

Algorithms for Cardiovascular Disease Prevention

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Abstract

Prevention of coronary artery disease requires control of risk factors. It is not enough to take out guidelines, it is necessary to implement the guidelines. There are a number of studies which have shown that quite often guidelines are not followed. In this article, we have abstracted the essence of the guidelines into simple to follow algorithms so that they are easy to remember and also teach. For Cardiovascular risk reduction, general measures include stopping smoking, perform 150 minutes of moderate activity per week and take a low fat and low salt diet. For hypertension: All classes of drugs are suitable but generally (NICE 2011) Angiotensin receptor blockers or Angiotensin converting enzyme inhibitors for young (<55 years), Beta blockers (only if other compelling indications). In elderly (>55 years, many with isolated systolic hypertension) Calcium channel blockers, diuretics if needed, are preferred. Combinations are used if monotherapy does not work. For dyslipidemia: Statin benefit groups are defined and manifest coronary artery disease and Diabetics above 40 years should get high dose statins. Lipid levels are only tested to look for compliance or further intensification of regime. Diabetes: Metformin is the drug of choice, Sulfonylureas can be used in combination. Glyptins are also safe and can be used. Other drugs should be used with the help of the endocrinologist.

Key words: Algorithms, CAD, cardiovascular disease guidelines, India, prevention

INTRODUCTION

Cardiovascular risk reduction requires focused reduction of the various cardiovascular disease (CVD) risk factors. Clear guidelines are available for the management of each risk factor, but it is often not possible for many physicians to stay abreast with the latest guidelines. In this article, we have tried to convert the latest and the best available guidelines for cardiovascular risk reduction into simple algorithms which are just one or two pages per risk factor and easy to read. They are not comprehensive, and many details have been removed for simplification. It is hoped that the algorithms will ensure that a basic level of prevention will be provided by all health-care providers in a similar and standardized manner. These have been designed in the form of two pages which are meant to be handouts along with supplementary material for each major risk factor (hypertension, diabetes, and dyslipidemia). These have been arrived by consensus and are not meant to replace existing guidelines but just to provide a starting point for therapy.

GENERAL PREVENTIVE MEASURES

- Stop smoking and tobacco use
- It is recommended for healthy adults of all ages to perform at least 150 min a week of moderate intensity or 75 min a week of vigorous-intensity aerobic physical activity^[1-12]
- Diet: Energy intake should be limited to the amount needed to maintain a body mass index between 20.0 and 25.0 kg/m². Saturated fatty acids (<10% of total energy intake) replacement by polyunsaturated fatty acids. Salt intake should be <5 g of salt per day, 2–3 servings of fruit per day, and 2–3 servings of vegetables per day. Consumption of sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.^[13]

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HYPERTENSION MANAGEMENT

The recommendations in this paper [Figures 1 and 2] have been adapted from multiple sources, mainly the NICE guidelines of 2011 and the ESC statement of CVD reduction 2016. Physicians are expected to take this statement into account, along with the individual needs and preferences of their patients.^[13,14]

Insert 1

It is the main algorithm for the management of hypertension. Most of the classes of antihypertensives (angiotensin converting enzyme [ACE] inhibitors/angiotensin receptor blockers [ARBs], calcium channel blockers [CCB], and diuretics) can be used initially unless there are specific indications but in the NICE guidelines, it was suggested that younger patients would be benefited by starting with ACE inhibitors or ARBs. Beta blockers are not preferred in young unless they have compelling reasons such as heart failure (HF) or angina. In elderly, where isolated systolic hypertension is more likely CCBs are preferred. Diuretics are not often preferred initially because of their tendency to cause metabolic problems.

The management starts usually with lifestyle modification (Insert 2) and one drug. Two drugs are used if the blood pressure (BP) is not controlled and a third drug is added if it is still not controlled. Combinations can be used.

Insert 2

It contains the targets. The targets are simple: Treat BP above 140/90 mmHg and bring it below 140/90 mmHg. If SPRINT results are to be followed then the ESC guidelines suggest that the targets can be lowered slightly to 130–139/80–85 mmHg, keeping in mind that the very strict control in SPRINT was also associated with adverse effects.

Physicians should use Insert 1 as a desktop reminder.

