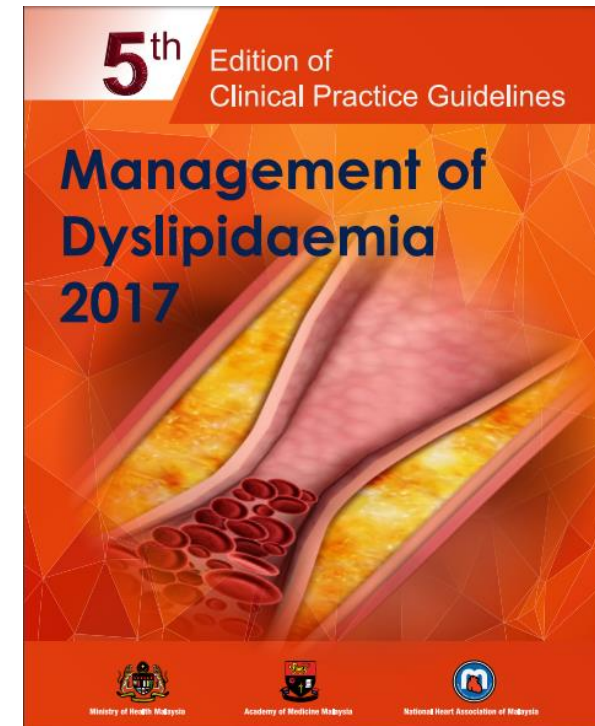


CLINICAL PRACTICE GUIDELINES
Management of Dyslipidaemia
2017
(5th Edition)

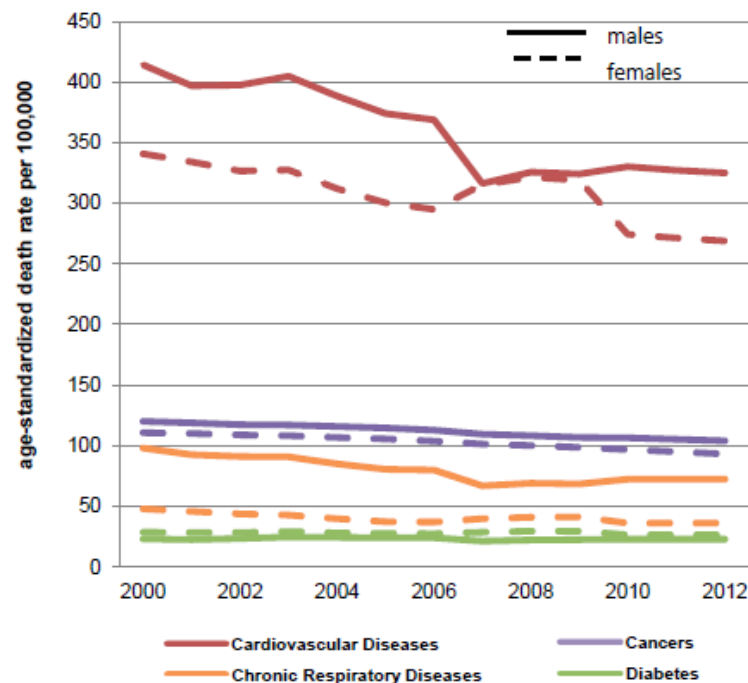


No Conflicts of Interest related to this presentation

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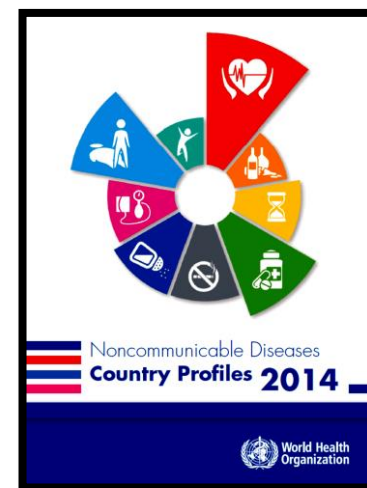
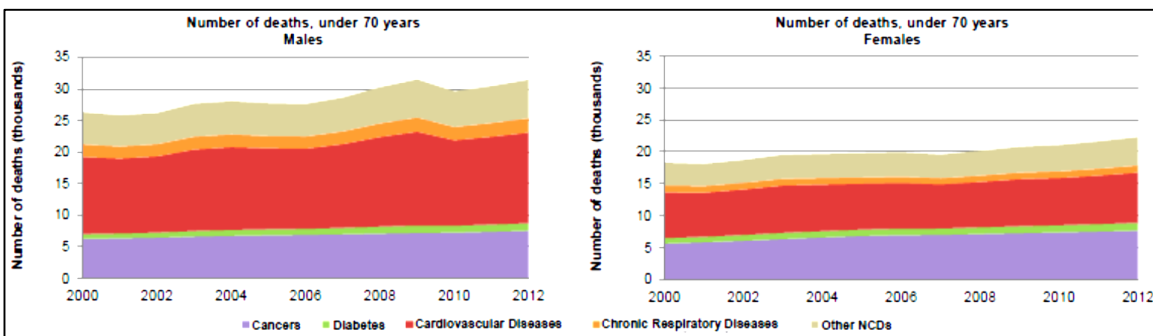
Age-standardized death rates*



