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Challenge the Guidelines

Consensus statement on the management of dyslipidemia in Indian subjects: A different perspective

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In the last 35 years we have witnessed an impressive 76%–80% decline in coronary artery disease (CAD) mortality rates in the United States (US), Finland and other countries.[1,2] This dramatic decline in CAD mortality rates is all the more impressive as the rates of obesity and diabetes markedly increased during this period.[3] The decline is largely due to control of 3 major established risk factors—smoking, high blood pressure, and elevated cholesterol.[1,3] Data review confirms that control of cholesterol was the eminent factor in reducing risk compared to all others; and notably, advances in invasive treatments (stents and coronary bypass surgery) contributed the least.[1,3] The escalating epidemic of CAD in India is due to absent or poor control of the same 3 risk factors, superimposed on a genetic predisposition to CAD.[4] Indians have a 2-fold risk of CAD and a 3-fold risk of diabetes compared to their western counterparts when adjusted for various risk factors.[4] Indians also develop CAD at a younger age.[5,6] These factors underscore the need for interventions at a lower threshold and at a younger age for Indians than their Western counterparts.[7,8]

We commend Sarat Chandra and colleagues for their initiative and effort in publishing the Consensus Statement on the Management of Dyslipidemia in Indian Subjects (CSMDIS).[9] This document fills a deep void and has many strengths that include an informative discussion on the burden of cardiovascular disease (CVD) in India, appropriate strategies for lifestyle intervention, and an excellent elucidation of lipid-lowering-treatment (LLT) thresholds for intervention and targets. However, we take exception to the risk prediction and stratification in primary prevention (Section 3) as this would stifle statin therapy for millions of Indians who are at risk and perpetuate the undertreatment of dyslipidemia.[10,11]

Treatment decisions are largely driven by pharmacoeconomics (cost-benefit ratio) in the United Kingdom (UK) where the health care cost is borne by the government, whereas risk-benefit ratio drives it in the US.[12,13] As Indian patients pay for their medical expenses one would expect India to be aligned with the US paradigm. Yet the CSMDIS set 20% CVD risk within 10 years as the high-risk threshold to qualify for LLT compared to 10% in the UK and 7.5% in the US.[12,13] Despite access to the same scientific data, recommendations for statin therapy from India are disparate and restrictive. The use of statins presently is very low in India, <5% in secondary

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prevention (compared to 71% in the US) and it is very likely that it is even lower in primary prevention.[10,11,14]

We appreciate the opportunity to present a different perspective to address the escalating epidemic of CAD in India [6,15] in a 6 question format followed by evidence-based answers on the first 5 questions and our considered opinions on the last one.

1. What is the best measure of atherogenic cholesterol and what is it's optimal level?

High-density lipoprotein cholesterol (HDLC) is anti-atherogenic and the remainder of cholesterol (total cholesterol minus HDLC) is atherogenic and termed non-high density lipoprotein cholesterol (NHDLC).[16] NHDLC includes all Apo B containing lipoproteins—low-density lipoprotein cholesterol (LDLC), very LDLC (VLDLC), intermediate density lipoprotein cholesterol (IDLC), lipoprotein (a) and remnant cholesterol. NHDLC is both a necessary and sufficient risk factor for atherosclerosis—the underlying pathophysiological process in CVD.[17] Necessary risk factor, because atherosclerosis does not develop in the absence of some elevation in NHDLC. Sufficient risk factor, because atherosclerosis develops when NHDLC concentration is markedly elevated, even in children as young as 6 years of age, without other risk factors.[17]

NHDLC, appropriately emphasized in CSMDIS, is being increasingly recognized as a better predictor of CVD risk than LDLC, and has the practical advantage of not requiring a fasting measurement.[16] For any given level of total cholesterol, Indians tend to have greater elevation in NHDLC by virtue of high triglycerides and low HDLC common in this population.[18,19]

The optimal NHDLC is defined as <130 mg/dL which corresponds to a LDLC <100 mg/dL and total cholesterol <150 mg/dL[16]. Evidence gathered in the past decade also supports a NHDLC of goal of <130 mg/dL for Indians with low, medium and high risks (Table 1).[16,20–25] In people with very high risk (established CVD, diabetes, and lifetime risk ≥45%) the NHDLC goal is < 100 mg/dL.[16,26] More stringent goals (NHDLC <75 mg/dL and LDLC< 50 mg/dL) have emanated from 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines and other studies.[12,23–26]

The best measure of atherogenic cholesterol is NHDLC and the optimal level is < 130 mg/dL for Indians.

