Dear Reader,

We are honoured to present you the 6th issue of "The State of the Heart", which explores the clinical evidence supporting the new understandings and happenings in the field of cardiology.

In India, the epidemiological transition from predominantly infectious disease conditions to non-communicable diseases has occurred over a rather succinct period of time. Despite wide heterogeneity in the prevalence of cardiovascular risk factors across different regions, CVD has emerged as the leading cause of death in all parts of India, including poorer states and rural areas. In this research driven time, management of these disorders is also constantly evolving towards the betterment whether it's pharmacological or non-pharmacological.

Being a healthcare custodian of the society, clinicians are constantly thriving to be abreast with the novel understandings of disease and its management. In this context, this is our initiative to provide you a compiled and to the point information.

Present booklet comprises of recent and latest deeds in the field of cardiovascular diseases like dyslipidemia, coronary artery disease, heart failure and its management. We hope that it will facilitate increased cooperation and innovation, and enthuse commitment to prevent these life-threatening and disabling disorders and providing the best possible care for people who suffer from these conditions.

Editor in chief

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Risk Factors of Sudden Cardiac Death(SCA) in the Young

Multiple-Year Community-Wide Assessment

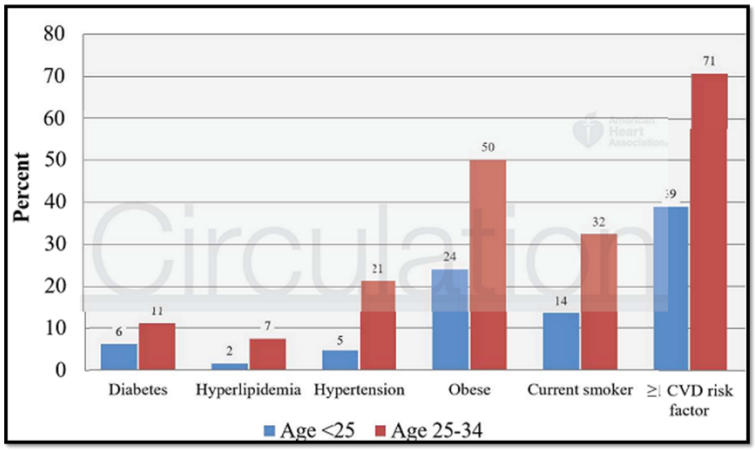

Fig. Prevalence of established cardiovascular risk factors in young subjects who suffered SCA

SCA between the ages of 5 and 34 years (2002–2015) catchment population ≈1 million

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SCA occurred without warning symptoms, Standard cardiovascular risk factors were found in over half of patients, suggesting the potential role of public health approaches that screen for cardiovascular risk factors at earlier ages.

Ref. Circulation. 2018;137:1561-1570

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Background: Prevention of sudden cardiac arrest (SCA) in the young remains a largely unsolved public health problem, and sports activity is an established trigger.

Methods: Prospectively ascertained subjects who experienced SCA between the ages of 5 and 34 years in the Portland, Oregon, metropolitan area (2002–2015, catchment population ≈1 million). They assessed the circumstances, resuscitation outcomes, and clinical profile of subjects who had SCA by a detailed evaluation of emergency response records, lifetime clinical records, and autopsy examinations.

Results: Of 3775 SCAs in all age groups, 186 (5%) occurred in the young (mean age 25.9±6.8, 67% male). In SCA in the young, overall prevalence of warning signs before SCA was low (29%), and 26 (14%) were associated with sports as a trigger. The remainder (n=160) occurred in other settings categorized as nonsports. Sports-related SCAs accounted for 39% of SCAs in patients aged ≤18, 13% of SCAs in patients aged 19 to 25, and 7% of SCAs in patients aged 25 to 34. Sports-related SCA cases were more likely to present with shockable rhythms, and survival from cardiac arrest was 2.5-fold higher in sports-related versus nonsports SCA (28% versus 11%; P=0.05). Overall, the most common SCA-related conditions were sudden arrhythmic death syndrome (31%), coronary artery disease (22%), and hypertrophic cardiomyopathy (14%). There was an unexpectedly high overall prevalence of established cardiovascular risk factors (obesity, diabetes mellitus, hypertension, hyperlipidemia, smoking) with ≥1 risk factors in 58% of SCA cases.

Conclusions: Sports was a trigger of SCA in a minority of cases, and, in most patients, SCA occurred without warning symptoms. Standard cardiovascular risk factors were found in over half of patients, suggesting the potential role of public health approaches that screen for cardiovascular risk factors at earlier ages.

2. Developing a Clinical Approach to Air Pollution and Cardiovascular Health

Developing a Clinical Approach to Air Pollution and Cardiovascular Health

Clinical Screening Tool for Air Pollution Risk
An affirmative answer to any question is associated with increased cardiovascular risk.

Household Air Pollution

Does your household burn solid fuels (wood, coal, charcoal, dung, or agricultural residues) for cooking, heating, lighting or other purposes? Yes No

If "yes": *What type of fuel do you use?*
What type of stove do you use?
How often do you burn solid fuel?
How much time do you spend around the fire?
Do you burn solid fuels inside the home?
How do you ventilate smoke from your house?

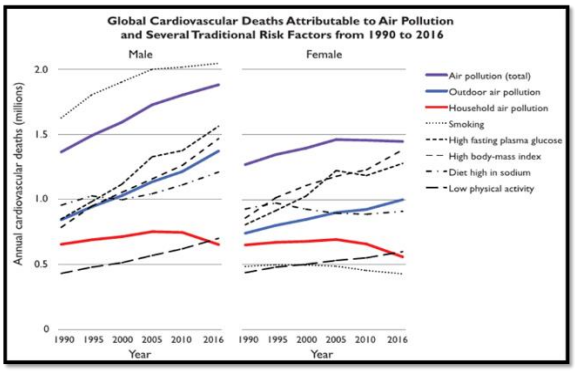
Outdoor Air Pollution

Do you live or work in an urban industrial center? Yes No

If "yes": *Are you aware of any sources of pollution near your home?*
Do you perform physical exertion outdoors?

