Systematic Review: Definition

A review of a clearly formulated question that uses systematic and explicit methods to:

1) Identify, select, critically appraise relevant research
2) Collect and analyse data from the studies that are included within the review

Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.

Systematic Review Process



2

OBJECTIVES & RESEARCH QUESTION

OBJECTIVE

- To synthesize the current evidence on the effects of palm oil on the following diseases:

❖ Hypercholesterolaemia

❖ Atherosclerosis

❖ Cardiovascular diseases (Coronary heart disease & Stroke)

❖ Diabetes mellitus

❖ Obesity

❖ Cancer: 3-MCPD, Glycidyl ester

RESEARCH QUESTION

Hypercholesterolaemia	▪ Does consumption of palm oil increase lipid profile levels in human as compared to other vegetable oils?
Atherosclerosis	▪ Does consumption of palm oil cause atherosclerotic plaque formation in human as compared to other vegetable oils?
CVD	▪ Does increased palm oil consumption leads to higher coronary heart disease (CHD) & stroke events and related mortality?

RESEARCH QUESTION

Diabetes

- Does consumption of palm oil increase risk of diabetes mellitus in human as compared to other vegetable oils?

Obesity

- Is there any association linking palm oil and obesity?

Cancer

- Does 3-MCPD content in palm oil have a role in carcinogenicity?
- Does glycidol and glycidyl esters content in palm oil have a role in carcinogenicity?

3

METHODOLOGY

METHODOLOGY

Formulation of Research Question

P	**P**atient, **P**opulation, or **P**roblem	**Human**
I	**I**ntervention, Prognostic Factor, or Exposure	**Palm oil consumption**
C	**C**omparison or Intervention (if appropriate)	**Other vegetable oils**
O	**O**utcome you would like to measure or achieve	**Disease** • Primary Outcome • Secondary Outcome

METHODOLOGY

Search Strategy Design

POPULATION	INTERVENTION		COMPARATOR	OUTCOME (DISEASE)
Human	*Elaeis guineesis*	Lauric acid	*Keywords defined by individual group*	
	Palm oil	Myristic acid		
	Palm olein	Palm kernel oil		
	Palm stearin	Palm kernel olein		
	Interesterified palm oil	Palm kernel stearin		
	Oleic acid	African oil palm		
	Linoleic acid	Red palm oil		
	Palmitic acid			

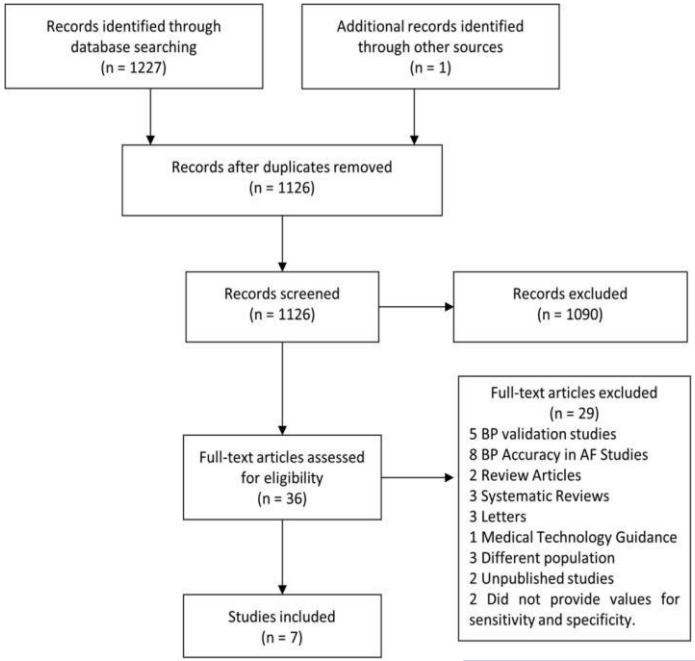
METHODOLOGY

Search Bibliographic Databases

a) **Electronic databases:**

- ✓ **MEDLINE**
- ✓ **CENTRAL**
- ✓ **Embase**
- ✓ **Scopus**
- ✓ **Clinicaltrial.gov**
- ✓ **LILAC**

b) **Process reported using 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)'**



