

Response: Role of the Pediatrician

Dr. Ninfa J. Villanueva

LECTURES:

- Lipid Profile of Filipinos

DR. JOSE DONATO A. MAGNO

- Cholesterol Metabolism and Plaque Formation

DR. LOURDES ELLA G. SANTOS

- Clinical features of Familial Hypercholesterolemia (FH)

ACD. RODY G. SY

- FH Registry and Screening in the Philippines

DR. CECILIA A. JIMENO

ADVOCACY on Familial Hypercholesterolemia

WHO Call to Action on FH – 2020

- Awareness – public, patient, medical community
- Advocacy – FH in children unrecognized...
- Screening, testing, diagnosis – cascade, universal
- Treatment – unrestricted access
- Severe and homozygous FH – very high risk
- Family-based care – integrated care needed
- Registries – essential, require sustained funding
- Research – basic science, genetic, epidemiologic, clinical
- Cost and value – understand value in FH care

JAMA Cardiol 2020, published online 01/02/20

Our Hope...

- Identify FH suspects and do cascade screening
- Enroll FH suspects in FH Registry to have our national data
- Include lipid profile of children in national surveys
- Find out 95th percentile of total cholesterol and LDL cholesterol in children
- Do universal or selective cholesterol screening of children at 5-10 years old
- Do universal cholesterol screening of college applicants (expected mean age of 18 years old)



ADVOCACY on Familial Hypercholesterolemia

WHO Call to Action on FH – 2020

- Awareness – public, patient, medical community

Our Hope...

- Identify FH suspects and do cascade screening

Call for support

- Severe and homozygous FH – very high risk
- Family-based care – integrated care needed
- Registries – essential, require sustained funding
- Research – basic science, genetic, epidemiologic, clinical
- Cost and value – understand value in FH care

JAMA Cardiol 2020, published online 01/02/20

Find out 95th percentile of total cholesterol and LDL cholesterol in children

- Do universal or selective cholesterol screening of children at 5-10 years old
- Do universal cholesterol screening of college applicants (expected mean age of 18 years old)

THE CHOLESTEROL DILEMMA

The **CLINICAL BURDEN** of **DYSLIPIDEMIA**



Jose Donato A. Magno, M.D.