Do you spend time near heavy tratraffic (e.g., multi-lane, high-speed roads) Yes No

If "yes": *Do you commute in traffic?*
Are you exposed to the open air when driving?
Is your home located near major roads?



Ref. Circulation. 2018;137:725-742

INTAS MEDICAL SERVICES

Key elements in a clinical approach to mitigating risks of air pollution and protecting CV health

Household air pollution

Adoption of low-emission stove-fuel combinations
- Prefer electric or clean-burning gas stoves
- Consider high-efficiency, low-emission biomass stoves

Improved household ventilation and air filtration
- Chimneys, hoods, windows, doors, eaves, fans, etc.
- Cook outdoors and/or away from living areas
- High efficiency particulate arrestance air filters and central air conditioners
- Home insulation, window seals, and pot lids to reduce fuel requirement for cooking or heating

Outdoor air pollution

Behavior changes to reduce exposures
- Build and connect to community pollution alert systems
- Avoid high-exposure locations and times
- Minimize traffic exposure, rush hour and major roadways
- Avoid prolonged/heavy exertion outdoors on polluted days
- Keep car and home windows closed

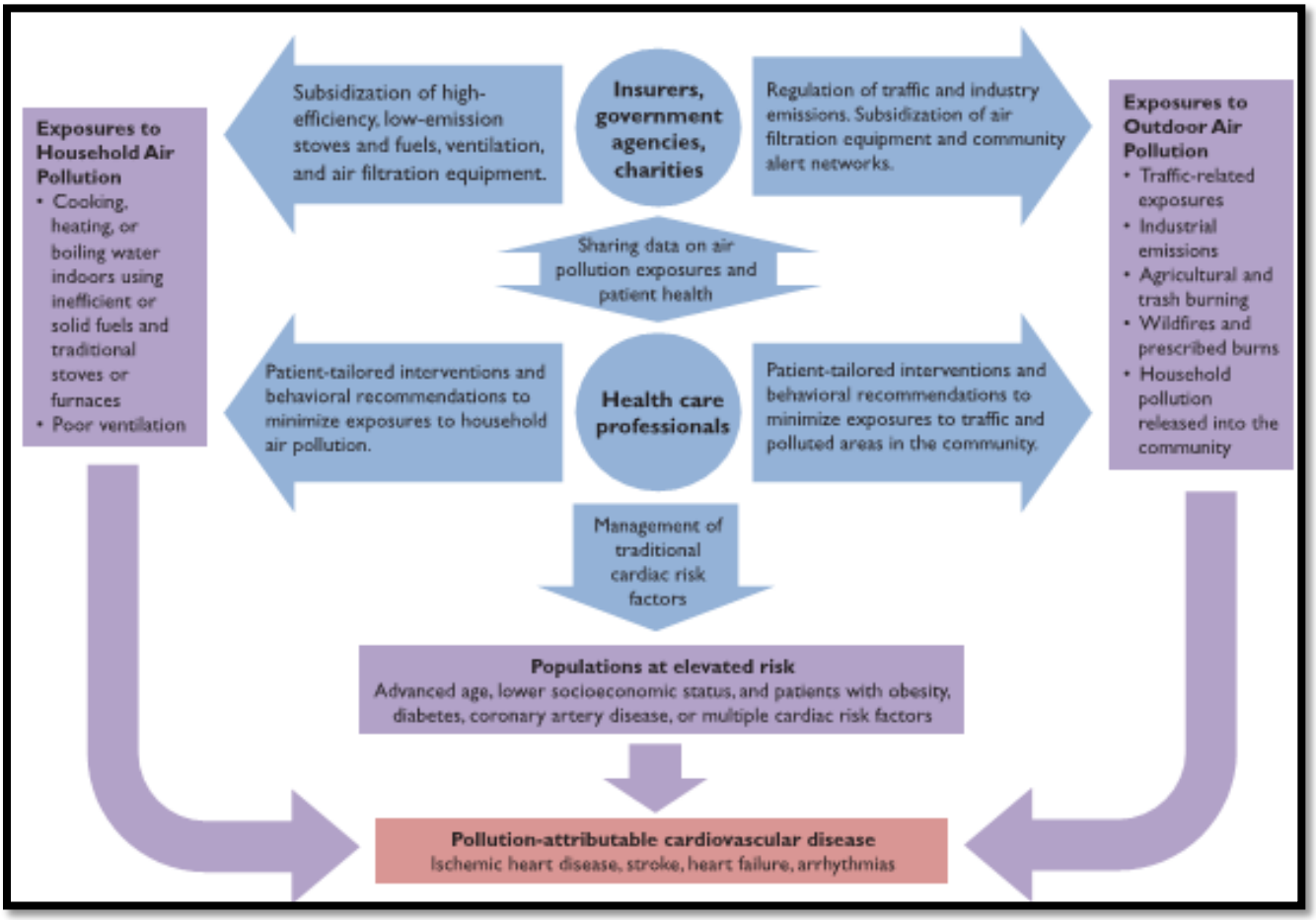
Equipment to reduce exposures
- Personal air filters (eg. N95 respirator, face mask, nasal plugs)
- Central air conditioners and high efficiency particulate arrestance air filters

Nearly 3 billion people are exposed to household air pollution emitted from inefficient cooking and heating stoves, and almost the entire global population is exposed to detectable levels of outdoor air pollution from traffic, industry, and other sources. Over 3 million people die annually of ischemic heart disease or stroke attributed to air pollution, more than from traditional cardiac risk factors such as obesity, diabetes mellitus, or smoking. Clinicians have a role to play in reducing the burden of pollution-attributable cardiovascular disease. However, there currently exists no clear clinical approach to this problem.

