Lipid Association of India Expert Consensus Statement on Management of Dyslipidemia in Indians 2016: Part 1
### TSUNAMI OF PREMATURE HEART DISEASE IN INDIA (IN MILLIONS)

<table>
<thead>
<tr>
<th>Number of Indians with CAD</th>
<th>2010 * (Millions)</th>
<th>2015** (Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>47.0</td>
<td>61.8</td>
</tr>
<tr>
<td>&lt; 50 yrs of age</td>
<td>28.4 (60%)</td>
<td>37.3 (60%)</td>
</tr>
<tr>
<td>&lt;40 yrs of age</td>
<td>17.4 (37%)</td>
<td>23.0 (37%)</td>
</tr>
<tr>
<td>&lt;30 years of age</td>
<td>8.3 (12%)</td>
<td>10.5 (17%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of deaths due to CAD</th>
<th>2010 *</th>
<th>2015**</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>2.3</td>
<td>2.9</td>
</tr>
<tr>
<td>&lt;50 years of age</td>
<td>1.14 (50%)</td>
<td>1.5 (52%)</td>
</tr>
<tr>
<td>&lt;40 years of age</td>
<td>0.70 (30%)</td>
<td>0.92 (32%)</td>
</tr>
<tr>
<td>&lt;30 years of age</td>
<td>0.33 (14%) 900/day</td>
<td>0.42 (14%) 1150/day</td>
</tr>
</tbody>
</table>

*780 million Adults > 20 years of age in 2010 and ** 800 million in 2015

Enas, EA. Indo-US Health Summit Report. Indian Heart J 2008; 60: 161–175
US age-standardized death rates attributable to CVD, 2000 to 2010


DECLINING IN DEVELOPED COUNTRIES
RISING PREVALENCE OF CAD IN INDIA

IT HAS GONE UP TO 20%

CORONARY ARTERY DISEASE IN INDIA

• WHO estimates that by 2020 more than 50% of cardiac patients worldwide will be Indians

• By 2020, Over 40 percent deaths in India would be due to CHD.

Is India set to be a

Heart disease capital of the world?
# Prevalence (%) of Dyslipidemia in General Adult Indian Population:

ICMR INDIAB STUDY - 2014 Study

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2042</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>13.9</td>
</tr>
<tr>
<td>Hyper Triglyceridemia</td>
<td>29.5</td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>72.3</td>
</tr>
<tr>
<td>High LDL-C</td>
<td>11.8</td>
</tr>
</tbody>
</table>

**Definitions:**
- **Hypercholesterolemia**: ≥200 mg/dl.
- **Hypertriglyceridemia**: ≥150 mg/dl.
- **Low HDL cholesterol**: <40 mg/dl for men and <50 mg/dl for women.
- **High LDL cholesterol**: ≥130 mg/dl (calculated using the Friedewald equation).
PREVALENCE OF DYSLIPIDEMIA IN SCHOOL GOING CHILDREN OF AGE GROUP 14-18 YEARS IN DELHI

Hypercholesterolemia: ≥170 mg/dl.
Hypertriglyceridemia: ≥90 mg/dl.
Low HDL cholesterol: <40 mg/dl.
High LDL cholesterol: ≥110 mg/dl.

Puri S. et al. J Am Coll Cardiol 2015; 65:A1486
WHY EXPERT RECOMMENDATION IS NEEDED?

Compared to other ethnic groups, South east Asians have:

• Higher prevalence of atherogenic dyslipidemia
• Higher prevalence of traditional risk factors & greater prevalence of risk factors at a younger age
• Lack of awareness on CAD prevention.
• Dietary Factors.
• Physical inactivity secondary to rapid urbanization.
## Background