 @doc_jdam

gaps in **CLINICAL** detection of FH exist

Awareness on FH
Access to testing
Health-seeking behavior

1

the local **BURDEN** is unique

Global burden of FH
Regional prevalence
Lipid profile of Filipinos

2

the CV impact of **DYSLIPIDEMIA** is established

CV complications
Recognition and referral
Benefits of early treatment

3

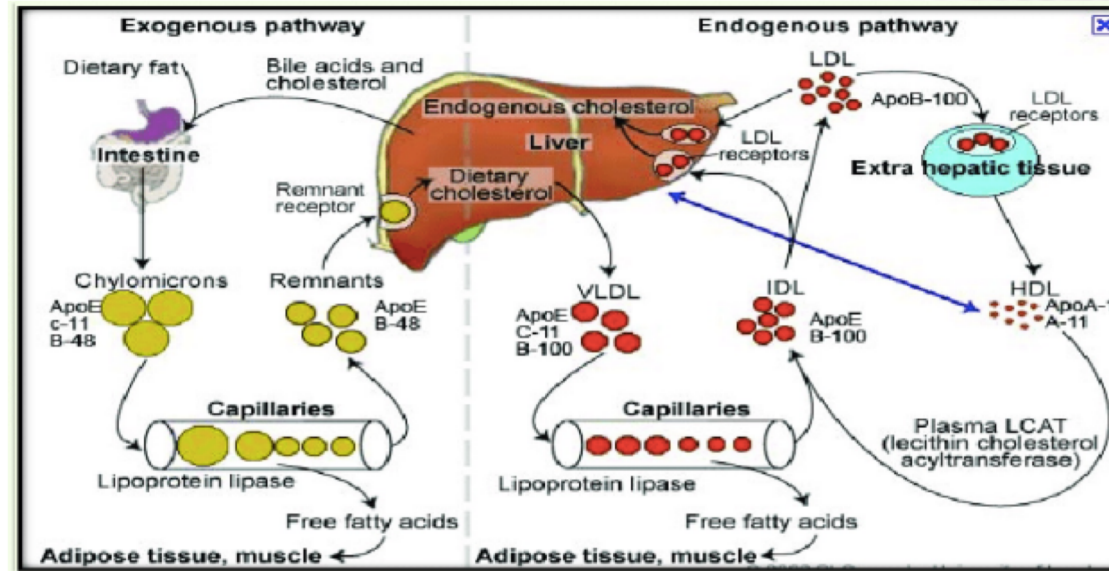
Cholesterol Synthesis

THE CHOLESTEROL DILEMMA

Cholesterol Metabolism and Plaque Formation Focus on FH Individuals

Lourdes Ella G. Santos, M.D.

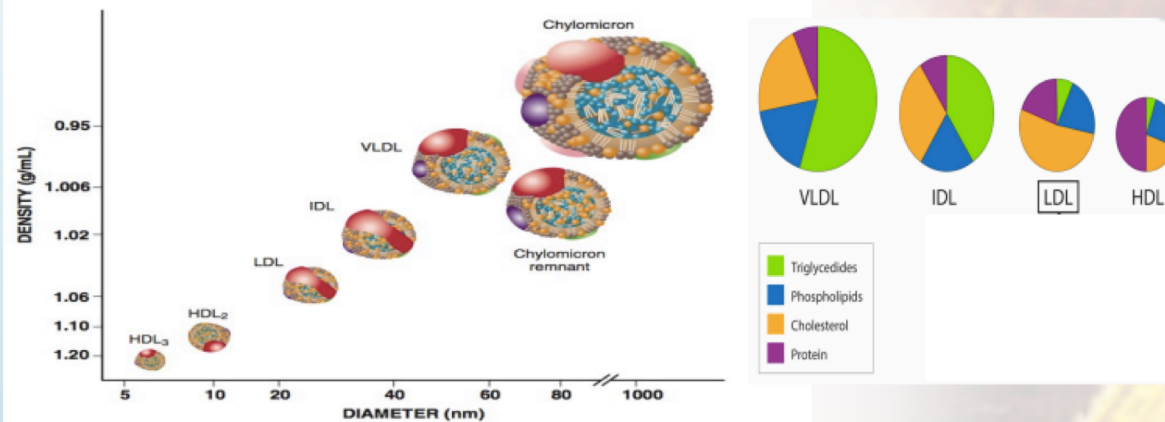
Preventive Cardiology, Clinical Lipidology and Hypertension



Karam I, Yang YJ and Li JY. Hyperlipidemia Background and Progress. SM Atheroscler J

Cholesterol Dilem

Lipoproteins Vary in Size and Composition



Dyslipidemia in children & adolescents

Genetic causes

Monogenic conditions

- Familial hypercholesterolemia
- Familial defective apolipoprotein B or PCSK9
- Familial hypertriglyceridemia

Polygenic defects

Secondary causes

Common:

- Obesity
- DM II
- Nephrotic syndrome

Dietary causes

Excessive intake of
saturated and trans fats

A dark blue arrow points to the right from the left edge of the slide. Below it, several thin, curved lines in shades of blue and grey sweep across the left side of the slide.