Here, they provide a blueprint for an evidence-based clinical approach to assessing and mitigating cardiovascular risk from exposure to air pollution. They begin with a discussion of the global burden of

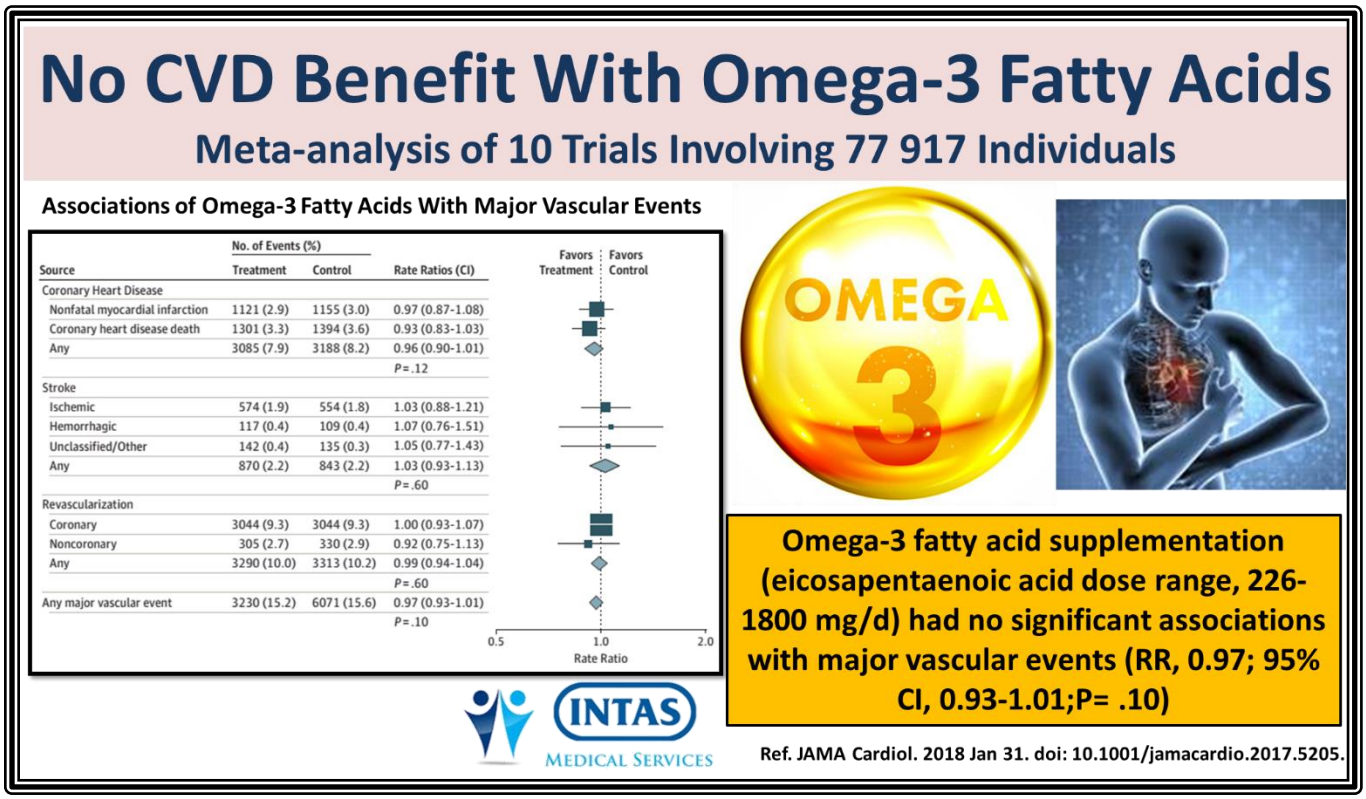
pollution-attributable cardiovascular disease, including a review of the mechanisms by which particulate matter air pollution leads to cardiovascular outcomes.

Next, They offer a simple patient-screening tool using known risk factors for pollution exposure. They then discuss approaches to quantifying air pollution exposures and cardiovascular risk, including the development of risk maps for clinical catchment areas. They review a collection of interventions for household and outdoor air pollution, which clinicians can tailor to patients and populations at risk. Finally, they identify future research needed to quantify pollution exposures and validate clinical interventions. Overall, they demonstrate that clinicians can be empowered to mitigate the global burden of cardiovascular disease attributable to air pollution.



Conclusion: Air pollution is a well-established risk factor for CVDs, responsible for a global burden of IHD and stroke that is greater than several traditional cardiac risk factors. Reductions in both HAP and OAP exposures would significantly increase life expectancy in the United States and abroad. Clinicians can play a significant role in mitigating pollution-attributable cardiovascular risk among the patients they serve. They have outlined a clinical approach for improving cardiovascular health. Clinicians, in partnership with government agencies, can use this approach to reduce pollution exposures in their service populations. They encourage clinicians and other health professionals to tailor this model to their specific populations and to collect prospective data to validate the efficacy of screening tools and interventions.