Prevalence of Cardiovascular Risk Factors among Adults > 18 years of age in Malaysia

Risk Factor	NHMS III (2006) ⁵	NHMS IV (2011) ⁶	NHMS V (2015) ⁷
Hypercholesterolemia*	20.7%	35.1%	47.7%
Hypertension**	32.2%	32.7%	30.3%
Diabetes***	11.5%	15.2%	17.5%
Smoking****	21.5%	23.1%	22.8%
Overweight /Obesity BMI >25 kg/ m ²	43.1%	44.5%	54.4%

Premature mortality due to NCDs



* total cholesterol ≥ 5.2 mmol/L by finger prick test

**BP > 140/>90mmHg

***fasting blood glucose ≥ 6.1 mmol/L by finger prick

****current smokers ≥ 15 years of age

**CPG : Management of Dyslipidaemia 2017
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Selection of Writing committee

**Declaration of
conflicts of Interest**

Clinical Questions to be addressed?

**Relevant and applicable
to the local context**

**Reviewing the Evidence specifically that
related to the Region and to Malaysia**

**International and
Regional Guidelines
Pubmed, Ovid, Cochrane**

Writing the document

Funding- from NHAM

**Sent to External Reviewers, End Users and
TAC , Ministry of Health**

**Public, Private Sectors
and Universities**

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- Dyslipidaemia has been well established as a CV risk factor. It refers to the following lipid levels:
 - Total cholesterol (TC) > 5.2 mmol/l
 - HDL-C < 1.0 mmol/l (males) < 1.2 mmol/l (females)
 - TG > 1.7 mmol/l
 - LDL-C levels - will depend on the patient's CV risk

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(5th Edition) - Summary

ROBUST CONSISTENT POSITIVE OUTCOME DATA ON CVD WITH INTERVENTIONS TO LOWER TC AND LDL-C ESP WITH STATINS

INCONSISTENT (AND SOMETIMES HARMFUL) OUTCOME DATA WITH INTERVENTIONS TO LOWER TG/RAISE HDL-C

CPG : Management of Dyslipidaemia 2017

(5th Edition) - Summary

- LDL Cholesterol is the primary target of therapy.
- Non-HDL-C may be considered as a secondary target when treating individuals with:
 - combined hyperlipidaemias
 - diabetes
 - metabolic syndrome
 - chronic kidney disease

CPG : Management of Dyslipidaemia 2017

(5th Edition) - Summary

- In measuring lipid levels:
 - A standard lipid profile includes measurement of plasma or serum total cholesterol (TC), LDL cholesterol (LDL-C), HDL-cholesterol (HDL-C) and triglycerides (TG).
 - LDL-C is usually calculated by the Friedewald equation which is not valid in the presence of elevated TG (TG > 4.5 mmol/L).
 - Both fasting and non-fasting samples may be used for lipid screening.

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(5th Edition) - Summary

- In management, the global CV risk of the individual should first be assessed.
- Patients with established CVD, CKD and diabetes fall into the **Very High** and **High Risk** Categories.
 - All other individuals should be risk stratified at the outset using the Framingham General CVD risk score to determine if they are at **High, Intermediate (Moderate)** or **Low Risk**. or online at <https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php>

**Table 1A: Estimation of 10 year CVD Points for MEN
(Framingham Point Scores)**

Points	Age, y	HDL-C	TC	SBP (not treated)	SBP (treated)	Smoker	Diabetes
-2		1.6+		<120			
-1		1.3-1.6					
0	30-34	1.2-<1.3	<4.2	120-129	<120	No	No
1		0.9-<1.2	4.2-<5.2	130-139			
2	35-39	<0.9	5.2-<6.3	140-159	120-129		
3			6.3-<7.4	160+	130-139		Yes
4			>7.4		140-159	Yes	
5	40-44				160+		
6	45-49						
7							
8	50-54						
9							
10	55-59						
11	60-64						
12	65-69						
13							
14	70-74						
15	75+						
Points allotted							

