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

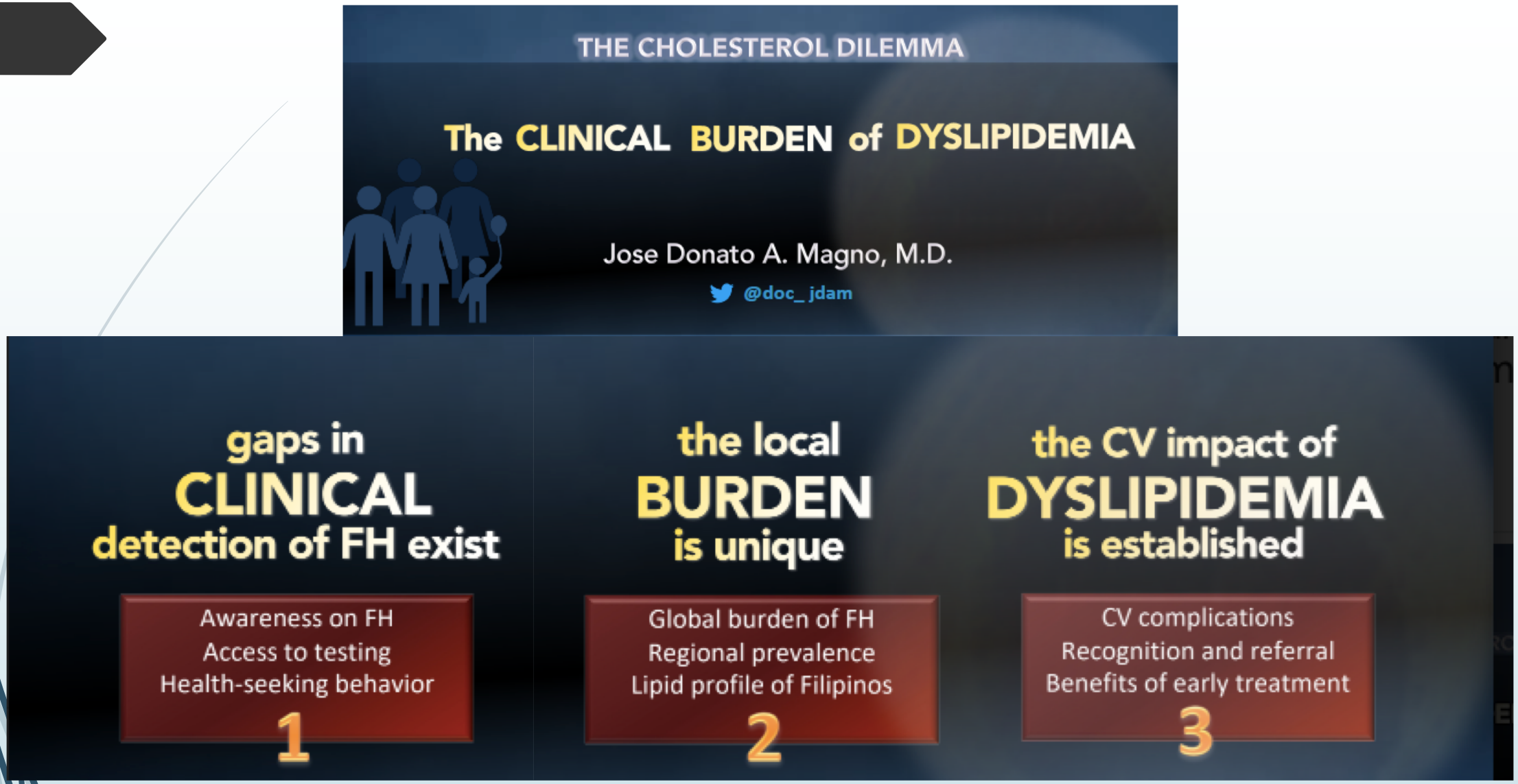
- Awareness – public, patient, medical community
- Severe and homozygous FH – very high risk
- Family-based care – integrated care needed
- Registries – essential, require sustained funding
- Research – basic science, genetic, epidemiologic, clinical
- Cost and value – understand value in FH care

JAMA Cardiol 2020, published online 01/02/20

Our Hope…

- Identify FH suspects and do cascade screening
- 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)