Management of dyslipidemia in children

- Heart-healthy lifestyle changes
 - Dietary modification
 - Physical activity
 - Weight loss for obese children
 - Avoidance of nicotine exposure
- Risk-based management
 - Use of statins- dosing, titration and monitoring

Evaluation and diagnosis of Familial Hypercholesterolemia in children & adolescents

CLINICAL SUSPICION

- elevated LDL in child
- elevated LDL or known FH in family members
- tendon xanthomas in child or family members
- premature atherosclerotic CVD in child or family member

Evaluation and diagnosis of Familial Hypercholesterolemia in children & adolescents

CLINICAL SUSPICION

- elevated LDL in child
- elevated LDL or known FH in family members
- tendon xanthomas in child or family members
- premature atherosclerotic CVD in child or family member

EVALUATION

- detailed history including family history
- complete PE
- look for secondary causes

Evaluation and diagnosis of Familial Hypercholesterolemia in children & adolescents

CLINICAL SUSPICION

- elevated LDL in child
- elevated LDL or known FH in family members
- tendon xanthomas in child or family members
- premature atherosclerotic CVD in child or family member

EVALUATION

- detailed history including family history
- complete PE
- look for secondary causes

LIPID PROFILE

- Elevated TC & LDL-C
- Normal or low HDL-C
- Normal TG (elevated TG if child is obese)

Evaluation and diagnosis of Familial Hypercholesterolemia in children & adolescents

CLINICAL SUSPICION

- elevated LDL in child
- elevated LDL or known FH in family members
- tendon xanthomas in child or family members
- premature atherosclerotic CVD in child or family member

EVALUATION

- detailed history including family history
- complete PE
- look for secondary causes

LIPID PROFILE

- Elevated TC & LDL-C
- Normal or low HDL-C
- Normal TG (elevated TG if child is obese)

GENETIC TESTING

- Mutations for
- LDR gene
 - APOB gene
 - PCSK9 gene

Heterozygous FH (HeFH)

1 in 200 – 300 individuals

- High levels of total and LDL-C

PLUS ≥ 1 of the following:

- Family history of hypercholesterolemia (especially in children) or known FH
- History of premature coronary heart disease in the patient or family members
- PE findings of abnormal deposition of cholesterol in extravascular tissues (eg. tendon xanthomas)



Homozygous FH (HoFH)

1 in 200,000 - 400,000
individuals

- Untreated LDL-C > 500 mg/dL (> 13 mmol/L)

PLUS either of the following:

- Tendon or cutaneous xanthomas before age 10 years
- Elevated LDL-C consistent with HeFH in both parents