### 2004 National Cholesterol Education Program: Adult Treatment Panel III Update

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Target Goal</th>
<th>Initiate TLC</th>
<th>Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk:</strong> CHD or CHD risk equivalents (10-y risk &gt;20%)</td>
<td>LDL-C &lt;100 mg/dL (optional goal: &lt;70 mg/dL)</td>
<td>≥100 mg/dL</td>
<td>≥100 mg/dL (&lt;100 mg/dL: consider drug options)</td>
</tr>
<tr>
<td>Secondary Consideration (TG ≥ 200 mg/dL)</td>
<td>non HDL-C &lt;130 mg/dL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Achieve at least 30%-40% reduction in LDL-C, regardless of baseline level*

## Comparison of Recent Major Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Treat Based on</th>
<th>Treat to Specific Target</th>
<th>First-Line Therapy</th>
<th>Alternative or Add-On Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA[^a] (2013)</td>
<td>Risk group</td>
<td>No</td>
<td>Statin</td>
<td>None</td>
</tr>
<tr>
<td>ADA (2014)[^b]</td>
<td>Risk group</td>
<td>No</td>
<td>Statin</td>
<td>Generally not recommended</td>
</tr>
<tr>
<td>ESC/EAS (2011)[^c]</td>
<td>Risk group and LDL-C</td>
<td>Yes (LDL-C ± non-HDL or ApoB)</td>
<td>Statin</td>
<td>BAS, CAI, nicotinic acid, fibrate, omega-3</td>
</tr>
<tr>
<td>IAS (2013)[^d]</td>
<td>Risk group</td>
<td>No</td>
<td>Statin</td>
<td>BAS, CAI, nicotinic acid, fibrate</td>
</tr>
</tbody>
</table>

# NLA Recommendations

- Initiate therapy based on risk and lipid levels and treat to specific goal

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Initiate Drug Therapy Non-HDL-C (LDL-C), mg/dL</th>
<th>Treatment Goal Non-HDL-C (LDL-C), mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>• 0 or 1 major RF*</td>
<td>&gt; 190 (&gt; 160)</td>
<td>&lt; 130 (&lt; 100)</td>
</tr>
<tr>
<td>Moderate</td>
<td>• At least 2 major RFs and 10-y risk &lt; 10%*</td>
<td>&gt; 160 (&gt; 130)</td>
<td>&lt; 130 (&lt; 100)</td>
</tr>
<tr>
<td>High</td>
<td>• At least 2 major RFs and 10-y risk &gt; 10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• At least 3 RFs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DM with 0 or 1 other RF and no end organ damage</td>
<td>&gt; 130 (&gt; 100)†</td>
<td>&lt; 130 (&lt; 100)</td>
</tr>
<tr>
<td></td>
<td>• CKD stage 3 or 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LDL-C &gt; 190 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very high</td>
<td>• Established ASCVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DM with at least 2 other RFs or end organ damage</td>
<td>&gt; 100 (&gt; 70)†</td>
<td>&lt; 100 (&lt; 70)</td>
</tr>
</tbody>
</table>

*Consider other risk markers.
†Consider moderate- or high-intensity statin in patient with ASCVD or DM regardless of baseline lipid levels.

Non-HDL cholesterol should be used in preference to LDL-C as the treatment goal for lipid lowering therapy.

JBS3 Heart 2014;
What Indian experts feel
LAI BRAINSTORMING MEETS

Delhi 12.4.15, 19.4.15 & 12.7.15

Lucknow (09.8.15)

Mumbai (17.5.15)

Bengaluru (15.6.15)

Chennai (21.6.15)

Kolkata (24.5.15)

8 MEETINGS
6 METROS
Regional experts

- Jammu & Kashmir
- Mohali
- Rohtak
- Jaipur
- Delhi
- Gurgaon
- Karnal
- Meerut
- Lucknow
- Kanpur
- Varanasi
- Patna
- Shillong
- Guwahati
- Kolkata
- Bhubaneswar
- Nagpur
- Secunderabad
- Indore
- Baroda
- Surat
- Pune
- Ahmadabad
- Mumbai
- Bengaluru
- Coimbatore
- Chennai
- Kochi
- Trichy

153 Experts / 18 States / 30 cities
**METHODOLOGY**

- Each meeting was conducted using a standardized format.
- Key issues related to dyslipidemia management in Indians were first presented in the form of lectures followed by a discussion.
- Discussions were based on the existing data on the epidemiology and RCTs.
METHODOLOGY

• At the end of each discussion, a standardized questionnaire was given to all the participating experts to record their opinion on the various aspects of dyslipidemia management in Indians.