3. No CVD Benefit With Omega-3 Fatty Acids
Meta-analysis of 10 Trials Involving 77 917 Individuals



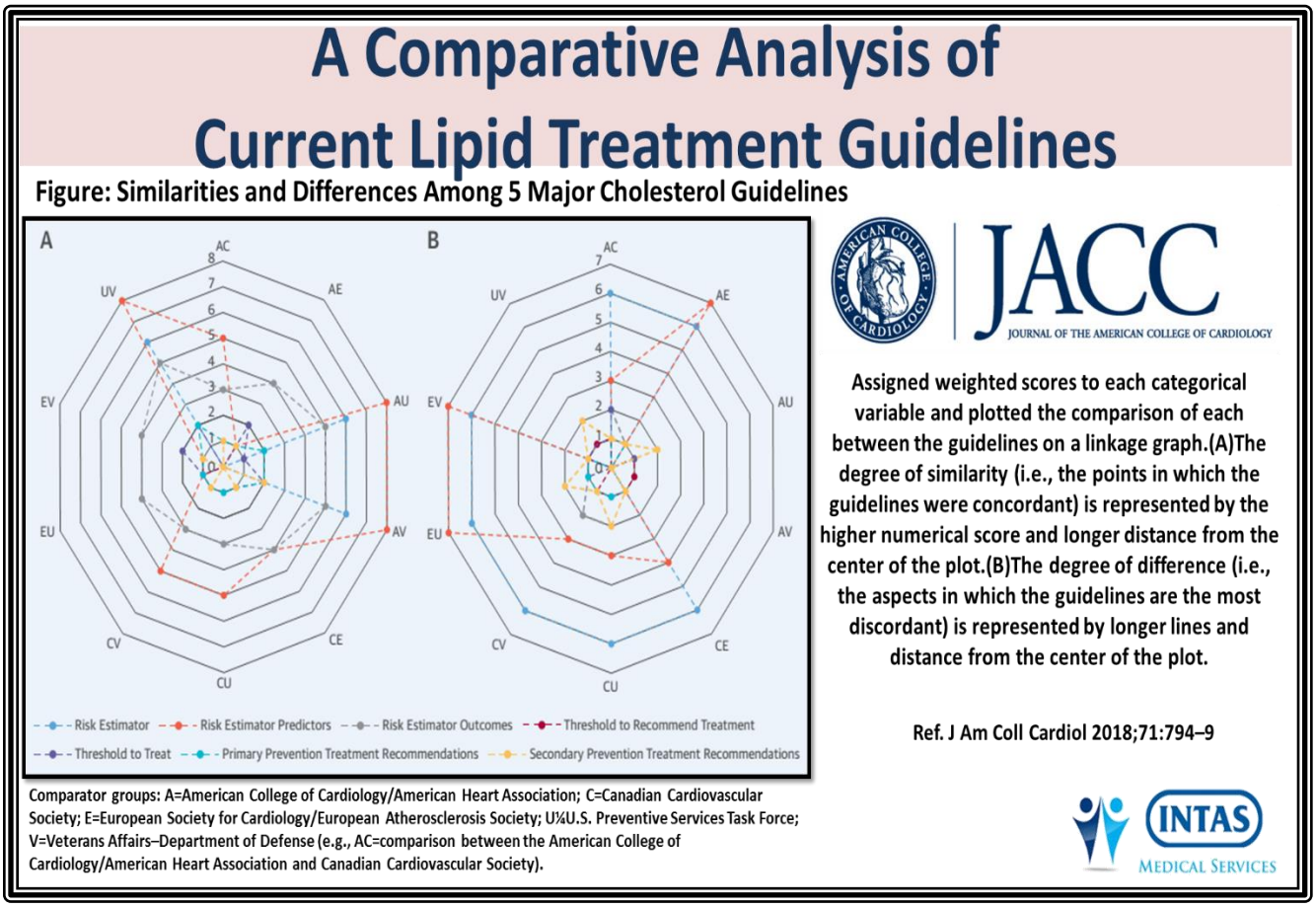
Objective: To conduct a meta-analysis of all large trials assessing the associations of omega-3 fatty acid supplements with the risk of fatal and nonfatal coronary heart disease and major vascular events in the full study population and prespecified subgroups.

Main Outcomes and Measures: The main outcomes included fatal coronary heart disease, nonfatal myocardial infarction, stroke, major vascular events, and all-cause mortality, as well as major vascular events in study population subgroups.

Results: Of the 77 917 high-risk individuals participating in the 10 trials, 47 803 (61.4%) were men, and the mean age at entry was 64.0 years; the trials lasted a mean of 4.4 years. The associations of treatment with outcomes were assessed on 6273 coronary heart disease events (2695 coronary heart disease deaths and 2276 nonfatal myocardial infarctions) and 12 001 major vascular events. Randomization to omega-3 fatty acid supplementation (eicosapentaenoic acid dose range, 226-1800 mg/d) had no significant associations with coronary heart disease death (rate ratio [RR], 0.93; 99% CI, 0.83-1.03; P = .05), nonfatal myocardial infarction (RR, 0.97; 99% CI, 0.87-1.08; P = .43) or any coronary heart disease events (RR, 0.96; 95% CI, 0.90-1.01; P = .12).

Conclusions and Relevance: This meta-analysis demonstrated that omega-3 fatty acids had no significant association with fatal or nonfatal coronary heart disease or any major vascular events. It provides no support for current recommendations for the use of such supplements in people with a history of coronary heart disease