2. How effective and safe is statin therapy?

Statins offer the most effective treatment to lower NHDLC by lowering both LDLC and triglycerides >50% (1:1 ratio).[18,27] More than 200 million people worldwide have taken statins since it was first introduced in 1987 and 170,000 were studied in well-designed randomized clinical trials; its excellent safety record surpass all other lipid-lowering medications.[12,27–30]

A recent discovery is that statin is the most effective medication to lower CVD risk.[12,27–30] Hence its use is not limited to patients with dyslipidemia or CAD but extends to all patients with elevated CVD risk.[12,27–30] Because of the impressive effect of statin medications in reducing CVD risk, a paradigm shift in statin therapy has occurred in that it's use is no longer restricted to those with high LDLC or NHDLC.[12,27–30] The broader use of statins in CVD risk reduction is analogous to the use of ACE inhibitors for cardiac and renal protection in the absence of hypertension.[18] The absolute CVD benefits of statin therapy are proportional to the intensity of therapy, the age of initiation of such therapy and the baseline risk of the individual (but not necessarily the baseline cholesterol level).[18] Most importantly, the benefit of statin therapy in primary prevention far outweighs the risk even in people with 5% CVD risk within 10 years.[29]

A meta-analysis of statin trials has demonstrated that every 80 mg/dL decrease in LDLC safely reduces the 5-year incidence of major CVD events by 42% and total mortality by 24%.[31] In primary prevention in every one million very high-risk persons (60% risk of CVD within 10 years), high-intensity statin therapy (that lowers LDLC by 98 mg/dL) prevents 9200 deaths and 28,400 CVD events.[29] Most importantly among those with <10% CVD risk within 10 years, high-intensity statin therapy can prevent 600 deaths and 1200 to 2400 CVD events.[29]

Many physicians and patients underestimate the absolute benefits and overestimate the absolute risks of statin therapy.[18] The absolute number of CVD events prevented (as discussed above) are 100 times greater than the absolute number of adverse events produced—an average excess of 3 deaths, 20 rhabdomyolysis, 100 myopathy, and 100 hemorrhagic stroke, per one million persons-years of statin therapy.[12,18] Contrary to a popular misconception, statins do not cause dementia and may actually decrease its risk by 29%[32]. The increased CVD risk resulting from statin-related new-onset diabetes is 60 times smaller than CVD prevented from statin therapy.[12] The excess risk of diabetes is 0.1% per year for low to moderate intensity and 0.3% per year for high intensity statin therapy. The risk of diabetes is also limited to those who are obese, sedentary and already on the path to diabetes.[12,18] The evidence suggests that statin therapy might shorten the time to diabetes by a few weeks or months but not years.[18] Statins may affect diabetes risk in the complex interplay between lipids, glycemia, LDL receptor function and obesity.[33] The safety and efficacy of statins is much greater than other forms of LLT.[12,18]

Statin therapy is effective and safe; the benefits far outweigh safety concerns.

3. What is the minimum age to measure lipid levels in Indians?

The range of recommendations available must be viewed in the context of the populations studied whether based on cost-benefit or risk-benefit analysis, and in conjunction with advances in scientific information on the topic. European guidelines recommend measuring lipid levels at age 40, whereas the 2013 AHA/ACC guidelines recommend lipid measurements at 20 years of age.[12] The National Institute of Health (NIH) of US sponsored major report "Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents" (202 pages and 841 references),

Table 1 – Recommendations for lifetime risk estimation, stratification, and management of dyslipidemia among Indians.