• These questionnaires were also sent to experts who could not attend the meeting.

• The information collected was summarized and the key findings were further discussed amongst the members of core expert group before preparation of the final draft.
RECOMMENDATIONS
1. **Universal screening of all Indians**

- By 20 years of age or,
- At the time of college admission or,
- At the earliest opportunity.

For the purpose of early detection of high-risk individuals.
2. Rule out secondary causes of dyslipidemia
3. Fasting lipid profile is not mandatory
   Non-HDL –C should be calculated in every subject
4. Identify patient risk category based on conventional and non-conventional risk factors
### Major risk factors for atherosclerotic cardiovascular disease.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Parameter</th>
</tr>
</thead>
</table>
| Age                                                   | Male  > 45 Years  
   Female  > 55 years                                                |
| Family history of Premature CAD / CVD                 | < 55 year of age in a male first-degree relative  
   < 65 Year of age in a female first-degree relative         |
| Current cigarette smoking / Tobacco chewing           |                                                                           |
| High blood pressure                                  | >140/>90 mm Hg or on BP medication                                    |
| Low high-density lipoprotein cholesterol              | Males  <40 mg /dl  
   Females  <50 mg/dL                                             |
NON-CONVENTIONAL RISK FACTORS

- Coronary artery calcification (CAC) score $\geq 300$ Agatston units
- Carotid intima-media thickness (carotid IMT)
- Presence of Atheromatous plaque.
- Aortic pulse wave velocity
- High-sensitivity C-reactive protein (hs-CRP) $\geq 2.0$ mg/L
- Lipoprotein (a) $\geq 50$ mg/dl
RECOMMENDED APPROACH TO ASCVD RISK STRATIFICATION IN INDIANS

Patients requiring ASCVD risk assessment

‘Very high risk’
- Pre-existing ASCVD, or
- Diabetes with ≥2 other major ASCVD risk factors or evidence of target organ damage, or
- Familial homozygous hypercholesterolemia

‘High risk’
≥3 major ASCVD risk factors*
Or
≥1 other high-risk features³

Count number of major ASCVD risk factors*
Look for other high-risk features³

‘Low risk’
0-1 major ASCVD risk factor*

Estimate lifetime CVD risk

≥1 moderate-risk non-conventional risk factors⁶

‘Moderate risk’
2 major ASCVD risk factors*

≥1 moderate-risk non-conventional risk factors⁶

≥30% lifetime CVD risk

*Major ASCVD risk factors
1. Age ≥45 years in males and ≥55 years in females
2. Family history of premature CVD
3. Current cigarette smoking or tobacco use
4. High blood pressure
5. Low HDL-C

*Other high-risk features
1. Diabetes with 0-1 other major ASCVD risk factors and no evidence of target organ damage
2. CKD stage 3B or 4
3. Familial hypercholesterolemia (other than familial homozygous hypercholesterolemia)
4. Extreme of a single risk factor
5. Coronary calcium score ≥300
6. Non-stenotic carotid plaque
7. Lipoprotein (a) ≥50 mg/dL

*Moderate-risk non-conventional risk factors
1. Coronary calcium score 100-299
2. Increased carotid IMT or aortic pulse wave velocity
3. Lipoprotein (a) 20-49 mg/dL
4. Metabolic syndrome
5. Estimate lifetime ASCVD risk in all low risk individuals
10-YEAR RISK VERSUS LIFETIME RISK

Calculate life time risk assessment rather than 10 years risk
• Higher prevalence of CAD in young Indian population.
• Short-term risk does not become high until later in life thereby losing the opportunity for timely prevention of CAD.

