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2014 Evidence Based Guideline for Management of High Blood Pressure in Adults: An Overview

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Since its publication in 2004, the primary resource for the management of hypertension has been the Seventh Report of the Joint National Committee (JNC 7) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[1] This comprehensive document includes not only hypertension treatment guidelines, but also recommendations on diagnosis and classification of hypertension, management of "special situations" in hypertension, blood pressure devices, public health challenges, and description of common substances that may affect blood pressure. The basis of the recommendations made for JNC 7 came from pooled data gathered from meta-analyses, randomized controlled trials, prospective studies, cross-sectional surveys, previous review/position statements and expert opinion.

Although JNC 7 has provided much needed guidance for the clinical management of hypertension, new data has become available leaving some of its content outdated and requiring an update, JNC 8. The U.S. National Heart, Lung, and Blood Institute (NHLBI) appointed JNC 8 panel members in 2008 and work began on developing updates to the previous version. In June 2013, the Institute announced that it would no longer participate in the development of any clinical guidelines, including the blood pressure guidelines leaving many clinicians disillusioned. The authors from the original JNC 8 panel chose to publish the recommendations independently in the form of the "2014 Guideline for Management of High Blood Pressure" published in the Journal of the American Medical Association on December 18, 2013.[2]

Unlike its predecessor, the 2014 guideline commonly referred to as JNC 8 is a hypertension management focused document. The recommendations and statements contained in this "evidence-based" guideline are as a result of data and expert opinions gathered from randomized controlled trials. Observational studies, systematic reviews, and meta-analyses were omitted.

This new guideline contains a total of 9 "evidence-based" recommendations for the management of hypertension. These recommendations address 3 key concepts that the panelists identified as specifically leading to improved health outcomes. They include: initiation of antihypertensive pharmacologic therapy at specific blood pressure thresholds, treatment with antihypertensive pharmacologic therapy to a specified blood pressure goal and comparative benefits versus harms on specific health outcomes as a

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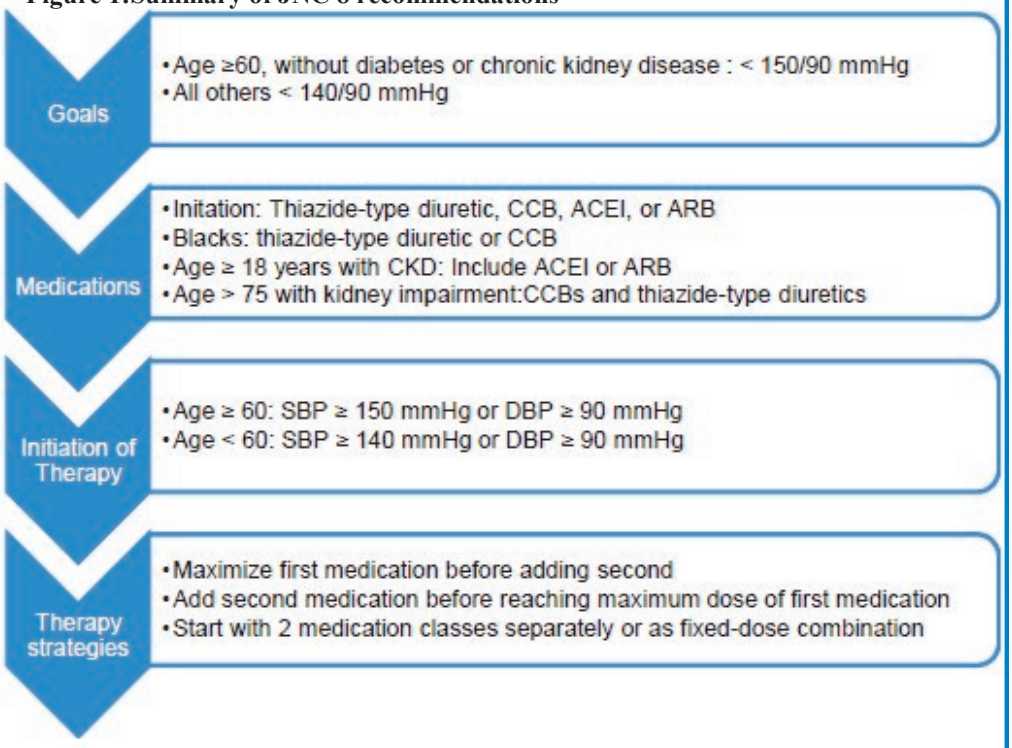
result of various antihypertensive drugs or drug classes.