4

OUTCOMES

OUTCOMES

HYPERCHOLESTEROLAEMIA	ATHEROSCLEROSIS
Acceptable serum lipid profile levels: ➢ **LDL levels less than 4.1 mmol/L** ➢ **HDL levels more than 1.0 mmol/L** ➢ **Total glycerides levels less than 1.7 mmol/L** ➢ **Total cholesterol levels less than 6.2 mmol/L**	**Primary outcome :Atherosclerosis diagnosed by plaque build-up measured by various method** **Secondary outcomes:** ➢ **Indirect measures of atherosclerotic plaque formation** ➢ **Health related quality of life** ➢ **Adverse effects** ➢ **Mortality secondary to palm oil consumption**

OUTCOMES

CARDIOVASCULAR DISEASE	DIABETES
Risk of CHD & Stroke and its related outcomes, expressed as the following: ➢ **Prevalence rate** ➢ **Incidence rate** ➢ **Hazard ratio** **Cause specific death rates**	**Risk of diabetes and related outcomes, expressed as the following:** **a) Clinical outcomes:** **Diabetic symptoms, admission, complication (cardiovascular complications, retinopathy, nephropathy and neuropathy).** **b) Laboratory surrogate outcomes:** **HbA1c, fasting blood glucose, HOMA, C-peptide, fasting insulin, change in glucose (%), peak glucose, 2 Hr glucose**

OUTCOMES

OBESITY	CANCER
Risk of obesity and related outcomes, expressed as the following: ➢ **Change in body weight** ➢ **Change in body mass index** ➢ **Change in body fat measurement**	**To evaluate cancer related activities of 3-MCPD, glycidol and GEs based on histopathological findings** **Secondary outcomes:** ➢ **Mode of action in causing cancer**

5

RESULTS

SEARCH RESULTS

DISEASE	TOTAL SCREENED	TOTAL INCLUDED
Hypercholesterolaemia	26547	22
Atherosclerosis	3459	9
CHD	1777	3
Stroke	2738	1
Diabetes	1706	6
Obesity	7735	5
Cancer – 3-MCPD	7940	19
Cancer – Glycidol & GEs	7940	11

CHARACTERISTICS OF INCLUDED STUDIES

Hypercholesterolaemia
2 parallel RCTs
20 randomized crossover trials

Atherosclerosis
4 parallel RCTs
5 crossover trials

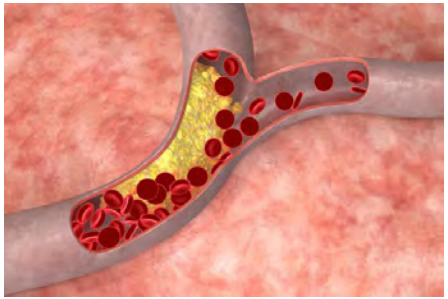
CHD:
1 ecological study
2 case-control studies
Stroke:
1 ecological study

Diabetes
6 parallel RCTs

Obesity
4 parallel RCTs
1 crossover trial

Cancer
14 carcinogenicity studies
16 *in vitro* & *in vivo* genotoxicity studies

RESULTS: HYPERCHOLESTEROLAEMIA

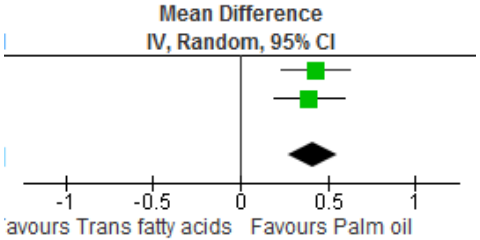


Palm oil vs Trans-fatty acids diet on risk of hypercholesterolaemia

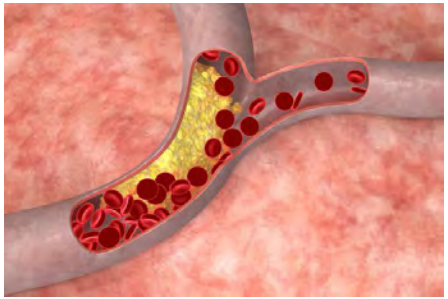
There was a moderate level of evidence to suggest that consumption of palm oil significantly increased HDL compared to trans fatty acids diet consisting of partially hydrogenated soybean oil and mixed vegetable oils (MD= 0.41 mmol/L ; 95% CI= 0.27, 0.55, p < 0.00001, 2 cross-over studies, 61 participants) (de Roos 2001, de Roos 2001b).