Call for support


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

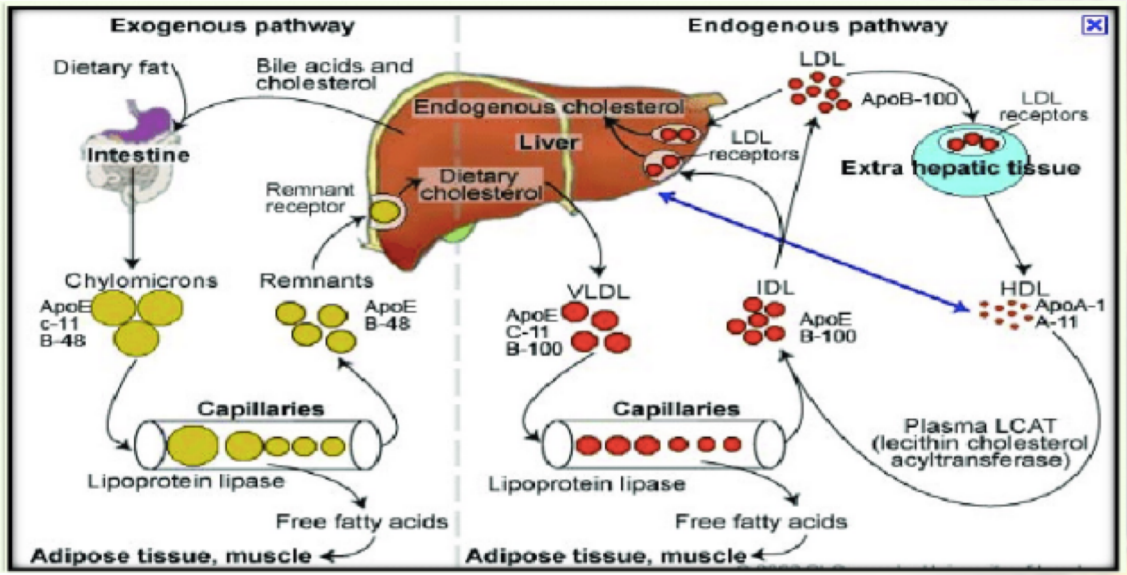
THE CHOLESTEROL DILEMMA

Cholesterol Metabolism and Plaque Formation

Focus on FH Individuals

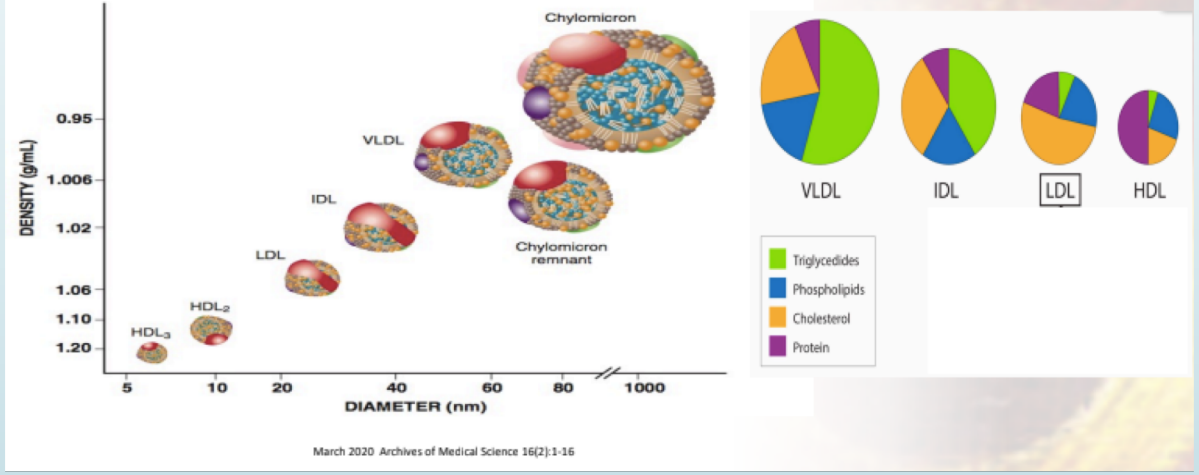
Lourdes Ella G. Santos, M.D.
Preventive Cardiology, Clinical Lipidology and Hypertension