A 4 Risk factors categorized as minor, moderate, and major

Risk factor category	Smoking	Diabetes	Systolic blood pressure	Total cholesterol
Minor	N/A	N/A	120–139 mm Hg	180–199 mg/dL
Moderate	N/A	N/A	140–159 mm Hg	200–239 mg/dL
Major	+++	+++	≥160 mm Hg	≥240 mg/dL

B Lifetime CVD risk estimation men and women in urban and rural India

	Men			Women		
	White	Urban Indian	Rural Indian	White	Urban Indian	Rural Indian
No risk factor	5%	9%	5%	8%	12%	6%
≥1 minor	25%	45%	25%	10%	15%	8%
≥1moderate	38%	69%	38%	22%	34%	18%
1 major	45%	81%	45%	25%	39%	20%
≥2 Major	60%	109%	60%	45%	64%	36%
Calibration factor	1.0	1.81	1.0	1.0	1.54	0.8

C Lifetime CVD risk stratification to match the severity of risk with intensity of preventive interventions

Lifetime risk stratification		Intensity of intervention	Lifestyle therapy[a]	Statin therapy[b]	Treatment goal (mg/dL) NHDLC	LDLC
Low	<15%	Low	+	Usually no	<130	<100
Medium	15–29%	Moderate	++	Optional	<130	<100
High	30–44%	Moderately high	+++	Strongly consider	<130	<100
Very high	≥45%	High	++++	Strongly Indicated	<100	<70[c]

LDLC = low-density lipoprotein cholesterol; N/A = not applicable; NHDLC = non-high density lipoprotein cholesterol.
[a] Includes not smoking, regular exercise, consuming a healthy diet, and maintaining ideal body weight and waist circumference.
[b] Unless contraindicated or not tolerated.
[c] Optional goal is NHDLC <75 mg/dL and LDLC <50 mg/dL.[16,20–26]

recommends universal screening of children for dyslipidemia between the ages of 9 and 11 and again between the ages of 15 and 17 years.[34]

The CSMDIS recommendation to delay lipid measurement to 30 years of age is questionable for a population with the highest risk of premature CAD.[5] This delay potentially allows unfettered plaque buildup for 3 decades in Indian residents, where more Indians <30 years of age die from CAD (420,000 per year) than people of all ages in the US (375,000 per year).[2,6] The landmark Framingham Offspring Study has demonstrated CAD risk is higher in those exposed to hyperlipidemia for longer periods.[35] For example, CAD risk was 2-fold among those exposed for 10 years, increasing 4-fold among those with 2 decades of exposure to moderate hyperlipidemia (NHDLC ≥160 mg/dL or LDLC ≥130 mg/dL).[35]

Meta-analysis of statin trials in middle-aged adults showed reduction of CVD of 21% for every 39 mg/dL reduction in LDLC[31]; notably the risk reduction was nearly 3 times higher with statin therapy initiated at age 35 (54%) compared to statin begun at age 65 (20%).[36,37] Mendelian randomization studies have demonstrated that a 38 mg/dL lifetime difference in LDLC (100 mg/dL vs 138 mg/dL) is associated with 88% lower rates of CAD.[37–39] Genetic and epidemiological studies confirm that CVD risk reduction with lifelong low LDLC levels is 3–5 times greater than lowering LDLC in middle-aged adults.[37–39] The fact that CVD risk reduction with lifelong low LDLC levels is far better, provides the rationale for early initiation of Maximal Lifestyle Therapy (MLT), beginning in childhood.[37–39] American guidelines recommend statin therapy for high-risk children as young as 10 years of age and is indicated when LDLC is ≥ 190 mg/dL without other risk factors.[34] Among children with LDLC 130–189 mg/dL, statin therapy is indicated in the presence of other risk factors.[34] Several statins are FDA approved for pediatric use.

We recommend measurement of lipid levels at age 20 for all Indians and at age 10 for those with a family history of dyslipidemia or CVD.