Table 1B: CVD Risk for Men

Total Points	10 year Risk %	Total Points	10 year Risk %
≤-3	<1	8	6.7
-2	1.1	9	7.9
-1	1.4	10	9.4
0	1.6	11	11.2
1	1.9	12	13.2
2	2.3	13	15.6
3	2.8	14	18.4
4	3.3	15	21.6
5	3.9	16	25.3
6	4.7	17	29.4
7	5.6	18+	>30

Grand Total: _____points

Table 2A: Estimation of 10 year CVD Points for Women
(Framingham Point Scores)

Points	Age, y	HDL-C	TC	SBP (not treated)	SBP (treated)	Smoker	Diabetes
-3				<120			
-2		1.6+					
-1		1.3-1.6			<120		
0	30-34	1.2-<1.3	<4.2	120-129		No	No
1		0.9-<1.2	4.2-<5.2	130-139			
2	35-39	<0.9		140-149	120-129		
3			5.2-<6.3		130-139	Yes	
4	40-44		6.3-<7.4	150-159			Yes
5	45-49		>7.4	160+	140-149		
6					150-159		
7	50-54				160+		
8	55-59						
9	60-64						
10	65-69						
11	70-74						
12	75+						
Points allotted							

Table 2B: CVD Risk for Women

Total Points	10 year Risk %	Total Points	10 year Risk %
≤-2	<1	10	6.3
-1	1.0	11	7.3
0	1.2	12	8.6
1	1.5	13	10.0
2	1.7	14	11.7
3	2.0	15	13.7
4	2.4	16	15.9
5	2.8	17	18.5
6	3.3	18	21.5
7	3.9	19	24.8
8	4.5	20	28.5
9	5.3	21+	>30

Grand Total: _____points

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- The intensity of risk factor reduction and target lipid levels will depend on the individual's CV risk
- The amount of CV risk reduction seen will depend on the absolute risk of the individual and the degree of LDL-C lowering that is achieved (level of LDL-C achieved and/or the percentage reduction).

Risk Stratification of Cardiovascular Risk

- **Very High Risk** individuals are those with:
 - Established CVD
 - Diabetes with proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia
 - CKD with GFR $<30 \text{ ml} / \text{min}^{-1} / 1.73 \text{ m}^2$
- **High Risk** Individuals include:
 - Diabetes without target organ damage
 - CKD with GFR $\geq 30 - <60 \text{ ml} / \text{min}^{-1} / 1.73 \text{ m}^2$
 - Very high levels of individual risk factors (LDL-C $>4.9 \text{ mmol/L}$, BP $>180/110 \text{ mmHg}$)
 - Multiple risk factors that confer a 10-year risk for CVD $>20\%$ based on the Framingham General (FRS)CVD Risk Score
- **Intermediate (Moderate) Risk** Individuals:
 - Have a FRS-CVD score that confer a 10-year risk for CVD of 10-20%
- **Low Risk** Individuals:
 - Have a FRS-CVD score that confer a 10-year risk for CVD $<10\%$

Target LDL-C levels

Global Risk	LDL-C Levels to Initiate Drug Therapy (mmol/L)	Target LDL-C Levels (mmol/L)
Low CV Risk*	clinical judgement**	<3.0
Intermediate (Moderate) CV Risk*	>3.4 **	<3.0
High CV risk <ul style="list-style-type: none"> ➤ > 20% 10-year CVD risk ➤ diabetes without target organ damage ➤ CKD with GFR 30-<60 ml / min⁻¹ /1.73 m² 	> 2.6	≤2.6 or a reduction of >50% from baseline***
Very high CV risk <ul style="list-style-type: none"> ➤ established CVD, ➤ diabetes with proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia ➤ CKD with GFR <30 ml / min⁻¹ /1.73 m² but not dialysis dependent) 	>1.8	<1.8 or a reduction of > 50% from baseline***

*Low and Intermediate (Moderate) CV risk is assessed using the Framingham General CVD Risk Score

**After a therapeutic trial of 8-12 weeks of TLC and following discussion of the risk: benefit ratio of drug therapy with the patient

***whichever results in a lower level of LDL-C

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- An achieved on-treatment LDL-C level of < 1.8 mmol/L appears to significantly slow down progression of atherosclerosis.
- Lower levels of LDL-C have been shown to be associated with atherosclerotic regression.

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(5th Edition) - Summary

- Therapeutic Lifestyle Changes i.e.
 - adhering to a healthy diet,
 - regular exercise,
 - avoidance of tobacco smoking and
 - maintenance of an ideal weight,

remain a critical component of health promotion and CVD risk reduction.