	Palm oil			Trans fatty acids diet				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
de Roos 2001	1.89	0.46	32	1.46	0.33	32	51.7%	0.43 [0.23, 0.63]
de Roos 2001b	1.87	0.45	29	1.48	0.33	29	48.3%	0.39 [0.19, 0.59]
Total (95% CI)			**61**			**61**	**100.0%**	**0.41 [0.27, 0.55]**

Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 5.71 (P < 0.00001)

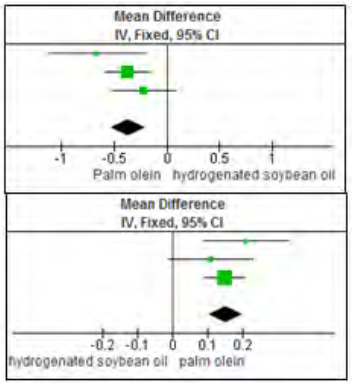


RESULTS: HYPERCHOLESTEROLAEMIA



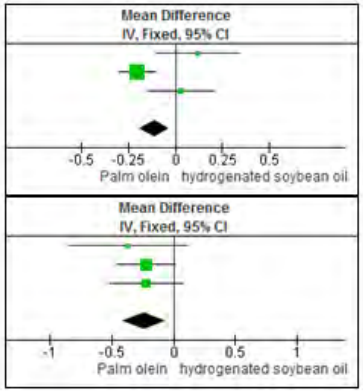
Palm olein vs Trans-fatty acids diet on risk of hypercholesterolaemia

There was a **moderate level of evidence** to suggest that consumption of palm olein significantly **better in all outcomes (HDL, LDL, TG & TC)** compared to partially hydrogenated soybean oil (3 cross-over studies, 67 participants) (Sundram 1997,2003,2007).



LDL

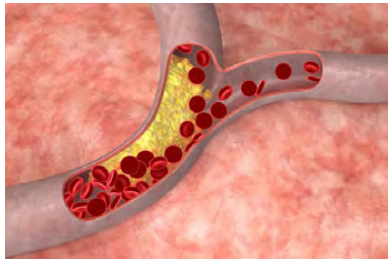
HDL



TG

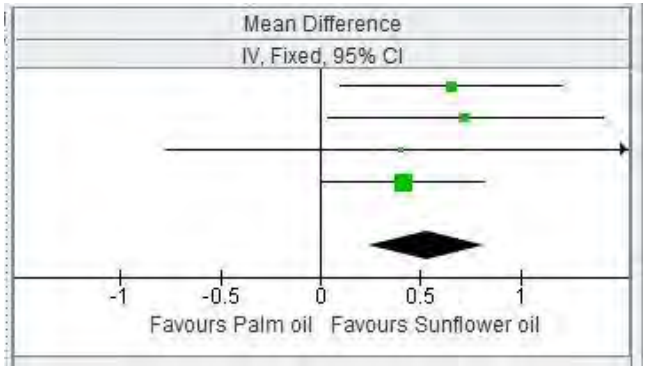
TC

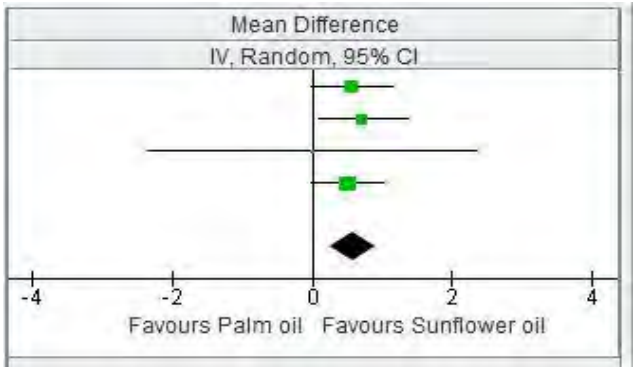
RESULTS: HYPERCHOLESTEROLAEMIA



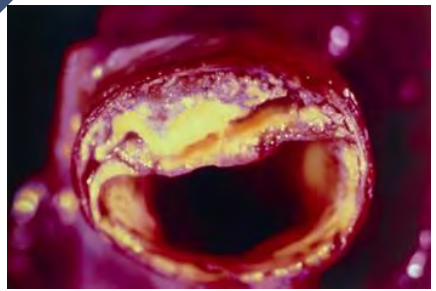
Palm oil vs Sunflower oil on risk of hypercholesterolaemia

- Evidence suggested that consumption of Palm Oil increases LDL and TC as compared to sunflower oil
- (Cater 1997, 2001; Noakes 1996; Iggman 2014) showed LDL change (MD= 0.53 mmol/L; 95% CI= 0.24,0.81, p = 0.0003, 58 participants, I2 = 0%) and TC (MD= 0.57 mmol/L; 95% CI= 0.25,0.90, p = 0.0006, 58 participants, I2 = 0%) both favouring the use of sunflower oil
- HDL and TG levels were not significant .