The first and most notable difference from previous guidelines is the recommendation of targeting a systolic blood pressure (SBP) goal of <150 mmHg in patients aged 60 years or older. The data that supports this recommendation demonstrates a reduction in stroke, heart failure, and coronary heart disease when targeting this goal. Moreover, the panel states that no additional benefit is seen in patients over the age of 60 who target goal SBP of <140 mmHg compared to those who target SBP <160mmHg or <150mmHg.

With respect to diastolic blood pressure (DBP), JNC 8 recommends the initiation of pharmacotherapy in the general population <60 years when DBP is ≥ 90 mmHg and treatment to goal DBP <90 mmHg. This recommendation is supported by findings of decrease in cerebrovascular events, heart failure, and overall mortality in adults aged 30-69 with hypertension. Additionally, the HOT trial reported no statistically significant difference in additional benefits by treating patients to a goal of either < 80mmHg or < 85mmHg compared to <90mmHg.[3]

Figure 1:Summary of JNC 8 recommendations



CCB: Calcium channel blocker, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, SBP: Systolic blood pressure, and DBP: Diastolic blood pressure

Another key difference in the new guidelines is with respect to comorbidities such as diabetes and chronic kidney disease (CKD). In JNC 7, the recommended blood pressure goal for patients with CKD is <130/80 mmHg. However, JNC 8 recommends that patients age >18 years with CKD target a goal blood pressure of <140/90 mmHg. Ultimately, the panelists found that there was no evidence demonstrating a benefit in mortality, cardiovascular, or cerebrovascular health outcomes in adults <70 years with CKD that targeted lower blood pressure goal (<130/80 mmHg). Evidence that the progression of kidney disease was not slowed when targeting a lower blood pressure goal of <130/80 mmHg compared with a goal of <140/90 mmHg solidified the overall expert opinion and recommendation to target blood pressure of <140/90 mmHg.

Similarly, in diabetic patients JNC 8 recommends to target a goal blood pressure of <140/90 mmHg. This new target is a deviation from JNC 7 and the American Diabetes Association (ADA) recommendations, 130/80 mmHg and 140/80 mmHg respectively. In this case, the recommendation made by the panelists was based on expert opinion. No randomized controlled trials were found to meet the inclusion criteria and demonstrate improved health outcomes in diabetics by targeting SBP goal of <140 mmHg compared to <150 mmHg. As for the DBP goal, insufficient evidence was found to support the previous recommendation of <80 mmHg. The consensus from the panelists was that using a consistent blood pressure goal among the general population and diabetics would facilitate implementation of the guidelines.

When initiating pharmacotherapy, one major change to be aware of is the elimination of β-blockers as first line agents. The new guidelines recommend initiating antihypertensive treatment with one of the following: thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker

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(ARB). The panel does not recommend the use of β-blockers in hypertension due to reported higher rate of cardiovascular events, more specifically stroke, in participants involved in a study comparing β-blockers and ARBs.[4]

While the blood pressure targets have been "loosened" when compared to previous recommendations, management of patients already controlled by the standards of JNC 7 should not be altered. Instead, these recommendations should be applied to uncontrolled and newly diagnosed patients. Limitations, such as exclusion of "landmark" trials (UKPDS and ADVANCE), systemic reviews, meta-analyses and the limited scope of the document may deter some from implementing these new recommendations in practice. However, this guideline attempts to base its recommendations and expert opinions from strict evidence supplied by randomized controlled trials. Additionally, it addresses the assumption that by targeting lower blood pressure levels, patients may improve outcomes irrespective of the type of agent used. Unlike its predecessor, JNC 8 is able to provide "evidence- based" dosing regimens for studied antihypertensive medications. Overall, the recommendations made in JNC 8 are just that, it is up to clinicians to interpret and apply them in practice. A summary of recommendations from JNC 8 are listed in Figure 1.