DIABETES

The key points a cardiologist needs to focus on are as follows [Figure 3 and 4]:

- The multifactorial approach is very important. Intensive management of hyperglycemia reduces the risk of microvascular complications and CVD. Intensive treatment of BP in diabetes mellitus (DM), with a target of 140 mmHg systolic for the majority, reduces the risk of microvascular and macrovascular outcomes. A lower systolic blood pressure target further lessens the risks for stroke, retinopathy, and albuminuria and should be applied to selected patients. All patients >40 years of age and selected younger patients at elevated risk are recommended for the statin therapy. In DM patients with existing CVD, the use of a sodium-glucose co-transporter-2 (SGLT-2) inhibitor substantially lessened CVD and total mortality and HF hospitalization without major adverse effects^[13,15,16]

- A target HbA1c for the reduction in risk of CVD and microvascular complications in DM of <7.0% is recommended for the majority of adults with DM
- BP targets in Type 2 DM are <140/85 mmHg, with a lower target of <130/80 mmHg recommended for some patients (younger patients at elevated risk for complications) for additional gains on stroke, retinopathy, and albuminuria risk. Renin-angiotensin-aldosterone system blocker is recommended in the treatment of hypertension in DM, particularly in the presence of proteinuria or microalbuminuria. Recommended BP target in patients with Type 1 DM is <130/80 mmHg
- In DM patients at very high-risk, a low-density lipoprotein cholesterol (LDL-C) target <70 mg/dL or a reduction of at least 50% if the baseline LDL-C is between 70 and 135 mg/dL is recommended.
- Choice of drugs for diabetes control:
 - Metformins are the first choice of drug
 - Sulfonylureas can be used if metformins cannot be used as the first choice
 - Gliptins can be considered as the first line only if either of metformin or sulfonylurea cannot be used
 - After 3 months of these drugs, combinations of these or dose increase or adding insulin can be done. Beyond this, the other drugs should be used with the help of an endocrinologist.

HYPERLIPIDEMIA MANAGEMENT FOR THE CARDIOLOGIST

These have been adapted from the AHA and ESC guidelines (2016 and 2013 and also with some suggestions picked up from the lipid association of India statements and other publications from India).^[17-27]

The main message clear from all the lipid control guidelines is that there are four sets of patients who need to be defined as the statin benefit groups. These are as follows [Figures 5 and 6]:

Individuals

1. Adults >21 years with clinical atherosclerotic CVD (ASCVD)
2. Adults >21 years with primary elevations of LDL-C >190 mg/dL
3. Diabetes aged 40–75 years with LDL-C 70–189 mg/dL and without clinical ASCVD
4. Individuals without clinical ASCVD or diabetes with LDL-C 70–189 mg/dL and estimated 10-year ASCVD risk >7.5%.

The last group which involves primary prevention is the group where for India we would probably need to lower the age to first start looking at risk to 21 years. Moreover, we would also need to use different calculators for risk calculation. Some of the risk calculators which have Indian data available include QRISK2 (use a cutoff of 10%) and JBS3, International Atherosclerosis Society 2013 (lifetime risk: Intervene in high and very high risk, uses smoking, diabetes, BP and cholesterol,

Suggested algorithm for hypertension (adapted from NICE Guidelines/ESC 2016.)