4. A Comparative Analysis of Current Lipid Treatment Guidelines

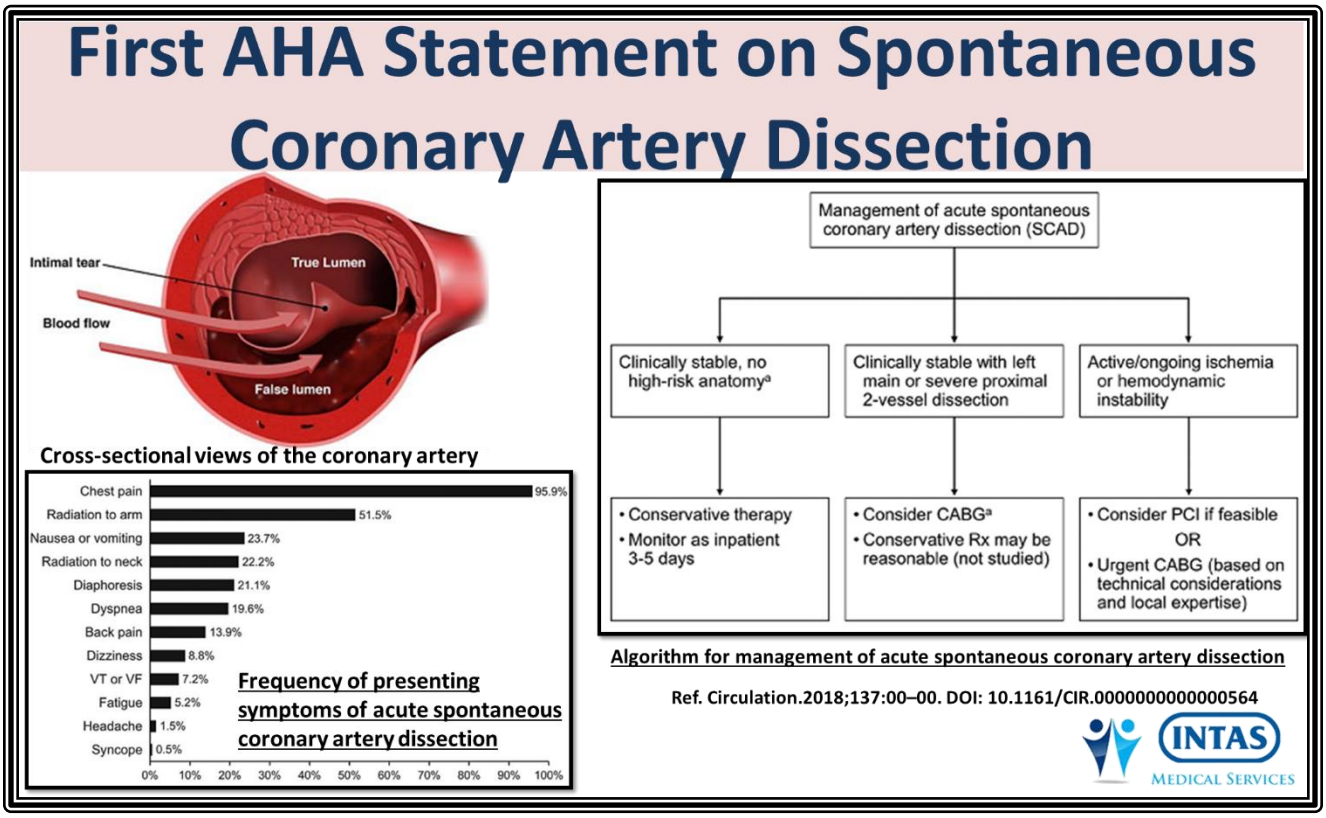


Lipid treatment guidelines have continued to evolve as new evidence emerges. They sought to review similarities and differences of 5 lipid treatment guidelines from the American College of Cardiology/American Heart Association, Canadian Cardiovascular Society, European Society for Cardiology/European Atherosclerosis Society, U.S. Preventive Services Task Force, and U.S. Veterans Affairs/Department of Defense.

All guidelines utilize rigorous evidentiary review, highlight statin therapy for primary and secondary prevention of atherosclerotic cardiovascular disease, and emphasize a clinician-patient risk discussion. However, there are differences in statin intensities, use of risk estimators, treatment of specific patient subgroups, and consideration of safety concerns.

Clinicians should understand these similarities and differences in current and future guideline recommendations when considering if and how to treat their patients with statin therapy.

5. First AHA Statement on Spontaneous Coronary Artery Dissection



Spontaneous coronary artery dissection (SCAD) has emerged as an important cause of acute coronary syndrome, myocardial infarction, and sudden death, particularly among young women and individuals with few conventional atherosclerotic risk factors.

Patient-initiated research has spurred increased awareness of SCAD, and improved diagnostic capabilities and findings from large case series have led to changes in approaches to initial and long-term management and increasing evidence that SCAD not only is more common than previously believed but also must be evaluated and treated differently from atherosclerotic myocardial infarction.

High rates of recurrent SCAD; its association with female sex, pregnancy, and physical and emotional stress triggers; and concurrent systemic arteriopathies, particularly fibromuscular dysplasia, highlight the differences in clinical characteristics of SCAD compared with atherosclerotic disease.

Recent insights into the causes of, clinical course of, treatment options for, outcomes of, and associated conditions of SCAD and the many persistent knowledge gaps are presented.