<Click here for references>

Summarizing the Revisions made in the 2014 ADA Standards of Care

By Alexander D. Covey, PharmD Candidate; Marcus Campbell, PharmD, BC-ADM

Diabetes is a complex chronic disease that requires constant management from both patients and practitioners . Since its founding in 1940, the American Diabetes Association (ADA) has been a leader in promoting research and compiling clinical data for the treatment of diabetes. In order to keep up with the fast pace of medical science, the ADA publishes an annual revision of its Standards of Care. With the exception of major drug advances or groundbreaking clinical data, the guidelines do not typically change dramatically from year to year. However, the subtle changes made over time accumulate to form a finely tuned disease management algorithm. It is therefore critically important that healthcare providers keep up to date on this information to best serve their patients. Below is a summary of the changes made for the 2014 ADA Standards of Care.[1]

Screening and Diagnosis

The 2014 guidelines include data from a study published in JAMA in 2013 that looked at the rate of progression to type 1 diabetes in children who had seroconversion of islet autoantibodies.[2] The study found that children who had seroconversion with multiple autoantibodies had risks of 70% and 84% of developing type 1 diabetes within 10 and 15 years, respectively. This is notable because the data was pooled from cohorts of children from 3 different countries who had a first degree relative with type 1 diabetes, lending evidence to support screening in patients who have a first degree relative with type 1 diabetes. There are currently no accepted screening programs for this type of patient, but the ADA recommends having them screened in a clinical trial setting.[1]

Detection and Diagnosis of Gestational Diabetes: There has been some debate about the diagnostic criteria for gestational diabetes mellitus (GDM). As a result of the HAPO study, the 2011 ADA Standards of Care began recommending a "One-step" diagnostic approach wherein all pregnant patients without prior diabetes diagnoses should undergo a 2 hour 75gm oral glucose tolerance test (OGTT) at 24-28 weeks of gestation.[3] The threshold for diagnosis of GDM with this method was based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) and anticipated an increase in the prevalence of GDM from 5-6% to 15-20%. The burdens of this increased prevalence of GDM were thought to be justified by improved

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Summary of ADA 2014 Standards of Care Revisions (continued)

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pregnancy outcomes for both mothers and offspring, although there was an admitted lack of clinical data to substantiate this claim.

In 2013, the National Institutes of Health (NIH) completed a consensus development conference to address the IADPSG recommendations. After reviewing the available data, the NIH recommended continuation of the "two-step" diagnostic approach that had previously been the standard. The decision was based on the lack of clinical data to support the one-step method, as well as the concern for the negative effects of identifying a large new group of patients with GDM under the IADPSG recommendations. The ADA 2014 Standards of Care still include the one-step approach as an option, but there is clear language that more evidence is needed to determine the superiority of one method over the other.[1]

Drug Therapy

Pharmacologic Therapy for Hyperglycemia in Type 2 Diabetes: Monotherapy with metformin is the recommended first step in managing a type 2 diabetic if they are eligible for non-insulin therapy and do not have any contraindications. It was previously recommended that monotherapy be administered for 3-6 months to achieve goal A1C levels, and failure would indicate adding a second agent. The 2014 standards of care have cut the time frame for monotherapy to 3 months if A1C goals are not achieved.[1]

Antiplatelet Agents: Patients who had experienced an ACS were previously recommended to use clopidogrel as an adjunct or alternative to aspirin for a year after their event to reduce the risk of future CVD events. The 2014 guidelines have changed the language to reflect more recent evidence that suggests dual therapy with a P2Y12 inhibitor in addition to aspirin can reduce future CVD events. Specifically, clopidogrel or ticagrelor should be used if no percutaneous coronary intervention (PCI) was performed, and clopidogrel, ticagrelor, or prasugrel could be used if PCI was performed.

Neuropathy: In previous guidelines, the treatment options were fairly vague and mostly pointed the reader to other sources of information. The 2014 guidelines revised this section to include a much more detailed discussion of the treatment options for specific types of neuropathy including: distal symmetric polyneuropathy, autonomic neuropathy, orthostatic hypotension, gastroparesis, and erectile dysfunction. The new subsections include discussions of the challenges, goals, and specific drugs or strategies used to treat the respective neuropathy.

Diabetes Care in the Hospital: The sole use of sliding scale insulin regimens has previously been frowned upon by the ADA with clinical evidence that demonstrates increased risks of hyper and hypoglycemia, as well as adverse outcomes for general surgery patients. In the 2014 guidelines, the ADA uses very direct language to strongly discourage the sole use of sliding scale insulin for glycemic control of any type of diabetic. The preferred method is to take a more physiological approach that includes basal, prandial, and correctional insulin.[1]

Monitoring

Glucose Monitoring: There was a small change to this section due to recent FDA approval of a sensor augmented insulin pump device equipped with an automatic low glucose suspend feature. These pumps are used as a tool for continuous glucose monitoring (CGM) which has been shown to be particularly beneficial to patients who have hypoglycemic unawareness. The ASPIRE trial looked at 247 patients who used augmented insulin pumps with the suspend feature and found that patients older than 16 had significantly reduced nocturnal hypoglycemic episodes without significantly increasing A1C levels. CGM devices with the suspend feature are useful for preventing severe hypoglycemic events in patients with nocturnal hypoglycemia, but more data and standardization is needed before CGM will be widely recommended to all insulin dependent diabetics.