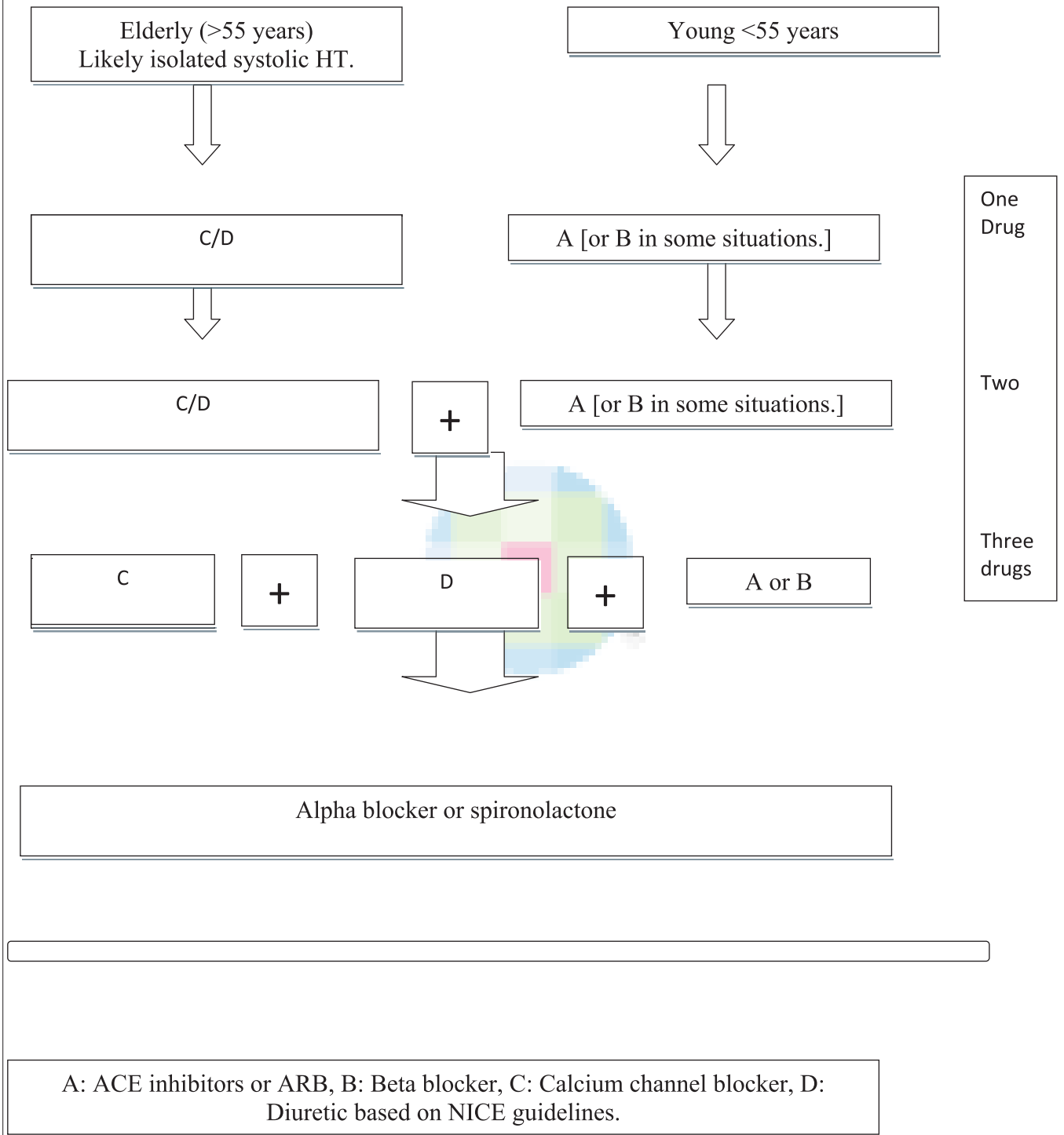


Figure 1: Hypertension management (insert one).

Hypertension: When to treat with drugs

Systolic BP >140 mmHg (>140 mm, if cardiovascular risk factors or macrovascular target organ damage). Above 80 years, treat above systolic blood pressure of 160 mm, unless there is diabetes or target organ damage.

or

Diastolic BP >90

Investigations: Urinalysis, blood (potassium, sodium, creatinine, fasting glucose, and lipid profile), electrocardiogram, and urine albumin excretion (in diabetics)

Initial treatment:

Lifestyle measures (weight control; increased physical activity; alcohol moderation; sodium restriction; and increased consumption of fruits, vegetables, and low-fat dairy products) are recommended.

One or combination: Diuretics (thiazide, chlorthalidone, and indapamide) or calcium channel-blockers (CCB); angiotensin converting enzyme (ACE) and inhibitors/angiotensin-2 receptor blocker (ARB). Below 55 years of age, offer ACE or ARB (except women of child bearing age), above 55 years, a CCB or a thiazide-like chlorthalidone/indapamide. Beta blockers are not the preferred initial therapy but are often used in younger patients and can be combined with CCBs.

Second stage: Use a CCB or thiazide-like diuretic with ACE or ARB.

Third stage: Ensure all drugs are at optimum doses. If three drugs are needed, then CCB plus ACE/ARB plus thiazide-like diuretic should be used.

Fourth stage: At this stage, spironolactone can be considered or a beta blocker or an alpha blocker.

Compelling indications: Beta blockers in heart failure and coronary artery disease, ACE inhibitors in diabetes and heart failure and CKD.