Familial Hypercholesterolemia
FH
Champions
in children



FH Champions in children

PEDIATRICIANS

Pediatric
Cardiologists

Pediatric
Endocrinologists

Pediatric
Gastroenterologists

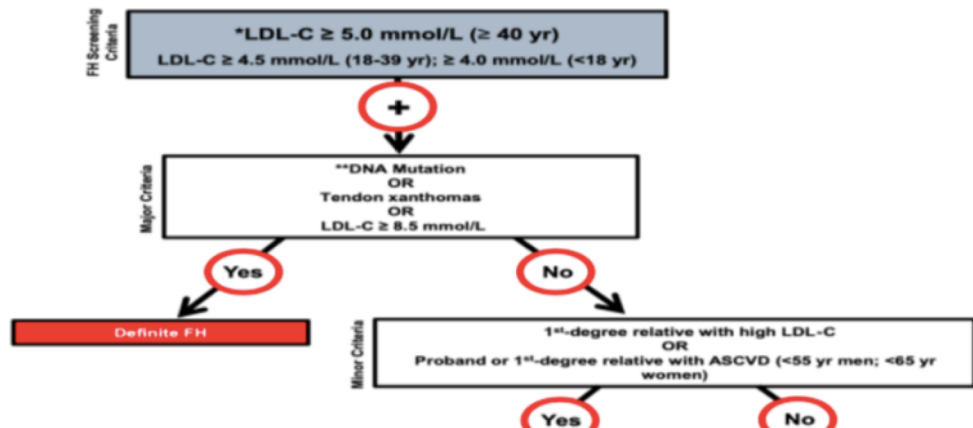


FH Champions in children

PEDIATRICIANS

Step 1: Commitment to an advocacy on FH
among pediatricians: **COLLABORATION**

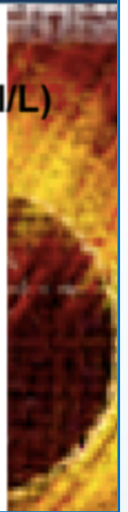
CANADA – Simplified FH Diagnosis



Diagnostic criteria for FH (Adults) in Japan

1. LDL-cholesterol > 180 mg/dL (4.8 mmol/L)
2. Tendon or tuberous xanthomata
3. Close relative with FH or early CAD

Diagnosis
 Definite FH: at least 2 of 3



Need for FH Diagnostic Criteria for Filipinos

China: FH Diagnostic Criteria

LDL-based Criteria

- LDLC \geq 6 mmol/L or
- LDL-C \geq 3.5 mmol/L plus a personal or family history of premature CHD



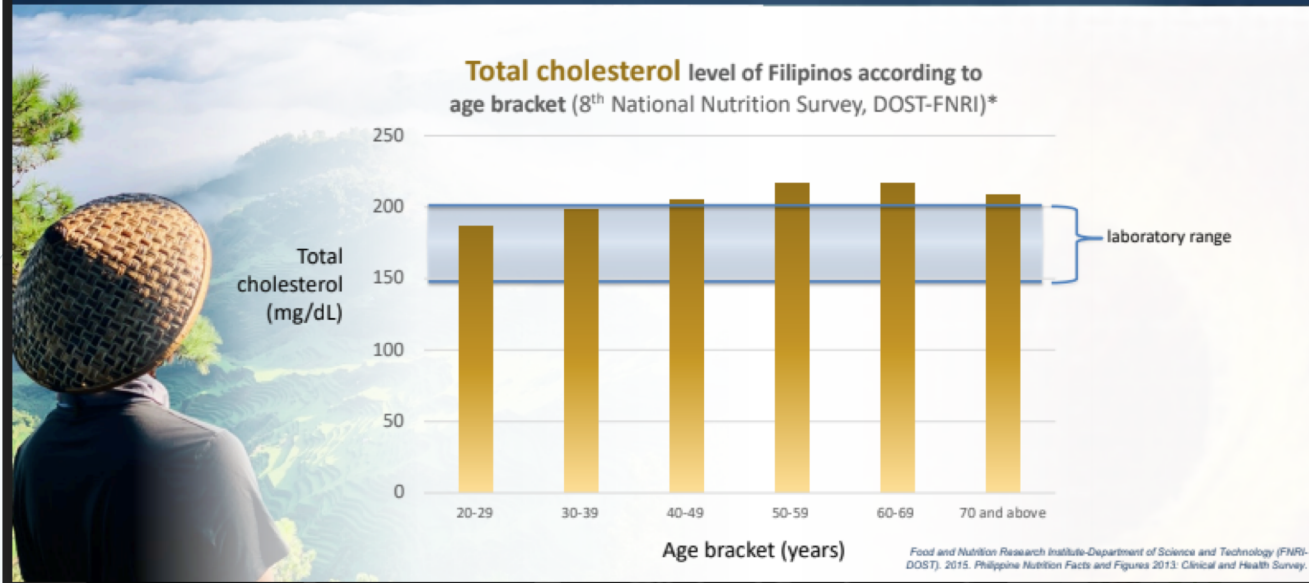
1. Zhou M et al. *J Atheroscler Thromb* 2016;23:539-549.
 2. Shi Z et al. *Int J Cardiol* 2014;174:834-836.

Modified Dutch Lipid Clinic Network Criteria

- Family history of a 1st degree relative with known premature CAD or vascular disease (1 pt)
- Personal history of premature CAD (2 pts)
- Premature cerebral vascular disease (1 pt)
- LDL-C >6.0 mmol/L (8 pts); 5.0-5.9 mmol/L (5 pts); 3.5-4.9 mmol/L (3 pts); 2.5-3.4 mmol/L (1 pt)
- Total score: >8 (definite), 6-8 (probable), 3-5 (possible), <3 (unlikely)

Lipid profile of Filipinos

Clinical Burden of Dyslipidemia
@doc_dam



Step 2: Need for a nation-wide study to formulate lipid profile of Filipino children