The goal of primary prevention is to reduce lifetime CV risk, not just 5- or 10-year risk.

LIFETIME RISK CALCULATORS ARE NEEDED
The following risk calculators have been proposed for life long risk assessment:

- ACC Pooled Cohort
- JBS 3 risk calculator
- Lloyed Jones / Framingham risk algorithm (IAS)

*The JBS 3 risk calculator is found to be most comprehensive in Indian Population.*
<table>
<thead>
<tr>
<th>Risk category</th>
<th>Treatment Goal</th>
<th>Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDL-C (mg/dL)</td>
<td>Non-HDL-C (mg/dL)</td>
</tr>
<tr>
<td>Very high risk</td>
<td>&lt; 50</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>High risk</td>
<td>&lt; 70</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>&lt; 100</td>
<td>&lt; 130</td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt; 100</td>
<td>&lt; 130</td>
</tr>
</tbody>
</table>

* After an initial adequate non-pharmacological intervention for at least 3 months
6. ROLE OF PRIMORDIAL PREVENTION

Primordial Prevention i.e. prevention of risk factors causative to the disease, thereby reducing the likelihood of development of disease should start from early childhood.
7. ROLE OF THERAPEUTIC LIFESTYLE CHANGES

*Life style changes are an integral part of prevention and treatment of dyslipidemia*

- Choosing appropriate diet.
  Calorie reduction is the key to weight loss and dyslipidemia treatment.
- Smoking cessation.
- Abstinence from alcohol.
- Physical activity [PA]
  Moderate intense PA is recommended for everyone.
- Role of Yoga and stress management
Primary target for treatment is LDL-C
- LDL-C of 50 mg/dl is safe

Statins are the primary modality for reducing LDL-C.
- Except in high risk and very high risk group, start with moderate intensity statin and titrate up as tolerated to achieve goal
- Discuss risk and benefit of treatment with patients.

Lipid profile should be checked at the time of diagnosis and then every 3-6 months on treatment.
9. TARGETS OF THERAPY – LDL-C (CONTD)

• The maximally tolerated statin dose should be used before add-on therapy is considered
  ➢ Add-on therapy which can be used are:
    ✓ Cholesterol absorption inhibitors
    ✓ Fibrates
    ✓ Dual PPAR
    ✓ Bile Acid Sequestrants
  ➢ These drugs should be used in patients with statin intolerance.

• Lifestyle modification should be encouraged at every visit.
Non-HDL-C = Total Cholesterol – HDL-C.

- It includes all atherogenic particles: VLDL, VLDL remnant, Chylomicron, Chylomicron remnant, IDL, LDL-C and Lp(a).
- Measurement of Non HDL-C does not require fasting blood sample.

Experts consider it as a co-primary target for treatment.

Statins are effective agents for decreasing levels of Non-HDL-C, even if LDL-C is at goal.

GOAL FOR NON-HDL-C: 30mg more than that of LDL-C goal
9. TARGETS OF THERAPY – TRIGLYCERIDES

• Elevated Triglyceride (TG) levels should be treated.

• Patients should be evaluated for possible secondary causes of hypertriglyceridemia.

• Goal TG levels is ≤ 150mg/dl preferably ≤ 100mg/dl.
9. TARGETS OF THERAPY – TRIGLYCERIDES

- First step to reduce TG: Life style modification,
  - Lifestyle modification alone can help reduce TG levels by 50%.

- Achieving non HDL-C goal will correct hypertriglyceridemia

- Statins are the treatment of choice to achieve target levels for TG level 200-500mg/dl.
  - For TG levels > 500mg/dl, Fibrates should be used.
9. TARGETS OF THERAPY – HDL-C

- Pharmacotherapy aimed at raising HDL-C does not appear to improve overall cardiovascular outcome.
  - Current evidence does not support the use of niacin to increase HDL levels.

- Physiologic measures that include exercise may increase HDL-C.