The NICE guidelines suggest starting with ACE/ARB in young, while ESC 2016 suggests that any drug can be used to start treatment.

Recommendations for BP control.

Standard goals: Systolic blood pressure <140 mmHg (elderly <150 mmHg), DBP <90 mmHg.

Intense BP control (based on the SPRINT trial): Systolic blood pressure <120 mm in high risk individuals (not diabetes or stroke). This was linked with increased complications. Prudent to bring down to 130–139/80–85.

Figure 2: Hypertension management (part 2).

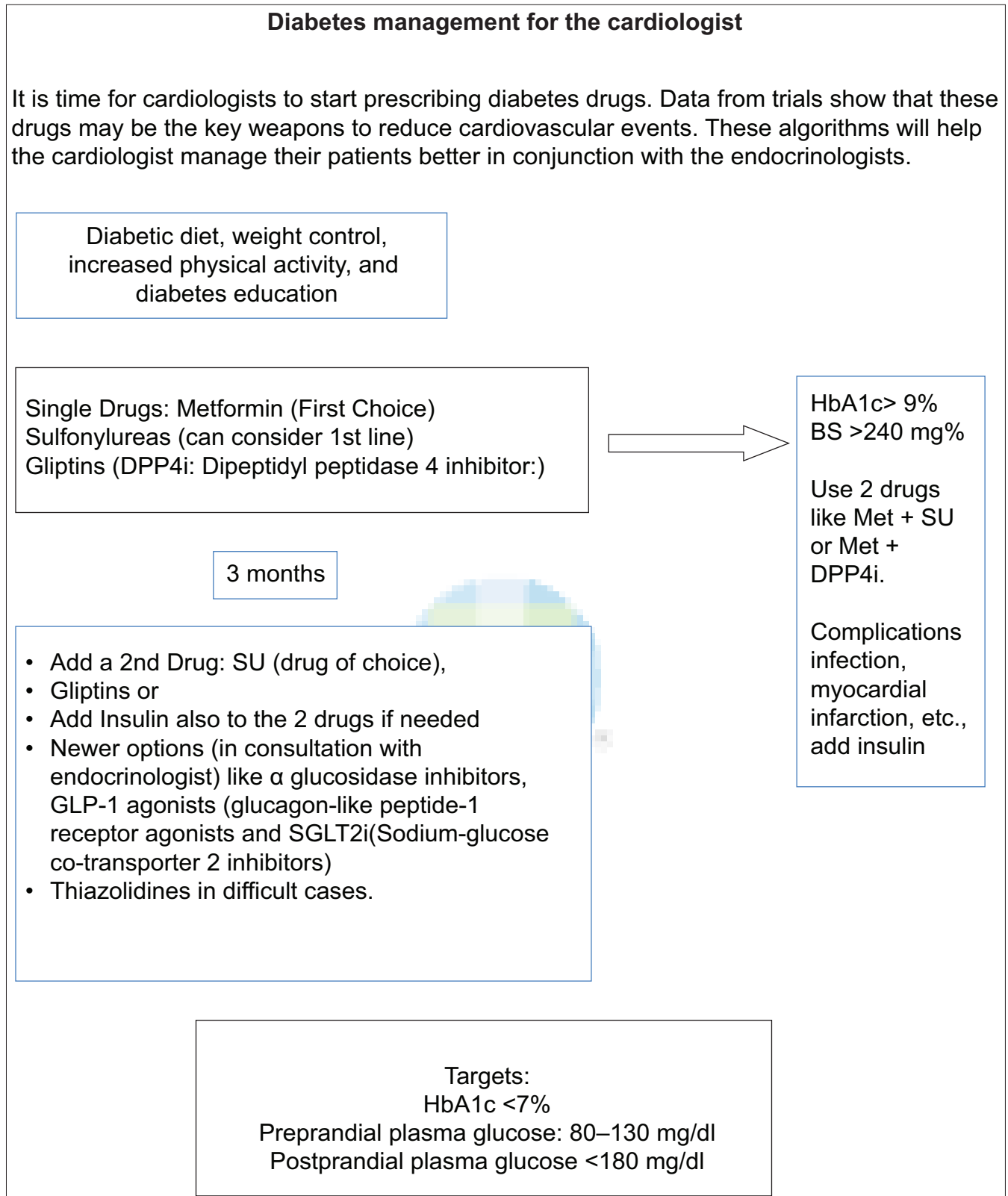


Figure 3: Diabetes management (part one).