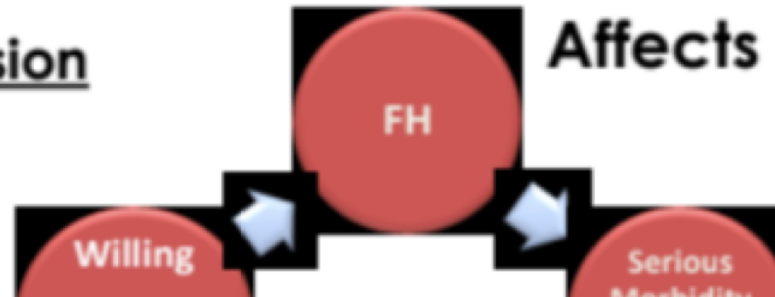
All	19002	131.5	1.5	525.9	127.8	185.3	205.0	252.5
Sex								
Male	8898	123.9	4.3	467.2	120.5	176.1	193.8	244.0
Female	10104	138.0	1.5	525.9	133.6	191.9	212.0	256.8
Age group								
20-29 years old	4070	117.3	24.3	340.2	113.5	162.9	181.1	220.5
30-39 years old	3639	127.7	12.0	397.3	124.7	176.5	194.6	243.6
40-49 years old	4173	134.0	4.3	361.4	131.3	184.6	202.7	248.3
50-59 years old	3529	145.4	1.5	525.9	142.9	203.5	225.9	270.3
60-69 years old	2108	145.9	8.5	498.8	142.1	202.7	225.9	274.1
70 years old and above	1483	141.8	5.8	410.4	137.1	196.5	222.4	273.7

Principles of Screening Familial Hypercholesterolemia

Shared Decision

- Physician
- Parent

Affects 1:250



Premature CVD

- MI
- CVA

Step 3: Consolidate efforts for the establishment
of UNIVERSAL SCREENING
among Filipino children & adolescents

• New agents*

* Not FDA approved <18 yr

- Accurate
- Accessible
- Inexpensive



OFFICIAL PUBLICATION OF THE PHILIPPINE PEDIATRIC SOCIETY

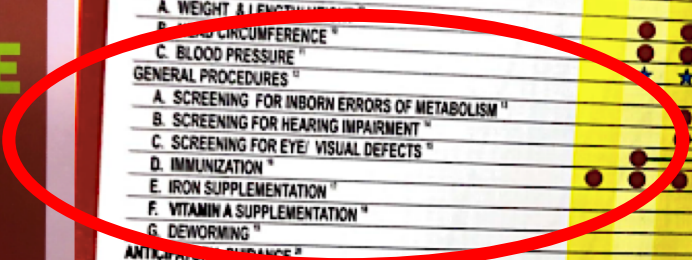
PREVENTIVE PEDIATRIC HEALTH CARE HANDBOOK

2018

Philippine Pediatric Society, Inc. Recommendations for Preventive Pediatric Health Care 2018

N.B. The recommendations in this table and optional procedures are described in detail in the ANNOTATIONS.