4. What are the limitations of 10-year risk estimation and a high-risk threshold of 20%?

In primary prevention, the fundamental tenet is to match the intensity of preventive interventions with the severity of CVD risk.[12,13,40] The severity of risk is typically evaluated by using various risk prediction equations that traditionally assess the risk of developing CVD within 10 years.[41] High-risk thresholds vary between countries, depending primarily on whether the risk-benefit ratio or cost-benefit ratio is factored.[12,13] In the UK, which follows the cost-benefit ratio, adoption of 40% CVD risk within 10 years was considered economical; although this would deny statin therapy to 99% of the population the opportunity to stem CAD.[13] As the costs of statins have fallen, the high-risk threshold for statin therapy has also fallen precipitously in the UK from 40% in 1990 to 20% in 2004, and to 10% in 2014, with a corresponding increase statin-eligible population from 1% in 1990 to 19% in 2004 and half the population in 2014.[13]

The ACC/AHA guidelines state a high-risk threshold of ≥7.5% (within 10 years) with an option for statin therapy at threshold of ≥5% after consideration of secondary factors.[12] The difference in the high-risk threshold for statin therapy between the US and UK is partly due to the difference in the Risk Prediction Equations used, which in turn have different CVD endpoints. The Pooled Cohort Equations (PCE) used in the US includes only hard CVD end points (fatal and nonfatal CAD, myocardial infarction, and stroke) whereas QRISK2 used in the UK includes hard CVD end points plus soft end points

(such as angina and transient ischemic attack).[41,42] As result, the 10% CVD risk by QRISK 2 and 7.5% by PCE are generally comparable. The use of statins was liberalized in the US in 2013 and in the UK in 2014, resulting in wider eligibility for primary prevention with statin therapy. Among US adults (>40 years of age), 26% are on statins including 63% of those with diabetes and 54% of those with elevated cholesterol.[14]

CSMDIS has restricted the wider use of statins in India when it set a 20% of CVD risk within 10 years as the high risk threshold for statin therapy in primary prevention.[9] The threshold is too high and indefensible based on accumulated evidence.[12,13,16,26,40] To illustrate this comment in clinical context, let us consider the statin eligibility for an Indian male (case 1) and a female (case 2), both having the following risk profile: Age 30, heavy smoker, family history of premature CAD, obesity (height 165 cm weight 70 Kg, BMI 26), systolic blood pressure (SBP) 160 mmHg without treatment, total cholesterol 280 mg/dL, and HDL 40 mg/dL). Would you not start these patients on statin therapy? QRISK2 risk calculator gave a 10-yr CVD risk of 9% for case 1 and 6% for case 2 — far below the 20% high-risk threshold recommended by CSMDIS. Case 1 would have to wait until age 40 and case 2 until age 49 to reach the 20% risk threshold for statin therapy (recommended by CSMDIS).[9] Nonetheless, both would have qualified for statin therapy if the ACC/AHA optional high-risk threshold of ≥5% were applied.[12]

A major problem with the 10-year CVD risk calculation is that it is heavily influenced by age.[12] As an example, 10-year CVD risk for a 70 year-old male without other risk factors (cholesterol 170 mg/dL, HDLC 50 mg/dL, SBP 110 mmHg without treatment, no smoking and no diabetes) is 13%,[12] whereas for a 30-yr old with multiple risk factors as described in cases 1 and 2 have a risk of 9% and 6% respectively. This underestimation of CVD risk at younger ages may not be a problem in developed countries such as the US, where 81% of CVD deaths occur in people ≥65 years of age and only 1% of deaths in whites and 4% of deaths in blacks occur in those <45 years.[2,6,43] In sharp contrast, underestimation of risk is a major problem in India, where 42% of all CAD deaths occur in people <45 years of age (1.2 million annually).[6]

Two thought provoking reports from India and Denmark highlight the importance of using appropriate risk thresholds when ACC/AHA/PCE is used to identify statin eligible patients among those presenting with the first acute myocardial infarction (AMI).[44,45] Among Indian patients (median age 59) only 30% would have qualified for statin therapy when CSMDIS criteria (20% CVD risk within 10 years) was applied.[44] However, among Danish patients <60 years of age, 65% of men and 12% of women would have qualified for statin therapy when ACC/AHA criteria (≥7.5% CVD risk within 10 years) was applied.[45] Further, 70% of men and 30% of women would have qualified for statin therapy when the optional criteria (≥5% CVD risk within 10 years) was applied.[45]These data underscore the importance of selecting not only the right risk prediction equation but also defining the appropriate threshold for statin therapy for Indians.