Guidelines on Specific Drugs

Metformin: Drug of choice, except when weight loss or underweight, start 500 mg BD with meals and up to 2000 mg per day. Increase 2 weekly. Side effects: GIT, lactic acidosis, muscle weakness. Contraindicated in renal failure.

Sulfonylureas: Good option for Indians as the first line/meat intolerance or MODY or as an add-on to metformin. Cause weight gain. Gliclazide (40–160 mg) and glipizide (2.5–5 mg) in renal failure.

Gliptins (DPP4i: Dipeptidyl peptidase 4 inhibitors) like teneligliptin and sitagliptin. Side effects: GIT and pancreatitis risk. Minimal weight gain or hypoglycemia risk. No dose adjustment in renal failure.

Thiazolidinediones or glitazones: Pioglitazone. 2nd line. Risk of heart failure.

Drugs used in consultation with endocrinologists:

α glucosidase inhibitors: Acarbose.

Glucagon peptide-1 receptor agonist: Injectable, costly, 3rd line of therapy,

Sodium-glucose cotransporter 2 inhibitors: New drugs, high efficacy, and costly. Reduce cardiovascular events.

Figure 4: Diabetes management (part 2).

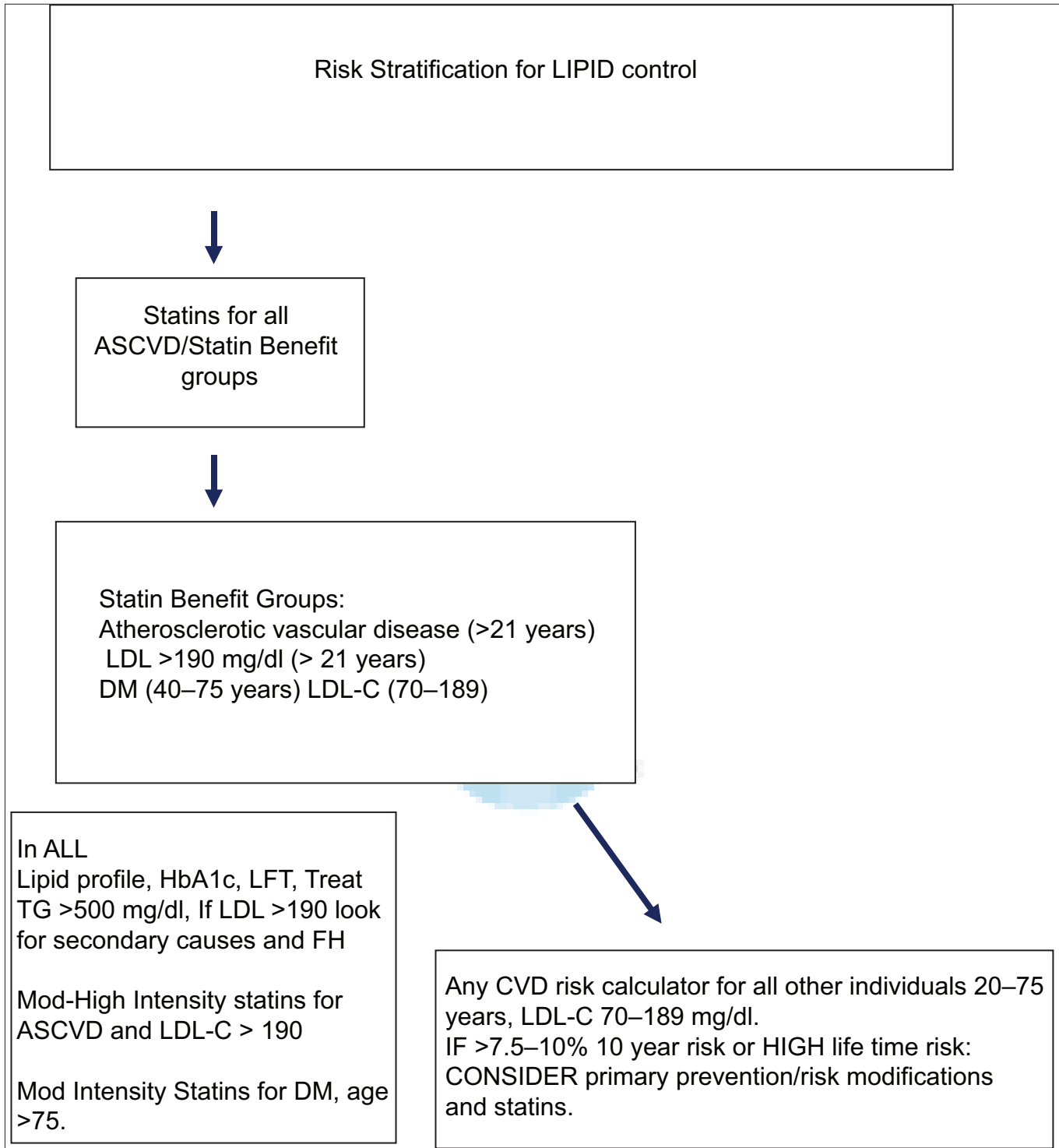


Figure 5: Dyslipidemia management (part one).

and ethnic correction). Any calculator can be used but the basic idea that Indians with increasing age and with addition of risk factors such as family history, smoking, and then diabetes; dyslipidemia should be considered for primary prevention at low thresholds with or without the use of these calculators.

The main purpose of the statins is that moderate-intensity therapy (lowering LDL-C by approximately 30–<50%) or high-intensity statin therapy (lowering LDL-C by approximately $\geq 50\%$) is a critical factor in reducing ASCVD events.

Targets