RESULTS: ATHEROSCLEROSIS



Primary outcome

- All primary outcome measures showed no significant effect on risk of atherosclerosis between participants who consumed palm oil and those who consumed comparator oil

Secondary outcome

- 20 (out of 21) secondary outcome measures showed no significant effect on risk of atherosclerosis between participants who consumed palm oil and those who consumed comparator oil except for one parameter which is LTB4 serum levels.
- LTB4 serum levels was higher in healthy participants who consumed palm oil compared to participants who consumed olive oil at 15 weeks (MD : 28.46; 95%CI 14.44 to 42.48)

RESULTS: ATHEROSCLEROSIS

ICAM-1

VCAM-1

IL-Iβ

SELECTIN

IL-6

LTB_4

TNF-α

CRP

NITROTYROSINE

FMD

PAI-1

tPA

vWF

Protein level

FIBRINOGEN

FACTOR VII

D-DIMER

Endostatin

PGE2

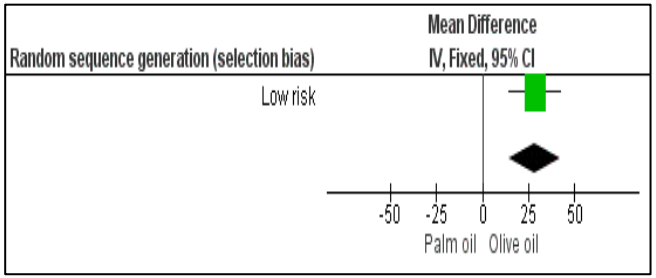
TXB2

PGF1α

Study or Subgroup	Palm oil Mean	SD	Total	Olive oil Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Voon	93.96	21.9401	15	65.5	16.92	15	100.0%	28.46 [14.44, 42.48]
Total (95% CI)			15			15	100.0%	28.46 [14.44, 42.48]

Heterogeneity: Not applicable

Test for overall effect: Z = 3.98 (P < 0.0001)



RESULTS: CARDIOVASCULAR DISEASE

Coronary Heart Disease

- CHD Event risk
  - Staple pattern diet (increasing palm oil intake, legumes, refined grains, red meat, organ meat etc.
    - Odds ratio ranges between 2.43 (1.56 – 3.79) and 3.70 (2.30 – 5.97)
  - Total saturated fats, across quintiles of energy
    - Odds ratio ranges between 1.61 (1.07 – 2.44) and 2.04 (1.37 – 3.05)

- CHD Mortality risk (**for every additional kilogram of palm oil consumed per-capita annually)**
  - In developing countries: **68 deaths per 100,000 (95% CI: [21 - 115])**
  - **In historically high income countries: 17 deaths per 100,000 (95% CI: [5.3 - 29])**

RESULTS: CARDIOVASCULAR DISEASE

Stroke

- Stroke mortality risk (for every additional kilogram of palm oil consumed per-capita annually)
  - In developing countries: 19 deaths per 100,000 (95% CI [-12 – 49]
  - In historically high income countries: 5.1 deaths per 100,000 (95% CI: [-1.2 – 11])

RESULTS: DIABETES

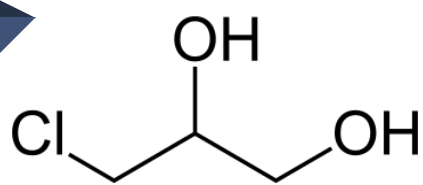
- Six types of vegetables oil were assessed (palm oil, palm olein, sunflower oil, olive oil, soybean oil, interesterified fat).
- No primary outcome was reported in the selected studies. No clear differences on fasting insulin, fasting C-peptide, peak glucose and 2 hr glucose.
- The evidence of positive or negative effect of palm oil on diabetes was inconclusive because other types of vegetable oils also showed similar patterns of effect.