A 10-year CVD risk of 5% is a more appropriate threshold for Indians for statin therapy than 20%. However, because of the many variables that potentially deprive statin therapy to millions of patients who would benefit from it and because of the need for cumbersome estimation tools, it is time to put the 10-year CVD risk estimation tool to rest. Instead consider a better alternative (discussed below).

5. What are the advantages of lifetime risk estimation and stratification of CAD in Indians?

The aim of preventive intervention in CVD should not be limited to 10 years but should be to reduce the morbidity and mortality due to CVD for a life time thus aiding healthy aging. A noteworthy publication from India highlighted the importance of estimating lifetime risk among Indians with low short-term risk.[46] In this study, 76% (approximately one in 2 men and 3 in 4 women) had low-risk of CAD (using 10% CVD risk within 10 years as the high-risk threshold).[39] However, half of those with low short-term risk had a high lifetime risk qualifying for intensive interventions. As a result, the proportion of high-risk individuals increased by 150% (from 24% using 10-yr risk estimates to 61% when lifetime risk was estimated).[46]

The Global Recommendations for the Management of Dyslipidemia by the International Atherosclerosis Society (IAS), published in 2013 estimates only lifetime risk (defined as risk to age 80) effectively eliminating the limitations of a 10-year risk estimation.[16] The full IAS document can be downloaded from the IAS website: http://www.athero.org/download/IASPPGuidelines_FullReport_20131011.pdf.

The IAS lifetime risk estimation and stratification has several advantages over other tools (Tables 1 and 2).[16,20–26] Most importantly, the IAS algorithm considers only 4 major risk factors and 4 levels of lifetime risk. Major risk factors are cholesterol >240 mg/dL, SBP >160 mmHg, smoking, and diabetes. Cholesterol 200–239 mg/dL and SBP 140–159 are moderate risk factors; cholesterol 170–199 mg/dL and SBP 120–139 mm Hg are minor risk factors. Levels of lifetime risk are: very high ≥45%, high 30–44%, moderate15 -29%, and low <15%. This stratification forms the basis for recommending LLT: indicated for those at very high risk, to be strongly considered for those at high risk, optional for those with moderate risk and not indicated for low risk individuals.[16]

To view risk stratification in the clinical context of the 2 illustrative cases mentioned earlier (under 4), and now reexamining them using the IAS tool, case 1 would have a lifetime risk of 109% and case 2, 64%, far above the 45% high-risk threshold (thereby qualifying for statin therapy).[16] This IAS lifetime risk estimation took less than a minute without the aid of a computer or internet access.

All CVD risk scores have different accuracy in different populations, tending to over predict CVD risk in low-risk populations (such as Chinese, Japanese, and Southern Europeans) and under predict the risk in high-risk populations (such as Indians and Russians).[2,22] A multitude of protective factors and harmful risk factors contribute to differences in baseline population risk. Several studies have shown 150%–220% higher CVD mortality among South Asians compared to whites in the UK, despite equal access to health care (and after adjustment for all major risk factors including

Table 2 – Advantages of International Atherosclerosis Society lifetime risk estimation and risk stratification for Indians.