In the AHA and ESC 2016 statements, clarification has been given regarding the statin use and lipid levels to be achieved. If the levels are not achieved as per the guidelines, then alternate drugs like ezetimibe as the next drug and then PCSK9 have been suggested after checking for compliance. Bile acid sequestrants are also considered as the second line treatments.

ASCVD

All patients get statins (ensure high intensity statins)

They should have a 50% reduction in LDL-C level

LDL-C <100 mg/dl if no comorbidity such as DM, acute ASCVD, or kidney disease

<70 mg/dl if any of the above comorbidities. Moreover, see NHDLC <100 in DM

Diabetes

All patients get statins

They should have a 50% reduction in LDL-C level

LDL-C < 100 mg/dl and NHDLC <130 mg/dl

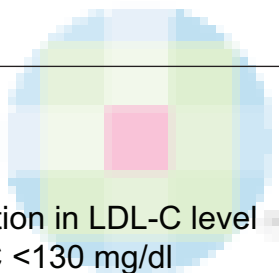


Figure 6: Dyslipidemia management (part two).

High intensity statins

Lower LDL-C by 50%: e.g., atorvastatin 40–80 mg, rosuvastatin 20–40 mg.

Moderate intensity statins

Lower LDL-C by 30%, e.g., atorvastatin 10–20 mg, rosuvastatin 10–20 mg.

Indian perspective

Indians are 5-fold more prone to myocardial infarction and cardiovascular death. They are prone to develop coronary artery disease before 40 years of age. Studies suggest that Indians achieve higher levels of circulating statins compared to the Caucasian population. Investigation of Rosuvastatin in South Asian Subjects Trial showed that LDL-C decreased by 45% with rosuvastatin 10 mg versus 40% with atorvastatin 10 mg and by 50% with rosuvastatin 20 mg versus 47% with atorvastatin 20 mg.

CONCLUSION

These algorithms have been developed with a view to disseminate the current guidelines to as wide an audience as possible and standardize cardiovascular risk management to simple principles. These should not be considered as very comprehensive statements but just initial guiding principles to start treatment in various areas of cardiovascular disease prevention.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: The evidence. *CMAJ* 2006;174:801-9.