Retinopathy: Previous guidelines both type 1 and type 2 patients who had normal eye exams should have repeat eye exams annually, but that could be extended to 2-3 years at the provider's discretion. The 2014 guidelines now recommend the maximum time between eye exams should be 2 years.[1]

Miscellaneous

Diabetes Care in Special Populations: This section was updated with information recently published by the CDC, including their projections of prevalence for type 2 diabetes using the SEARCH database. If the current trend of increased diagnosis continues, the number of type 2 diabetics under the age of 20 in the United States is due to quadruple in the next 40 years. This information is particularly disturbing because distinguishing type 1 from type 2 diabetes in patients this young can be difficult, but is critical in determining the best treatment options.[1]

<Click for references>

ACC/AHA Lipid Guidelines 2013 - In a nutshell

By Tim Gordon and Bryan Koronowski, PharmD Candidates; Justin D. Scholl, PharmD, BCACP

The American College of Cardiology (ACC) and the American Heart Association (AHA) recently developed a new guideline for the management of hyperlipidemia. The fundamental goal of this guideline is to identify a patient's risk for atherosclerotic cardiovascular disease (ASCVD) and effectively manage those already diagnosed [1]. The authors define ASCVD as coronary heart disease, stroke, peripheral arterial disease, transient ischemic attack, and stable/ unstable angina.[1] Depending on the presence of a prior event or risk factors for the event, patients are targeted for either primary or secondary prevention with statin therapy.[1] The strategy utilized within the new guideline departs from the previous guideline in that treatment is no longer initiated or adjusted predominantly in response to lipid values, but rather, is based upon targeting patients to fixed dose of statin therapy corresponding to ASCVD or other risk factors. The rationale for this shift in recommendation is based on evidence from randomized controlled trials showing high-value endpoints, such as reductions in cardiovascular events or mortality, in which statin therapy was targeted to a fixed-dose of medication and not to a target LDL-C goal.[1]

The four at-risk populations of individuals that will benefit from statin therapy based on the new guideline include:

1. Adult patients with clinical ASCVD
2. Adult patients with primary elevations of LDL–C ≥190 mg/dL
3. Patients 40-75 years of age with diabetes and LDL–C 70 to 189 mg/dL without clinical ASCVD
4. Patients 40-75 years of age without clinical ASCVD or diabetes with LDL–C 70 to 189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher

Another unique feature of the new ACC/AHA guideline is the use of an alternative Pooled Cohort Risk Assessment Equation to identify ten-year cardiovascular risk for patients aged 40-79, and lifetime cardiovascular risk for all patients, based upon pooled data from current literature[1]. This tool was developed using data from trials included within the guideline research and differs somewhat from the traditional Framingham Risk Assessment utilized previously. The calculator quantifies risk based on age, sex, race, lipid values, blood pressure, diabetes and smoking status. An online calculator can be found through the AHA website.[1]

Lifestyle modification still remains the foundation of therapy for lowering ASCVD risk and includes adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products and maintenance of a healthy weight.[1] According to the new guideline, lifestyle modifications should be used in combination with statins for the identified patients at risk.

Following lifestyle modifications, statins are the medication class of choice for reduction of cardiovascular events associated with ASCVD, because they provide the greatest mortality benefit, have the fewest safety issues, and possess the largest body of high quality evidence from randomized controlled trials (RCT) .[1] For patients at the highest risk of cardiovascular events, that is the four populations listed above, the guideline recommends the use of high-intensity statin therapy, regardless of LDL-C measurement. High intensity statins include atorvastatin 40-80mg and rosuvastatin 20-40mg (Figure 1). Lower doses or alternative statins may be used in this patient population in those patients who do not tolerate higher doses. The use of