RESULTS: OBESITY

- There is a paucity of studies that compared the association of dietary palm oil intake and obesity. No significant results when palm oil was compared to:

a) extra virgin olive oil on BMI
b) sunflower oil on body weight
c) sunflower oil on BMI
d) olive oil on body weight
e) lard on body weight

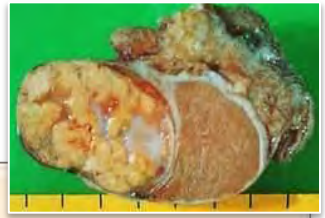
RESULTS: CANCER (3-MCPD)



- **There were mixed findings in animal studies and no human studies available**

Opinions on kidney tumor

- Occurred at 2 highest doses (100 & 500 mg/kg) – beyond actual human intake
- Also occurred in controlled animals (not significant) – species susceptibility
- Occurrence related to severity of nephropathy & tubular hyperplasia
- Possibly caused by 3-MCPD metabolites – ß chlorolactate & oxalic acid
- Different pathophysiology in human



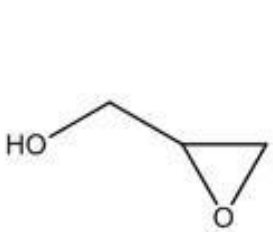
Opinions on Leydig cell tumor

- F344 rats were known for spontaneous Leydiq cell proliferation – high occurrence in controlled group
- However, Leydig cell tumor is considered rare in human (1-3% of all testicular neoplasm)

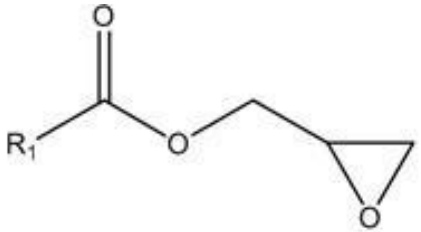
RESULTS: CANCER (Glycidol & GEs)

- From both *in vitro* and *in vivo* studies, it shows that glycidol is a genotoxic and carcinogenic compound as follows:

a) 2 toxicology (carcinogenicity) studies in animal
b) 5 genotoxicity studies
c) 4 consisting of neurotoxicity, reproductive and developmental toxicity studies in animal



Glycidol



Glycidyl Esters (GE)

6

QUALITY OF EVIDENCE ASSESSMENT

QUALITY OF EVIDENCE ASSESSMENT

- **Risk of bias assessment:**

a) **Randomized parallel trial:**
   - **Majority of the studies conduct randomization but sequence regeneration not mentioned**
   - **Allocation concealment not mentioned in most of the studies**
   - **Blinding on participants, personnel and outcome assessment conducted in most studies**
   - **No reporting bias as most studies report based on the outcome parameters set**
   - **No issue with period of study and proper repeated-measures analysis is conducted**

b) **Randomized crossover trials:**
   - **Most studies did not have a wash-out period which gives a carry-over effects risk**
   - **Cross-over design appropriate for majority of studies**

QUALITY OF EVIDENCE ASSESSMENT

- **GRADEPro assessment:**

Overall low-to-moderate quality of evidence across all outcomes due to following downgrading factors:

a) Indirectness, as all studies evaluated surrogate outcomes
b) Imprecision, reflected by wide 95% confidence intervals, partly contributed by small sample sizes.
c) Inconsistency: high level of heterogeneity among data
d) Carry-over effects, non-specified wash out period for certain randomised crossover studies

7

CONCLUSION

CONCLUSION

- **Limitation:**

  a) Limited number of studies which meet inclusion criteria
  b) Small sample sizes
  c) Non-standardised variety of comparators employed
  d) Quality of studies

- **Based on the findings, conclusions that are clearly in favour or against the effects of palm oil on diseases are not justified until more high-quality evidence is available**

CONCLUSION

- **Therefore, it is recommended to conduct high-scale quality clinical trials as suggested:**

a) **Sample size determination (e.g 85% power at α=0.05): Large scale studies**
b) **Intervention: Standardized intervention focusing on commercial cooking palm oil used in our country**
c) **Habitual intake should be studied**
d) **Study should be more focused on disease outcomes in addition to serum concentrations**
e) **Randomized parallel trial or cohort (for hazardous outcome) highly recommended**
f) **Serial measurements of the fatty acids for better linkage to the results outcome**
g) **Studies should include the energy intake of the intervention**

ACKNOWLEDGEMENTS

We would like to extend our gratitude to:

Y.B. Datuk Seri Dr S. Subramaniam, **Minister of Health,**
Director General of Health,
Deputy Director-General of Health(Research and Technical Support),
Deputy Director-General of Health (Public Health),
Director of Institute for Medical Research ,
Director of Clinical Research Centre and their members for their teamwork and support.
Coordinators and working group members for this project.

Many thanks to *Dr Lai Nai Ming* for his guidance and expert opinion in making this project a success.

THANK YOU

Any questions?
You can find me at
terencetyc@imr.gov.my