Cholesterol Synthesis



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

Lipoproteins Vary in Size and Composition



March 2020 Archives of Medical Science 16(2):1-16

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

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

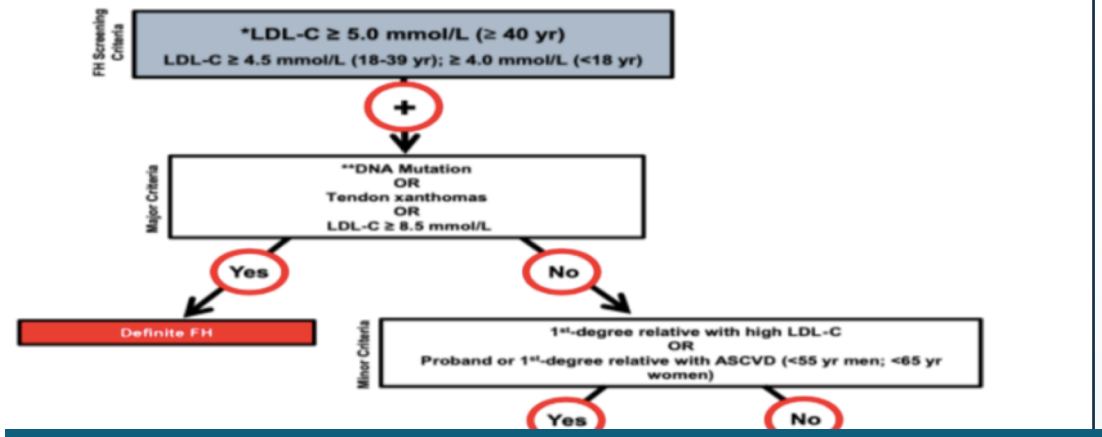
Pediatric Gastroenterologists

FH Champions in children

PEDIATRICIANS

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

CANADA – Simplified FH Diagnosis

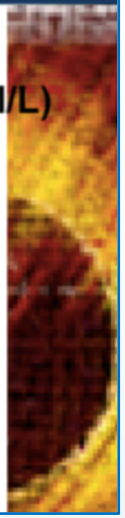


Diagnostic criteria for FH (Adults) in Japan

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

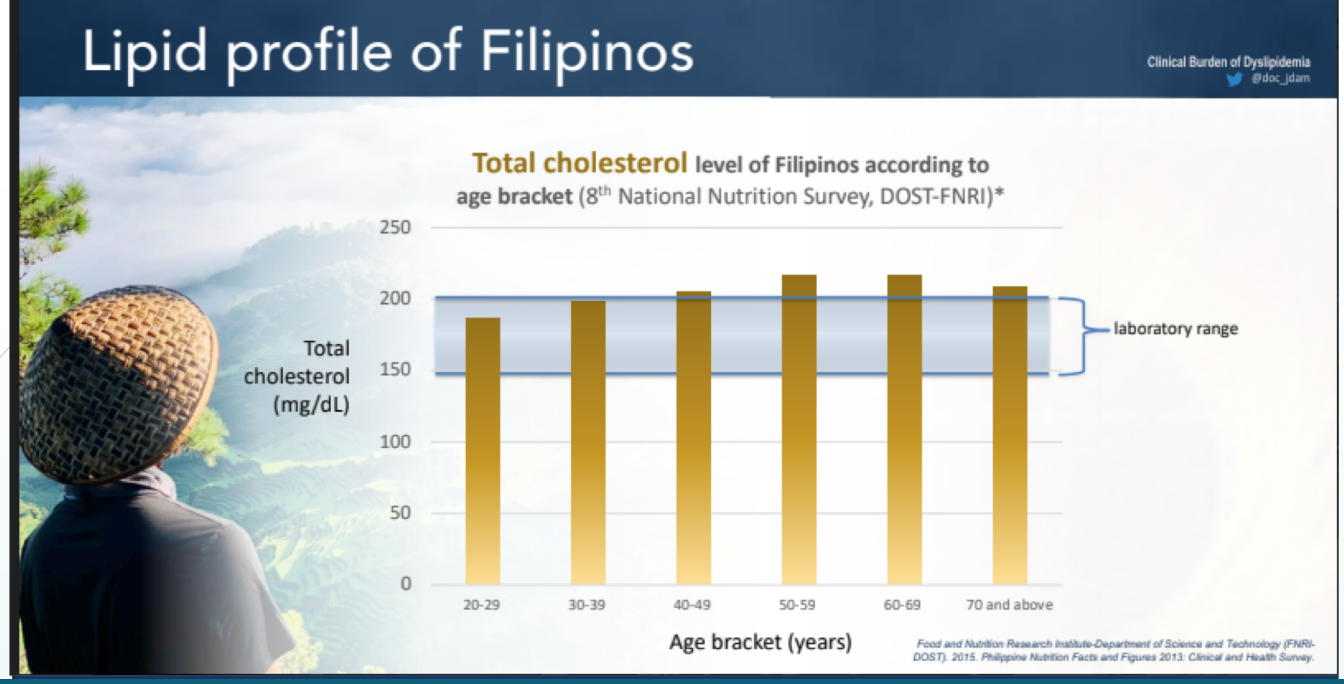
China: FH Diagnostic Criteria

LDL-based Criteria

- LDLC ≥ 6 mmol/L or
- LDL-C ≥ 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.