	AGE ^a	INFANCY ^b												EARLY CHILDHOOD ^c			MIDDLE CHILDHOOD ^d		ADOLESCENCE ^e										
		Pre Natal ^f	at birth ^g	2-4 days ^h	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	24 mos	3Y	4Y	5Y	6Y	8Y	10Y	11Y	12Y	13Y	14Y	15Y	16Y	17Y	18Y	19Y	
PRENATAL VISIT & COUNSELING		●																											
HISTORY: INITIAL/INTERVAL ⁱ		●																											
DEVELOPMENTAL SURVEILLANCE ^j		●																											
SCREENING FOR ATOPY ^k																													
PHYSICAL EXAMINATION ^l		●																											
MEASUREMENTS		●																											
A. WEIGHT & LENGTH ^m		●																											
B. HEAD CIRCUMFERENCE ⁿ		●																											
C. BLOOD PRESSURE ^o																													
GENERAL PROCEDURES ^p																													
A. SCREENING FOR INBORN ERRORS OF METABOLISM ^q				★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★
B. SCREENING FOR HEARING IMPAIRMENT ^r																													
C. SCREENING FOR EYE/ VISUAL DEFECTS ^s																													
D. IMMUNIZATION ^t		●																											
E. IRON SUPPLEMENTATION ^u																													
F. VITAMIN A SUPPLEMENTATION ^v																													
G. DEWORMING ^w																													
ANTICIPATORY CARE ^x																													
A. FIRST DENTAL VISIT ^y																													
B. NUTRITION COUNSELING ^z																													
C. PHYSICAL ACTIVITY ^{aa}																													
D. INJURY & POISONING PREVENTION ^{ab}																													
E. PREVENTION OF CHILD MALTREATMENT ^{ac}																													
F. COUNSELING ON EXPOSURE ON LEAD AND OTHER TOXICANTS ^{ad}																													
PROCEDURES FOR PATIENTS AT RISK ^{ae}																													
A. CBC ^{af}																													
B. URINALYSIS ^{ag}																													
C. WORK-UP FOR SEXUALLY ACTIVE ADOLESCENTS ^{ah}																													
D. MANTOUX TEST ^{ai}																													



**Add:
LIPID SCREENING**

- DONE AT EVERY VISIT OR AT RECOMMENDED INTERVALS FOLLOW-UPS DURING THE 1st YEAR OF LIFE DONE ON A MONTHLY BASIS
- ↔ AGE RANGE A PROCEDURE IS DONE AT LEAST ONCE OR AT RECOMMENDED INTERVALS
- ↔ (with red dot) AGE RANGE A PROCEDURE IS DONE AT LEAST ONCE FOR ALL CHILDREN THE DOT INDICATES THE PREFERRED AGE
- ★ DONE FOR THOSE AT HIGH RISK ONLY
- ↔ (with blue star) AGE RANGE A PROCEDURE IS DONE AT LEAST ONCE FOR THOSE AT HIGH RISK

Disclaimer: The recommendations contained in this document are intended to GUIDE practitioners in the conduct of anticipatory care and guidance and periodic health examinations of infants, children and adolescents. In no way should the recommendations be regarded as absolute rules, since practices and peculiarities in individual cases or particular communities may entail differences in the specific approach. In the end, the recommendations should supplement and not replace sound clinical judgment.



Risk Factors for development of atherosclerosis and early CVD in childhood

Traditional risk factors:

- Dyslipidemia
- Obesity
- Diabetes mellitus (types 1 and 2)
- Hypertension
- Family history of CVD
- Smoke exposure

Risk Factors for development of atherosclerosis and early CVD in childhood

Other conditions with increased CVD risk

- Familial hypercholesterolemia
- Chronic kidney disease
- Kawasaki disease
- Childhood cancer
- Transplant vasculopathy
- Certain congenital heart diseases (eg. CoA, AS, TGA, congenital coronary artery anomalies)
- Cardiomyopathy (eg. HCM)
- Chronic inflammatory disorders (eg. SLE, systemic JRA)
- HIV infection
- Adolescent depressive & bipolar disorders

Lipid Screening in children & adolescents

Assess CVD risk annually
Does the child have any CVD risk factor?

Child has ≥ 1 identified CVD risk factor

Perform lipid screening:

- begins when the CVD risk factor is first identified (but generally not before age 2 years)
- tailor interval of testing to the individual risk profile

Child has no identified CVD risk factor

Perform screening based on
the AGE of the child/
adolescent

Lipid Screening in children & adolescents

Assess CVD risk annually
Does the child have any CVD risk factor?