1	Assessment of lifetime risk	Lifetime risk provides more accurate estimation of CVD risk among Indians—a population with the highest rates of premature coronary artery disease (CAD). Age, the principal driver of underestimation of premature CVD risk is eliminated from the risk estimation algorithm
2	Simplicity	Simple algorithm requiring no internet access or calculators
3	4 risk categories	Very high (≥45%), high (30–44%), moderate (15–29%), and low (< 15%)
4	4 major risk factors only	Diabetes, smoking, cholesterol ≥240 mg/dL and SBP ≥160 mm Hg
5	2 moderate risk factors only	Cholesterol 200–239 mg/dL and SBP 140–159 mm Hg
6	2 minor risk factors only	Cholesterol 180–199 mg/dL and SBP 120–139 mm Hg
7	Country/Ethnic/gender specific calibration coefficients reflecting the baseline risk	China 0.36, Italy 0.37, France 0.41, Germany 0.43, UK and Ireland 0.74, US 1.0, rural Indian men 1.0, rural Indian women 0.8, urban Indian men 1.81, urban Indian women 1.54.
8	Absolute lifetime risk estimation	Multiply the estimated lifetime risk with the recalibration coefficient; this allows to compensate for significant over or underestimation of risk in certain populations.
9	Definition of atherogenic cholesterol	Atherogenic cholesterol is defined as NHDLC and it is calculated by subtracting HDLC from cholesterol level.
10	Definition of and its optimal level	The optimum level of NHDLC is <130 mg/dL, which corresponds to LDLC <100 mg/dL and total cholesterol <150 mg/dL.
11	Rationale for the use of NHDLC	NHDLC is a better predictor of CVD risk than LDLC, although LDLC has been the traditional target of lipid-lowering therapy for decades. NHDLC has the additional advantage of not requiring fasting or additional expense for estimation.
12	Reduction in lifetime CVD risk with treatment of risk factors	Unlike 10-year risk estimation which is fixed, lifetime CVD risk estimation is dynamic; lifetime CVD risk, therefore, risk can be substantially reduced by treatment of risk factors (such as treatment of high blood pressure, high cholesterol or smoking cessation).

CAD = coronary artery disease; CVD = cardiovascular disease; LDLC = low-density-lipoprotein cholesterol; NHDLC = non-high-density-lipoprotein cholesterol; SBP = systolic blood pressure; Refs. [16,20–23].

diabetes).[47–49] Taking this into account, IAS panel has delineated specific calibration coefficients to compensate for the underestimation and overestimation CVD risk among different populations in the world. This coefficients vary by ethnicity and range from as high as 1.8 for urban Indian men and 1.54 for urban Indian women to 1.0 for rural Indian men and 0.8 for rural Indian woman and as low as 0.5 for Japanese Americans and 0.36 for Chinese.[20–22] The estimated CVD risk is multiplied by these calibration coefficients to arrive at the true absolute CVD risk in a given population. The high calibration coefficient for urban Indians appears related to a higher prevalence of lipoprotein(a)[50] and metabolic syndrome,[51] combined with unhealthy diet (low intake of fruits, vegetables, whole grains, and fish, and high intake of full-fat dairy products and fried food, a surrogate for trans fats, etc.).[52] The high prevalence of protective factors among Chinese, Japanese and Italians, and Native Americans (American Indians) possibly account for their low calibration coefficients.[4]

Based on the preceding discussion, it follows that when the IAS algorithm is used compared to 10-year risk stratification, far more Indians would fall in the stratum for statin therapy even when the LDLC level is not significantly elevated. For example, an Indian male with 1 and Indian female with 2 major risk factors would have a lifetime CVD risk of 81% and 64% respectively and therefore require high-intensity statin therapy; this is because of their CVD risk exceeds the high risk threshold of ≥45%.[16]

Another advantage of lifetime risk calculation is that it is not a fixed entity and the risk would decrease with appropriate therapy.[16] For example, control of blood pressure or cessation of tobacco use can downgrade the lifetime risk to a lower category and reduce the dose of statin or possibly even obviate the need for it, provided the NHDLC level is in the optimal range. This is in sharp contrast to 10-yr risk estimation based on a single measurement that does not provide adjustments for changes in risk due to interventions such as smoking cessation or statin therapy started after enrollment.

The IAS risk estimation and stratification algorithm may be further refined, at a later date, by incorporating other factors such as chronic kidney disease, microalbuminuria, family history of premature CVD, ankle-brachial index <0.9, Coronary Artery Calcium Score (CACS) > 300 Agaston units, and lipoprotein (a) ≥50 mg/dL (>125 nanomol/L)[26].

Despite its simplicity and ease of use, some physicians may be unwilling to try the IAS and other risk prediction algorithms. Therefore, physicians may be offered the option to treat high cholesterol just the same way as they treat hypertension, based exclusively on the cholesterol levels. It seems reasonable to recommend statin therapy to individuals with cholesterol ≥180 mg/dL or NHDLC ≥160 mg/dL.[16,53] This option is particularly important in India, where many busy practitioners, including cardiologists see as many as 200 to 300 patients a day.[53] This option would reduce the number of patients requiring risks scoring. However, this would leave behind a large number of patients with multiple non-lipid risk factors that magnify the CVD risk and therefore should not be the preferred option.