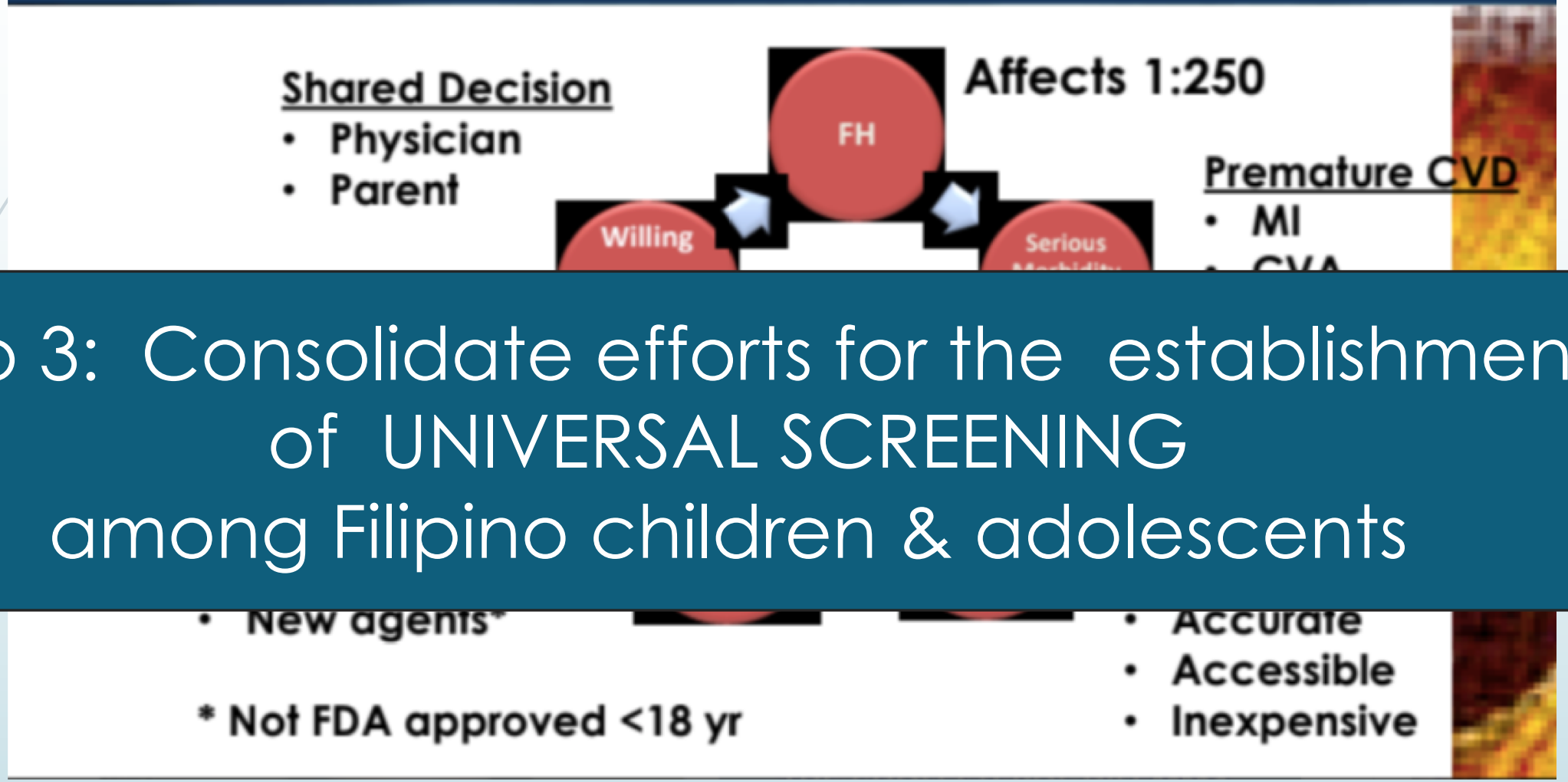
Modified Dutch Lipid Clinic Network Criteria
Family history of a 1st degree relative with known premature CAD or vascular disease (1 pt)
Personal history of premature CAD (2 pts)
Premature cerebral vascular disease (1 pt)
LDL-C >6.0 mmol/L (8 pts); 5.0–5.9 mmol/L (5 pts); 3.5–4.9 mmol/L (3 pts); 2.5-3.4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



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



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

Add:
LIPID SCREENING

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, PhD[1], Feiyan Chen, PhD[2], Jennifer A Faerber, PhD[2], 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