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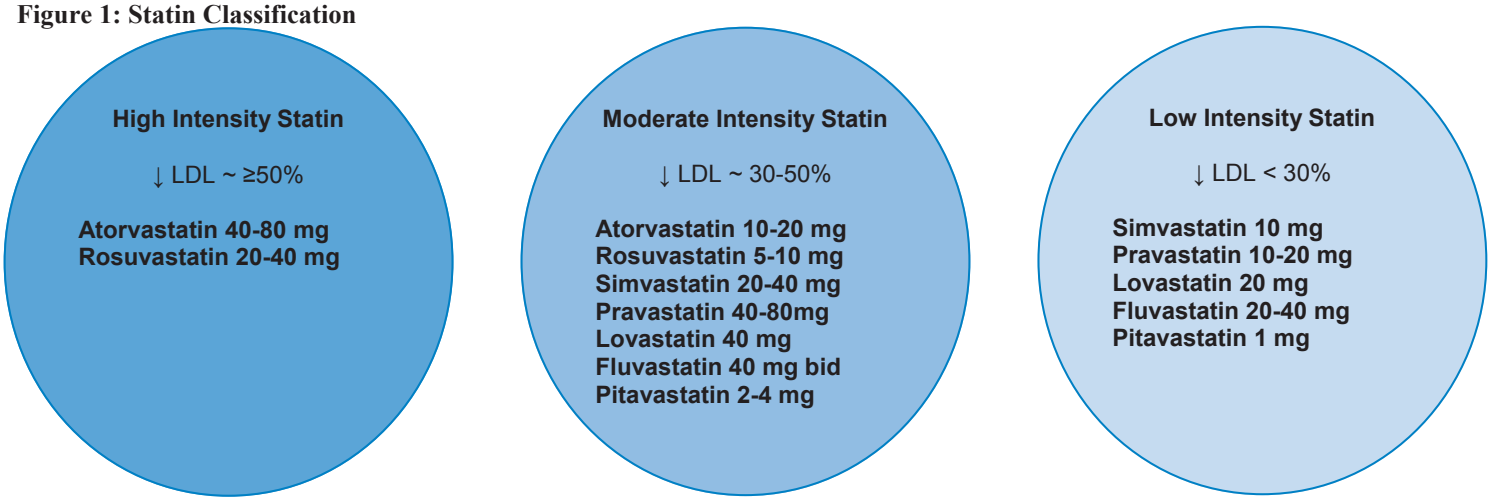
Figure 1: Statin Classification



ACC/AHA ASCVD review (continued)

additional lipid lowering agents is not specifically recommended in this guideline. In patients who do not fall into the high risk groups, the use of moderate intensity statins or lifestyle modifications alone may be warranted based on additional criteria outlined within the guideline itself.

This new guideline gives clinicians more freedom to practice clinical judgment when treating patients at risk for ASCVD events. It gives clinicians evidence to treat the patient to the extent of which both the clinician and patient are comfortable, taking into account individualized factors. Dr. Neil Stone, the chair of the expert panel that crafted the new guidelines, presents a scenario that addresses the aforementioned conundrum: "In secondary prevention, what if your patient is on high-intensity statin therapy and gets an LDL level of 78 mg/dL and is adhering to excellent lifestyle?...If he has to get to an optional goal of under 70 mg/dL as some would advocate, it means adding on medicines for which there is no proven benefit."[4]

Some critics have pointed out that the online risk calculator, which differs somewhat from the Framingham Risk Assessment used in ATP III, greatly overestimates patient's chances of having a heart attack or stroke leading to overtreatment. This may be further compounded by the reduction of the 10-year risk treatment threshold to 7.5%, rather than 10% in the previous ATP III guideline. Moreover, others point out that additional non-RCT data within the literature, which was omitted from the guideline, may have affected the recommendations had it been included. The National Lipid Association pulled their support just before the guideline was released, disagreeing with the abandonment of LDL targets once patients began taking statins.[5]

In summary, the 2013 ACC/AHA Lipid Guideline primarily focuses on statin treatment in four major at risk groups with the goal of preventing primary or secondary heart attack, stroke or death. This guideline focuses on the use of standard fixed-dose statin therapy as the means to improve cardiovascular outcomes in patients with ASCVD as opposed to targeting specific LDL-C goals. Expert opinion appears to be divided between supporters and critics. Nevertheless, clinicians now have more support to treat the individual patient, rather than the laboratory values, in such a fashion that utilizes both evidenced based medicine and clinical experience.

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