The IAS lifetime risk estimation and stratification algorithm is the best method to identify and treat Indians at high-risk for CAD at a younger age. The IAS algorithm with the calibration factors also lowers the bar for initiating statin therapy for millions of Indians, who would greatly benefit from it. Besides it is also easy to use and is flexible as therapy can be modified as risk factors change. For these reasons we endorse statin therapy on the basis of lifetime risk estimation and stratification.

6. How can we appropriately increase the use of statins for primary prevention of CVD in India?

Besides the issue of underestimating risk factors, a major impediment to combating CVD in India is the underuse of indicated medications, especially statins that reduce CVD morbidity and mortality.[10,11,54] In a broader context, the issue of under treatment is not confined to dyslipidemia but also to chronic diseases such as diabetes and hypertension.[10,11,54] The concept of lifelong treatment is not understood by many patients and unfortunately not fully understood or embraced by some physicians.

Some practitioners including cardiologists seem eager to reduce or stop life-saving medications as soon as the blood pressure or cholesterol level has barely reached the goal. Some also practice the provision of offering "drug holidays" to patients. Repeated reinforcements by educational programs may help change the mind set of some practitioners to remember the chronic disease management dictum "*treatment is lifelong, if not, life may not be long.*" Since they receive little information from doctors, pharmacists or pharmaceutical companies, many patients are totally in the dark as to "what medications are prescribed for what conditions" and fail to differentiate between life-saving medications, vitamin supplements and other non-essential medications.

Primary care physicians (general practitioners) write two-thirds of statin prescriptions in the US and Europe but not so in India. There is no compelling reason why Indian general practitioners should not manage dyslipidemia in their patients. In primary prevention, but not in secondary prevention, statin therapy is reserved for those who fail to achieve or maintain the risk adjusted NHDL levels with maximal lifestyle therapy, which should be started before and continued during statin therapy. It is important to continue statin therapy lifelong unless competing diseases have reduced the quality and quantity of life.

In the US, most prescriptions for high blood pressure and high cholesterol are written for three months at a time (and sometimes for 1 month with 3 refills). Bottles containing 100 tablets are the norm rather than the exception. In contrast, most patients in India buy "medication strips" that usually last one or 2 weeks. Many patients wait a week or 2 to buy the next strip. Cultural beliefs and socioeconomic status compound the woes. Patients consume a third or less of prescribed dosage contributing to poor control of hyperlipidemia. We are not unmindful of the financial, educational and cultural difficulties that patients in India face in understanding and dealing with chronic diseases and accepting the need for life long medications. While recognizing that there are no easy solutions, we encourage physicians to take leadership roles in educating patients and families directly and through print, visual and social media. Cardiologists, rightly so, should take the lead in the domains of CAD, its risk factors and management of dyslipidemia by teaching their primary care colleagues, medical students and physicians in training.

Strategies must be developed to enable Indian general practitioners champion the provision of statin therapy in primary prevention of CVD. Every effort should be made to make treatment of dyslipidemia as easy as the treatment of hypertension and diabetes by educating physicians and public.

The 2013 ACC/AHA cholesterol guidelines sparked efforts to promote statin use in many high-risk patients who were hitherto undertreated in the US.[12,55] We hope that this commentary will aid Indian physicians navigate through the occasionally differing recommendations in the American, European and Indian guidelines. While we agree on most of the CSMDIS guidelines we urge the guideline writers to make changes in Section 3 that deals with primary prevention giving due consideration to our perspective. We hope the revised guidelines would then foster a public health strategy that focuses on sustained reduction of NHLDLC throughout the lifespan that would reduce the excess burden of CAD among Indians. *It is time to expand the widely accepted LDLC and NHDLC dictum from "the lower the better" to "lower and earlier the better".*[18]

Conflicts of interest

All authors have none to declare.

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