Recommendations for Therapeutic Lifestyle Changes

Nutrition	Comments	Grade of Recommendation Level of Evidence
Total fats	20 – 25% with an upper limit of 30% of total energy	I, B
Saturated fat (SFA)	<p>< 10% of total calories.</p> <p>SFA should be replaced by :</p> <ul style="list-style-type: none"> ➤ PUFA ➤ MUFA or ➤ complex CHO e.g. whole grain, oatmeal 	<p>I, A</p> <p>IIa, B</p> <p>IIA, b</p>
Trans Fat	< 1% of total calories	I, A
Dietary cholesterol*	Keep to < 200 mg per day.* High cholesterol foods also contain high levels of SFA (e.g. meat, organ meats, full cream dairy products and some processed foods).	IIa, B
Carbohydrates (CHO)	<p>Total CHO 50 – 60% of total calories intake with emphasis on whole grains. To reduce intake of refined CHO foods e.g. white rice.</p> <p>In the presence of High TG and low HDL-C, CHO intake should be lower.</p>	<p>I, B</p> <p>I, B</p>

Recommendations for Therapeutic Lifestyle Changes

Nutrition	Comments	Grade of Recommendation Level of Evidence
Protein	15 - 20% of total calories intake with emphasis on vegetable protein.	I, B
Omega-3 fatty acids*	2 - 4 g per day from food and/or supplements in patients with hypertriglyceridemia.	II-a, B
Dietary fibre	<p>Incorporate fibre-rich foods that contribute at least 20 to 30g of fibre per day.</p> <p>Emphasis should be on soluble fibre sources (7 to 13g) such as fruits**, vegetables**, whole grains, high-fibre cereals, oatmeal, legumes and beans.</p>	I, B
Plant sterols and stanols	<p>2 - 3g per day.</p> <p>These include fortified milk, wheat germ, wheat bran, peanuts, vegetable oils (corn, sesame, canola and olive oil), oats***, almonds and food supplements.</p>	IIa, B
Weight reduction	<p>Achieve Body Mass Index (BMI) < 23 kg/m² or at least 5-10% reduction in body weight over 1-2 years</p> <p>Maintain waist circumference at:</p> <ul style="list-style-type: none"> ▪ < 90 cm for men ▪ < 80 cm for women 	I, B
Exercise	150 minutes a week of moderate aerobic or 75 minutes a week of vigorous aerobic exercise.	I, B
Smoking	Make efforts to stop smoking completely and avoid passive smoke.	I, B

** Juicing removes fibre from whole fruits and vegetables, thus it is not recommended

*** Adding ≥3 g OBG/d to the diet reduces LDL and total cholesterol by 0.25 mmol/L and 0.30 mmol/L, respectively, without changing HDL cholesterol or triglycerides

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- In most individuals at **Low** and **Intermediate (Moderate)** risk, therapeutic lifestyle changes alone should suffice. Occasionally drug therapy may be necessary to achieve target lipid levels. Only statins have been studied in these individuals.
- In individuals at **Very High** and **High** CV risk, drug therapy with statins should be initiated at the outset in conjunction with therapeutic lifestyle changes

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- Statin treatment has been clearly documented to reduce CV events in all age groups and irrespective of the baseline LDL-C.

Recommended Doses of Statin Therapy[#]

High-Intensity Statin Therapy* Daily dose lowers LDL-C on average, by approximately $\geq 50\%$	Moderate-Intensity Statin Therapy Daily dose lowers LDL-C on average, by approximately 30% - < 50%	Low-Intensity Statin Therapy** Daily dose lowers LDL-C on average, by < 30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg

[#]Adapted from: Stone NJ, Robinson JG, Lichtenstein AH, et al. *Circulation*. 2014;129:S76-S99

*High intensity statin therapy is for patients who are at **Very High** and **High** Risk

**Low intensity statin therapy is generally used for primary prevention after TLC and following a discussion with the patient of the risk: benefit ratio

Lipid Modifying Therapy for Dyslipidaemia
The Primary Target of Therapy is LDL-C:
The target will depend on the Individuals' CV Risk

Pharmacotherapy	Indication	Grade of Recommendation, Level Of Evidence
Statins	Very High and High CV Risk	I,A
	Intermediate (Moderate) and Low CV risk *	I,A
Statins + ezetimibe	Failure to achieve LDL-C goals	IIa,B
Statins + PCSK-9 inhibitors	Familial hypercholesterolemia	I,A
	Failure to achieve LDL-C goals	IIa, B
Statins + fibrates	Diabetic patients on maximally tolerated statins who have achieved the LDL-C target but have low HDL-C and high TG	IIb, B
Ezetimibe	Statin intolerance	IIa, C
PCSK-9 inhibitors	Very High and High CV risk with statin intolerance	IIa, B
Fibrates	Very High TG despite therapeutic lifestyle changes	IIa, C

* After Therapeutic Lifestyle changes

Thank you