6. The Effect of Intensive Statin Therapy on Symptomatic Intracranial Arterial Stenosis

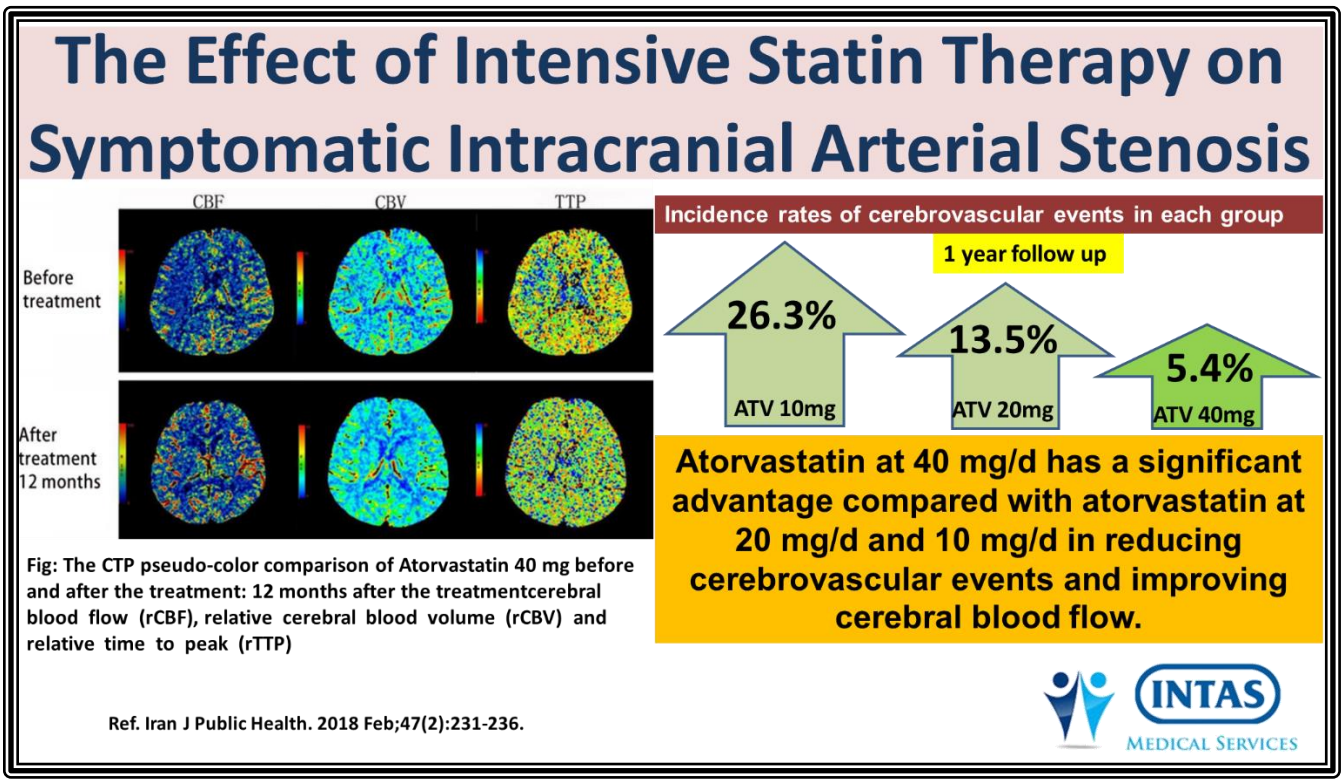


Fig: The CTP pseudo-color comparison of Atorvastatin 40 mg before and after the treatment: 12 months after the treatmentcerebral blood flow (rCBF), relative cerebral blood volume (rCBV) and relative time to peak (rTTP)

Background: The aim of this study was to observe the effect of intensive statin therapy on symptomatic intra-cranial arterial stenosis.

Methods: overall, 120 patients with symptomatic intracranial arterial stenosis were admitted to the Xiangyang No.1 People's Hospital, Hubei University of Medicine, Xiangyang, China from January 2010 to May 2013. They were randomly divided into three groups and were given different doses of atorvastatin orally for 1 year or more, and followed up for 12 months. The three groups were assessed for clinical end-point event rates and changes in cerebral blood flow value before and after treatment to assess the effectiveness of intensive statin therapy.

Results: The incidence rates of end-point cerebrovascular events in the low-dose group (10 mg/d), the general-dose group (20 mg/d) and the intensive treatment group (40 mg/d) were 26.3%, 13.5% and 5.4% respectively during the 12-month follow-up after treatment. There was a significant difference between the low dose group and the intensive treatment group (P<0.05). The relative cerebral blood flow and relative cerebral blood volume of the three groups were significantly higher than those before treatment (P<0.05), and the relative time to peak for the intensive treatment group was shorter than that before treatment (P<0.001).

Conclusion: Atorvastatin at 40 mg/d has a significant advantage compared with atorvastatin at 20 mg/d and 10 mg/d in reducing cerebrovascular events and improving cerebral blood flow.

7. Rosuvastatin does not adversely affect erectile function : HOPE-3

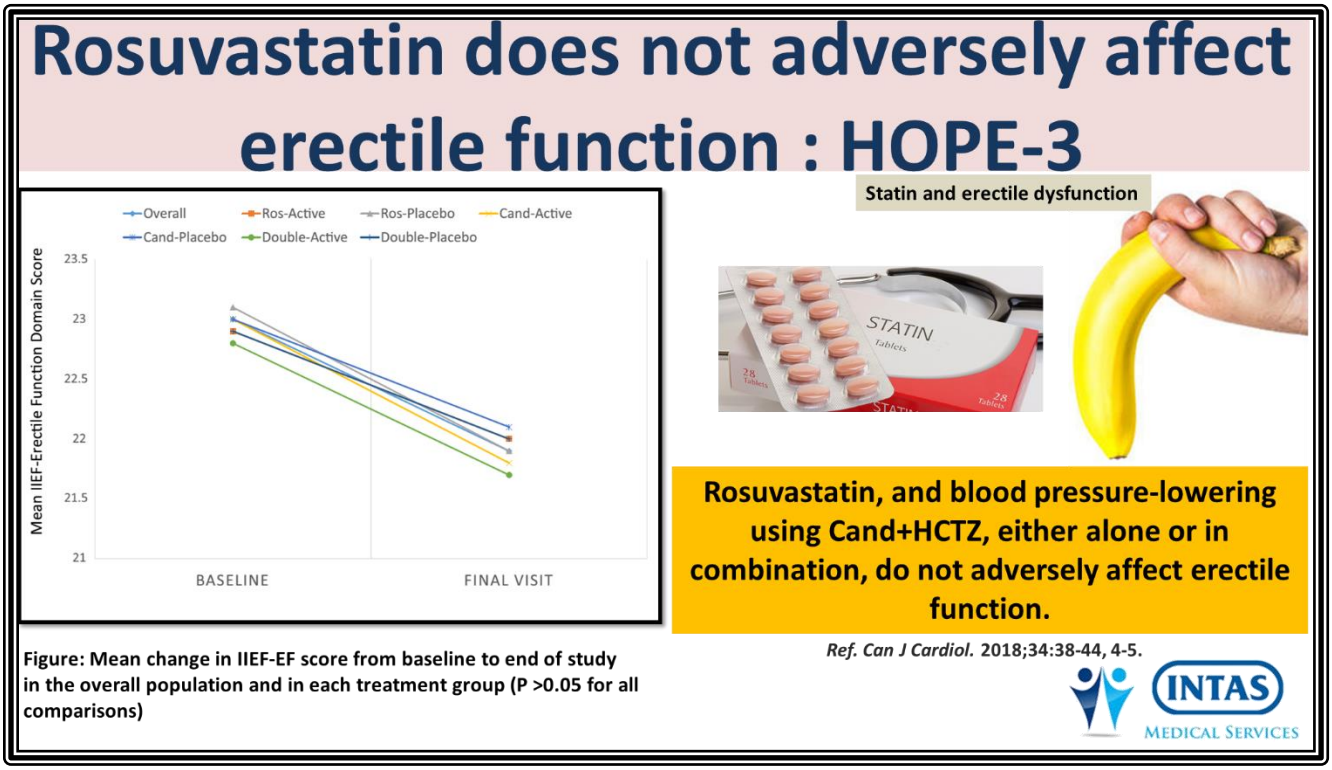


Figure: Mean change in IIEF-EF score from baseline to end of study in the overall population and in each treatment group (P >0.05 for all comparisons)