- Changes in our understanding of HDL physiology may lead to therapies targeting qualitative modifications of HDL in the future.
10. STATINS AND DIABETES

- Although statins are associated with an increase in the risk of new onset diabetes, this risk is significantly outweighed by the benefits.
  - The risk is greater with intensive statin therapy and in patients already predisposed to develop diabetes.

- Patients with risk factors for diabetes mellitus should be screened with fasting blood glucose or HbA1c, ideally prior to starting statin therapy. Thereafter, monitoring should be repeated within 1 year of initiation and at intervals no longer than 3 years.

- Aggressive lifestyle management is very important in preventing development of diabetes in patients receiving statin therapy.
STATINS INTOLERANCE: MYOPATHY

• Reported incidence is around 10%, however true incidence is not known.

• Routine monitoring of CK for statin induced myopathy is not recommended.

• Patients should be monitored for drug-drug interactions, vitamin D deficiency, hypothyroidism and other potential causes of statin induced myopathy.

• In patients with suspected statin induced myopathy treatment options include
  ➢ Lowering statin dose
  ➢ Reducing frequency of statins
  ➢ Use of alternative statins.
A very small relationship exists between statin therapy and hemorrhagic stroke, mainly in patients who have had a previous hemorrhagic stroke and who have poorly controlled blood pressure. *However, this risk is generally outweighed by the reduction in ischemic stroke with statins.*

There is no definitive evidence to suggest that statins lead to cognitive impairment or peripheral neuropathy.

If a patient presents with symptoms suggestive of cognitive impairment or peripheral neuropathy and no alternate etiology is found, statins may have to be withdrawn temporarily.
• An asymptomatic rise in hepatic enzyme activity is one of the most common adverse effect of statin therapy
  ➢ *The incidence of elevated aminotransferase activity >3 times ULN is still no greater than 3%.*
  ➢ Hepatitis, cholestasis and acute liver failure are extremely rare.

• In patients with non alcoholic steatohepatosis (NASH), statin treatment is safe, and it may even contribute to the resolution of NASH, and substantially reduce ASCVD risk by a greater margin than in those with normal liver function.
• Calculate life time risk score in age group of 20-50 years in absence of any CAD.

• Start statin in patients with high and moderately high life time risk.
  ➢ The decision to start statin therapy should be made after an informed discussion between the clinician and the patient about the risks and benefits of statin treatment.
  ➢ Before offering treatment for primary prevention, discuss the benefits of lifestyle modification and optimise the management of all other modifiable CVD risk factors if possible.

• Use low dose statin (i.e) 5mg of rosuvastatin or 10mg of atorvasatin.
RECOMMENDATIONS

• These recommendations in the statement are not mandatory to the medical community. These are opinions of lipidology experts from our country.

• Clinicians should use his judgment and experience to tailor the therapy for each patient.

• A detailed discussion with the patient prior to starting any medication for dyslipidemia is essential.
EXPERT CONSENSUS: SUMMARY

• Routine screening at age 20 yrs or at the time of college admission
• Exclude secondary causes of dyslipidemia
• Use LAI algorithm for ASCVD risk assessment. (It does not need calculators, and there is no class of recommendation or level of evidence)
• Use risk calculator preferably JBS3 to assess life time risk score especially in age group of 20-50yrs
• Stratify patients in various risk categories
• LDL-C is primary target and its monitoring is important during treatment
• LDL-C level of 50 mg/dl is safe
EXPERT CONSENSUS: SUMMARY

• Non- HDL-C is next target and it is equally important in Indian patients
• Non- statin drugs are important in dyslipidemia management
  • No role of Niacin.
  • Role of Omega 3 FA is debatable.
• Life style modifications are an integral for management and prevention of dyslipidemia.
• Practise primordial prevention
• Public awareness is essential to address this epidemic.
RECOMMENDATIONS ARE NOTHING WITHOUT IMPLEMENTATION
Help PROTECT OUR ENVIRONMENT & WILDLIFE

THANK YOU
THANK YOU