2. Ridker PM, Libby P. Risk marker for atherothrombotic disease. In: Bonow RO, Mann DL, Zipes DP, Libby P, editors. Braunwald's Heart Disease: A Text-book of Cardiovascular Medicine. Missouri: Saunders; 2012. p. 914-34.
3. Kelley GA, Kelley KS, Tran ZV. Walking and non-HDL-C in adults: A meta-analysis of randomized controlled trials. *Prev Cardiol* 2005;8:102-7.
4. Kamani CH, Gencer B, Montecucco F, Courvoisier D, Vuilleumier N, Meyer P, *et al.* Stairs instead of elevators at the workplace decreases PCSK9 levels in a healthy population. *Eur J Clin Invest* 2015;45:1017-24.
5. Kelley GA, Kelley KS. Aerobic exercise and lipids and lipoproteins in children and adolescents: A meta-analysis of randomized controlled trials. *Atherosclerosis* 2007;191:447-53.
6. Global Recommendations on Physical Activity for Health 2010. World Health Organization. Available from: http://www.apps.who.int/iris/bitstream/10665/44399/1/9789241599979_eng.Pdf. [Last accessed on 2015 Dec 10].
7. Anjana RM, Pradeepa R, Das AK, Deepa M, Bhansali A, Joshi SR, *et al.* Physical activity and inactivity patterns in India – Results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]. *Int J Behav Nutr Phys Act* 2014;11:26.
8. Mohan V, Gokulakrishnan K, Deepa R, Shanthirani CS, Datta M. Association of physical inactivity with components of metabolic syndrome and coronary artery disease-the Chennai urban population study (CUPS No. 15). *Diabet Med* 2005;22:1206-11.
9. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of Type 2 diabetes: Indian scenario. *Indian J Med Res* 2007;125:217-30.
10. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. *J Clin Endocrinol Metab* 2008;93 11 Suppl 1:S9-30.
11. Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, *et al.* Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: A statement from the council on clinical cardiology (subcommittee on exercise, rehabilitation, and prevention) and the council on nutrition, physical activity, and metabolism (subcommittee on physical activity). *Circulation* 2003;107:3109-16.
12. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, *et al.* Physical activity and public health: Updated recommendation for adults from the American college of sports medicine and the American Heart Association. *Med Sci Sports Exerc* 2007;39:1423-34.
13. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, *et al.* 2016 European guidelines on cardiovascular disease prevention in clinical practice: The sixth joint task force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European association for cardiovascular prevention & rehabilitation (EACPR). *Eur Heart J* 2016;37:2315-81.
14. Available from: <https://www.nice.org.uk/guidance/cg127/chapter/appendix-c-the-algorithms>. [Last accessed on 2016 Aug 11].
15. Anjana RM, Ali MK, Pradeepa R, Deepa M, Datta M, Unnikrishnan R, *et al.* The need for obtaining accurate nationwide estimates of diabetes prevalence in India-Rationale for a national study on diabetes. *Indian J Med Res* 2011;133:369-80.
16. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian diabetes prevention programme shows that lifestyle modification and metformin prevent Type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006;49:289-97.
17. Grundy SM. Promise of low-density lipoprotein-lowering therapy for primary and secondary prevention. *Circulation* 2008;117:569-73.
18. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G, *et al.* Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2013;1:CD004816.
19. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, *et al.* Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland coronary prevention study group. *N Engl J Med* 1995;333:1301-7.
20. Packard CJ, Ford I, Murray H, McCowan C. Lifetime Clinical and Economic Benefits of Statin-based LDL Lowering in the 20-year Follow-up of the West of Scotland Coronary Prevention Study. American Heart Association 2014 Scientific Sessions; 18, November, 2014. [Abstract].
21. Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, *et al.* Efficacy and safety of LDL-lowering therapy among men and women: Meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet* 2015;385:1397-405.
22. Smith SC Jr., Collins A, Ferrari R, Holmes DR, Jr, Logstrup S, Cand Jur, *et al.* Our time: A call to save preventable death from cardiovascular disease (heart disease and stroke). *Glob Heart* 2012;7:297-305.
23. Ajay VS, Prabhakaran D. Coronary heart disease in Indians: Implications of the INTERHEART study. *Indian J Med Res* 2010;132:561-6.
24. Bays HE, Jones PH, Brown WV, Jacobson TA. National lipid association annual summary of clinical lipidology 2015. *J Clin Lipidol* 2014;8 6 Suppl: S1-36.
25. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD Jr., DePalma SM, *et al.* 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2016;68:92-125.
26. Iyengar SS, Puri R, Narasingan SN, Wangnoo SK, Mohan V, Mohan JC, *et al.* Lipid association of India expert consensus statement on management of dyslipidemia in Indians 2016: Part 1. Special issue on LAI expert consensus statement on management of dyslipidemia in Indians. *Journal of Association of Physicians of India* 2016;64:7-52.
27. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, *et al.* 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;63(25_PA):2889-2934.