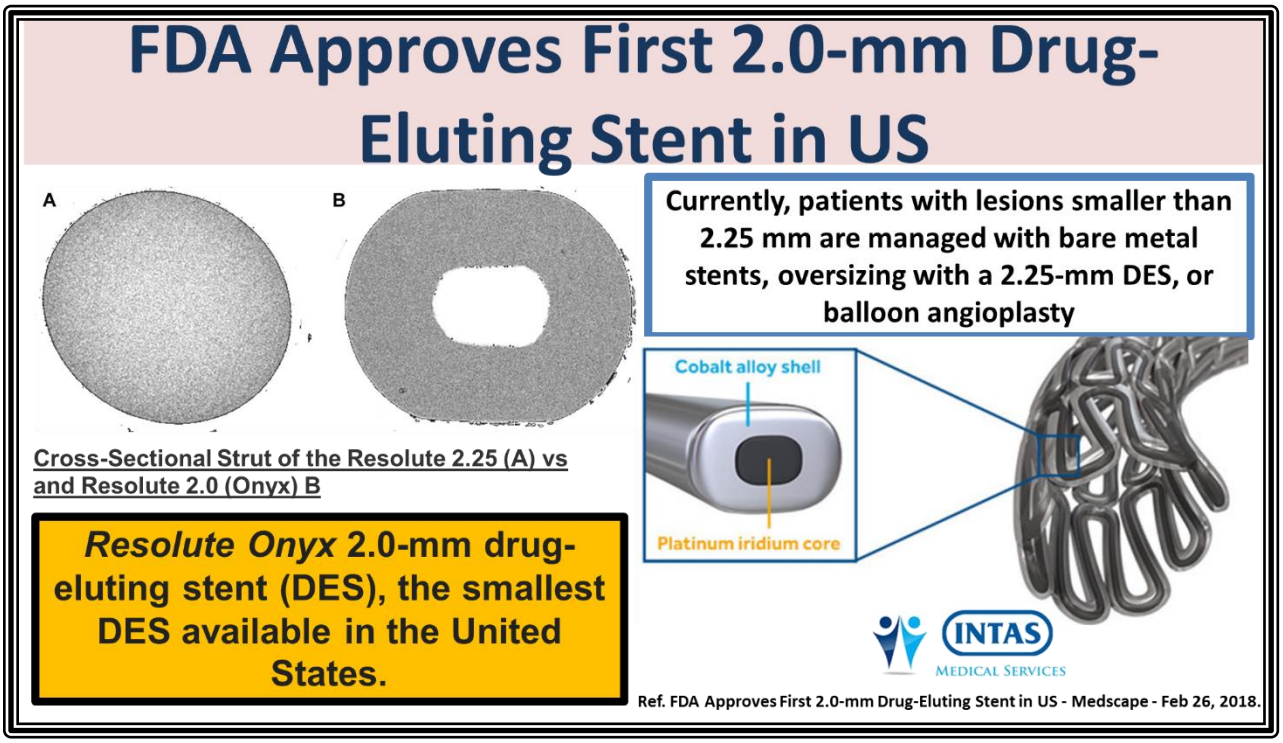
Objective: It is unclear whether modifying cholesterol, blood pressure, or both affect erectile dysfunction. Also, there are concerns that erectile dysfunction is worsened by common medications used to treat these risk factors. In this study, They evaluated the effect of: (1) cholesterol-lowering with a statin; (2) pharmacologic blood pressure reduction; and (3) their combination, on erectile function.

Methods: A priori, this was a secondary analysis of the Heart Outcomes Prevention Evaluation-3 (HOPE-3) randomized controlled trial. Men were 55 years of age or older with at least 1 cardiovascular risk factor. Erectile function was measured using the erectile function domain of the International Index of Erectile Function (IIEF-EF) score. Men with incomplete scores, or who did not engage in sexual activity, were excluded. Using a 2 × 2 factorial design, participants were randomized to rosuvastatin (10 mg/d) or placebo, and to candesartan with hydrochlorothiazide (HCTZ; 16 mg/12.5 mg/d; Cand+HCTZ) or placebo. Primary outcome was change in IIEF-EF from baseline to end of study follow-up.

Results: Two thousand one hundred fifty-three men were included; mean age was 61.5 years, and mean follow-up was 5.8 years. Mean IIEF-EF score at baseline was 23.0 (SD 5.6). Least square mean change in the IIEF-EF score did not differ with rosuvastatin compared with placebo (−1.4; standard error [SE], 0.3 vs −1.5; SE, 0.3; P = 0.74), Cand+HCTZ compared with placebo (−1.6; SE, 0.3 vs −1.3; SE, 0.3; P = 0.10), or combination therapy compared with double placebo (P = 0.35).

Conclusions: Cholesterol-lowering using a statin, and blood pressure-lowering using Cand+HCTZ, either alone or in combination, do not improve or adversely affect erectile function.

8. FDA Approves First 2.0-mm Drug-Eluting Stent in US



The U.S. Food and Drug Administration (FDA) has approved the Resolute Onyx 2.0-mm drug-eluting stent (DES), the smallest DES available in the United States.