Child has ≥ 1 identified CVD risk factor

Perform lipid screening:

- begins when the CVD risk factor is first identified (but generally not before age 2 years)
- tailor interval of testing to the individual risk profile

Child has no identified CVD risk factor

Perform screening based on the AGE of the child/adolescent

< 9 years

Lipid screening is NOT indicated

9 - 11 years


All children should undergo lipid screening once in this age range

12 - 16 years

Lipid screening is NOT RECOMMENDED in this age group

17 - 21 years

All adolescents & young adults should undergo lipid screening once in this age range



Why lipid screening is not recommended for children aged 12 - 16 years old

- Changes in lipid levels that normally occur during puberty decrease the sensitivity and specificity of screening

Published in final edited form as:

Am Heart J. 2021 February ; 232: 39–46. doi:10.1016/j.ahj.2020.10.058.

LOW rates

Adherence with lipid screening guidelines in standard- and high-risk children and adolescents

Justin H. Berger, MD, PhD¹, Feiyan Chen, PhD², Jennifer A Faerber, PhD², Michael L. O'Byrne, MD, MSCE^{*,1,3,4}, Julie A. Brothers, MD^{*,1}

Conclusions: Despite national recommendations, lipid screening was performed in a minority of children. Though subjects with high-risk conditions had a higher likelihood of screening, rates remained low. This study highlights the need for research and advocacy regarding obstacles to lipid screening of children in the United States.



Familial Hypercholesterolemia Registry and Screening in the Philippines

**Step 4: Start-up of FH Registry of Filipino
children & adolescents to be part of
National FH Registry**

Proposed Strategies: FH Advocacy in Children

1

- Get strong commitment of the pediatricians to support and join the advocacy

2

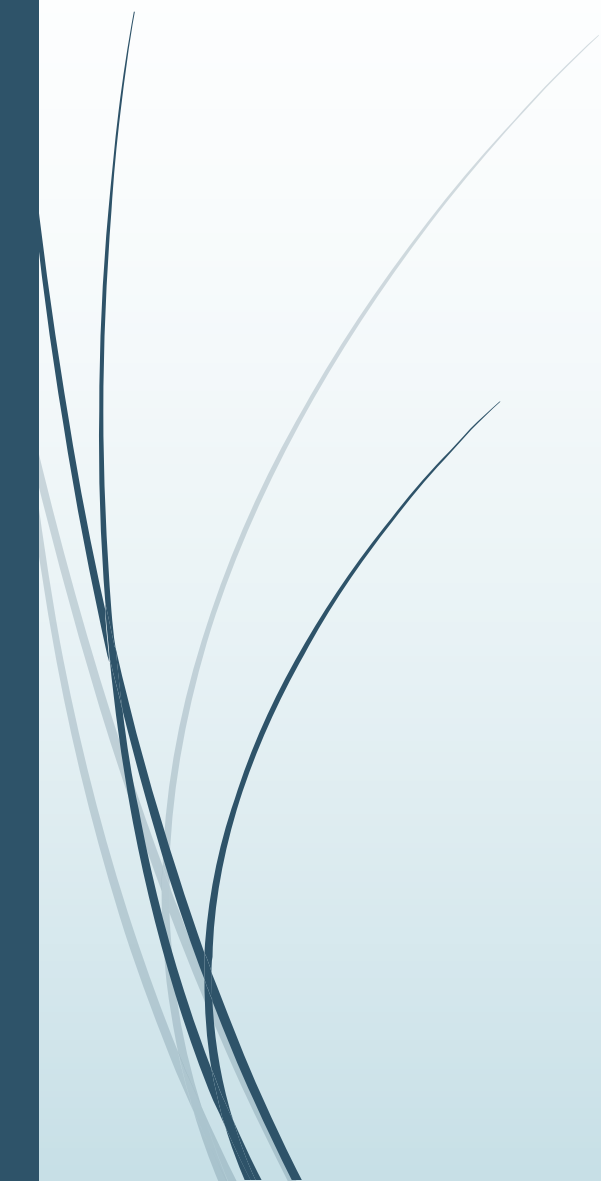
- Undertake a nation-wide study on the lipid profile of the pediatric population in the country

3

- Seek national support for Universal Screening of children and young adults

4

- Formulate a registry for Filipino children and adolescents which would then be a part of the National FH Registry.



Thank you