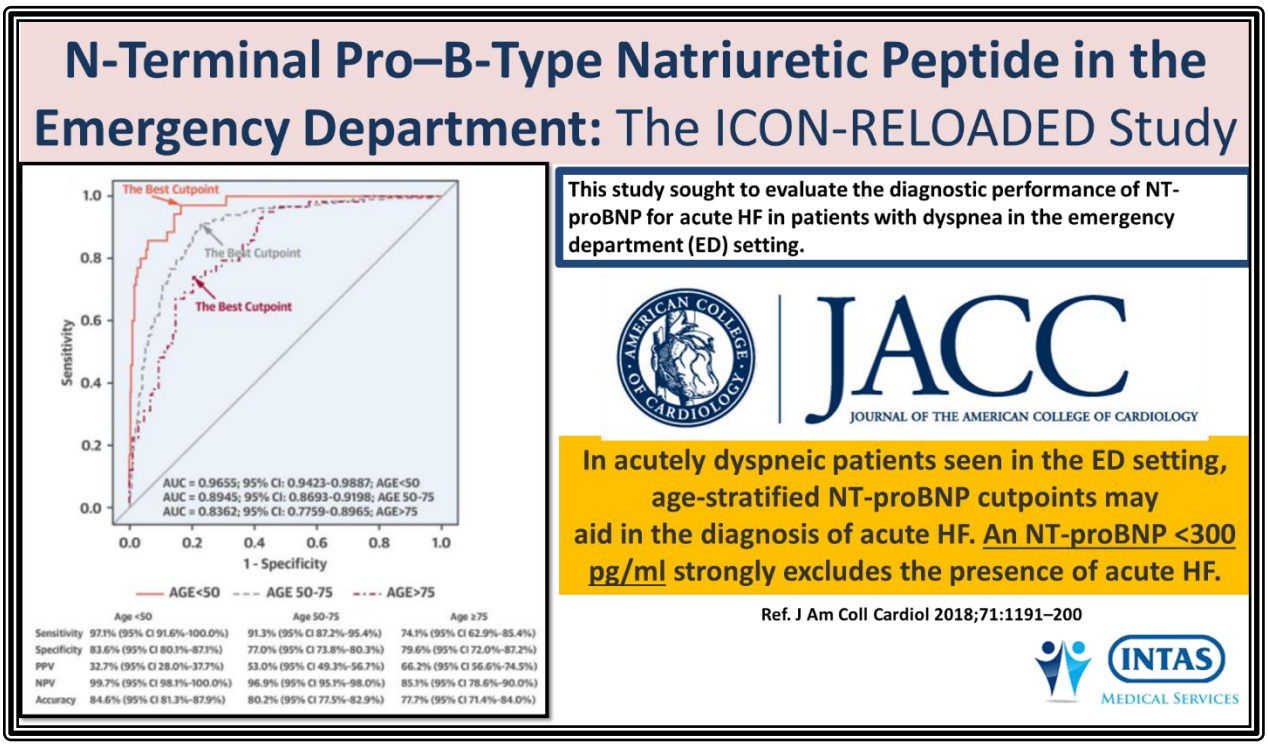
The approval addresses an unmet clinical need by expanding treatment options for patients with coronary artery disease in very small vessels, Medtronic noted in its announcement today.

Until now, the smallest-sized DES marketed in the United States was 2.25 mm.

Currently, patients with lesions smaller than 2.25 mm are managed with bare metal stents, oversizing with a 2.25-mm DES, or balloon angioplasty. Smaller preprocedural reference vessel diameter (RVD) is associated with increased target lesion revascularization and worse survival from major adverse cardiovascular events, even in the DES era.

"The Resolute Onyx 2.0 mm DES is an extremely deliverable stent that, when needed, can be post-dilated to 3.25 mm to treat lesions in difficult-to-reach areas of the heart," Matthew J Price, MD, from Scripps Clinic, La Jolla, California, who co-lead the RESOLUTE 2.0 mm Clinical Study supporting the FDA approval, said in the announcement.

9. N-Terminal Pro–B-Type Natriuretic Peptide in the Emergency Department: The ICON-RELOADED Study



Background Contemporary reconsideration of diagnostic N-terminal pro–B-type natriuretic peptide (NT-proBNP) cutoffs for diagnosis of heart failure (HF) is needed.

Objectives This study sought to evaluate the diagnostic performance of NT-proBNP for acute HF in patients with dyspnea in the emergency department (ED) setting.

Methods Dyspneic patients presenting to 19 EDs in North America were enrolled and had blood drawn for subsequent NT-proBNP measurement. Primary endpoints were positive predictive values of age-stratified cutoffs (450, 900, and 1,800 pg/ml) for diagnosis of acute HF and negative predictive value of the rule-out cutoff to exclude acute HF. Secondary endpoints included sensitivity, specificity, and positive (+) and negative (−) likelihood ratios (LRs) for acute HF.

Results Of 1,461 subjects, 277 (19%) were adjudicated as having acute HF. The area under the receiver-operating characteristic curve for diagnosis of acute HF was 0.91 (95% confidence interval [CI]: 0.90 to 0.93; $p < 0.001$). Sensitivity for age stratified cutoffs of 450, 900, and 1,800 pg/ml was 85.7%, 79.3%, and 75.9%, respectively; specificity was 93.9%, 84.0%, and 75.0%, respectively. Positive predictive values were 53.6%, 58.4%, and 62.0%, respectively. Overall LR+ across age-dependent cutoffs was 5.99 (95% CI: 5.05 to 6.93); individual LR+ for age-dependent cutoffs was 14.08, 4.95, and 3.03, respectively. The sensitivity and negative predictive value for the rule-out cutoff of 300 pg/ml were 93.9% and 98.0%, respectively; LR− was 0.09 (95% CI: 0.05 to 0.13).

Conclusions In acutely dyspneic patients seen in the ED setting, age-stratified NT-proBNP cut points may aid in the diagnosis of acute HF. An NT-proBNP <300 pg/ml strongly excludes the presence of acute HF.

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