

Clinical Briefs in Primary Care

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Evidence-based updates in primary care medicine

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Antiretroviral Therapy for HIV Patients

SOURCE: Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA* 2016;316:171-181.

Prevention of seroconversion in HIV serodiscordant couples (in which one partner is HIV positive and the other is not) is reduced by using barrier methods, especially when the HIV-positive partner is receiving antiretroviral therapy (ART). ART provides sustained reductions in HIV viral load and reduced infectivity, but would it be safe for serodiscordant couples to omit barrier methods entirely?

Rodger et al performed a prospective observational study ($n = 888$) of serodiscordant sexually active heterosexuals, men who have sex with men (MSM), and gay couples. The HIV-positive partners all were receiving ART, and $> 80\%$ presented with undetectable levels of HIV virus (some subjects on ART did not report viral load status, but are presumed to be similarly undetectable). Couples agreed to abstain from barriers during intravaginal or intra-anal intromission.

During 1.3 years (mean) of follow-up, there were no confirmed HIV conversions; any new HIV conversions were found to be from HIV strains not harbored by the HIV-positive partner and must have occurred from another external HIV-positive source.

Since intra-anal transmission is more common than intravaginal transmission, it is

particularly welcome that the rate of conversion was zero among all participants, including the 340 MSM. ■

Ticagrelor vs. Aspirin in Post-TIA and Stroke Patients

SOURCE: Johnston SC, Amarenco P, Albers GW, et al. Ticagrelor versus aspirin in acute stroke or transient ischemic attack. *N Engl J Med* 2016;375:35-43.

The first 90 days after a transient ischemic attack (TIA) or ischemic stroke is a high-risk period for recurrence of cardiovascular thrombotic events. Even with aspirin treatment, recurrences occur in as many as 10-15% of patients. Ticagrelor is an inhibitor of the P2Y12 receptor on platelets, similar in mechanism to clopidogrel. Ticagrelor is indicated for reduction of thrombotic events in persons with acute coronary syndromes or ST-elevation myocardial infarction. Might a different mechanism of action than aspirin treatment, as provided by ticagrelor, reduce thrombotic events in patients who experience a TIA?

The SOCRATES trial enrolled patients ($n = 13,199$) who had suffered an ischemic stroke or TIA within 24 hours of the event. Study subjects were randomized to ticagrelor (180 mg loading dose, then 90 mg twice per day) or aspirin (300 mg loading, then 100 mg once per day) for 90 days. The primary outcome was a composite of stroke, myocardial infarction, or death.

Although results trended favorably in the ticagrelor treatment arm (hazard ratio = 0.89), they were not statistically significant. Since the treatment costs of aspirin

are substantially less than ticagrelor, and the adverse bleeding effect profile is similar, aspirin should remain the drug of choice, except for patients who are aspirin-intolerant. ■

Many Treatment Choices for Type 2 Diabetes

SOURCE: Palmer SC, Mavridis D, Nicolucci A, et al. Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes: A meta-analysis. *JAMA* 2016;316:313-324.

The real goals of diabetes treatment are reduction in microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (myocardial infarction and stroke) endpoints. With that in mind, it should be sobering to review current FDA-approved labeling for antidiabetic meds: "There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with [insert drug name] or any other anti-diabetic drug."

A recent large meta-analysis (301 clinical trials) addressed cardiovascular mortality as well as all-cause mortality for the most commonly used antidiabetic drugs (metformin, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, insulin, DPP-4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists) seeking to discern any differences in cardiovascular events or mortality, as well as safety.

Despite an impressive amount of data, no particular class of agents — as monotherapy or in combination — provided distinct advantages for risk reduction of cardiovascular events or mortality.

Recent cardiovascular safety trials featuring two agents (empagliflozin and liraglutide) challenge the concept that diabetes treatment is ineffectual for cardiovascular risk reduction, but if clinicians believe in “class effects” of medications, it appears dubious that any clear winners will emerge any time soon in the quest for cardiovascular risk reduction. ■

SPRINT: Celebrating Benefits for Older Patients

SOURCE: Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged \geq 75 years: A randomized clinical trial. *JAMA* 2016;315:2673-2682.

Hypertension experts and generalists alike consider the Systolic Blood Pressure Intervention Trial (SPRINT) a game changer. Despite the advice from Eighth Joint National Committee that lowering blood pressure to $< 140/90$ mmHg was sufficient for most non-senior adults, the question of whether lower is better was never believed to have been adequately clarified. SPRINT determined that aiming for a systolic blood pressure of < 120

mmHg provided significant reductions in cardiovascular and all-cause mortality compared to “traditional” blood pressure goals (< 140 mmHg systolic blood pressure) in hypertensive non-diabetic adults. SPRINT also was large enough ($n = 9,361$) and included a sufficient number of patients > 75 years of age ($n = 2,636$) to make meaningful commentary about benefits in that specific age demographic.

After a median of 3.14 years follow-up in patients > 75 years of age (mean age = 80 years), major adverse cardiovascular events fell by approximately one-third in the intensively treated group, as was all-cause mortality, without incurring excess serious adverse events.

SPRINT is not the first clinical trial to confirm benefits of treating hypertension in super-seniors: the Hypertension in the Very Elderly Trial (HYVET; mean age = 83 years) ended early due to the important mortality reductions observed in treated seniors attributable to blood pressure control. Using available knowledge, age should not be considered a barrier to seeking good blood pressure control. ■

Updates on the USPSTF Colorectal Cancer Screening Recommendations

SOURCE: US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2016;315:2564-2575.

In accordance with previous recommendations, the United States Preventive Services Task Force still endorses colorectal cancer (CRC) screening in adults 50-75 years of age. For patients > 75 years of age, the decision has to be individualized, especially for those who have not received screening as recommended earlier in life.

Because of a lack of studies demonstrating particular advantage of one CRC screening method over another in head-to-head comparison trials, each of the recommended methods has to be evaluated on its own merits and tolerability. Taking that into consideration, it appears that of the nine CRC screening methods evaluated (including flexible sigmoidoscopy, fecal immunochemical stool testing, colonoscopy, CT colonography, etc.), each provides a substantial increase in life expectancy, with a very small margin of greater efficacy for colonoscopy.

Any harms related to CRC screening generally are associated with colonoscopy, whether it is used as the primary screening method or in follow-up of another screening method. Overall, either colonic perforation or major intestinal bleeding occurs in approximately 1/1,000 colonoscopies. In conjunction with previous American Cancer Society recommendations, rather than focus on particular advantages of one screening method vs. another (since all interventions improve outcomes, and demonstrated differences appear to be modest), it is more important to identify a screening method the patient will endorse than debate any between-method differences in efficacy. ■

Predicting Opioid Abuse and Dependence

SOURCE: Ciesielski T, Iyengar R, Bothra A, et al. A tool to assess risk of de novo opioid abuse or dependence. *Am J Med* 2016;129:699-705.

In an era in which opioid overdose has outstripped auto accidents as a cause of mortality in adults ≤ 45 years of age in many states, it is critical to learn how to better identify patients at risk of opioid addiction, abuse, and dependence. There already are several screening tools for opioid misuse screening available to clinicians such as the Opioid Risk Tool and the Screener and Opioid Assessor for Patients in Pain; however, patients who are willing to be untruthful and hide their risk factors render such tools meaningless.

Ciesielski et al retrospectively studied a large sample from a health insurance database ($n = 649,851$), from which the authors identified 2,067 cases of opioid abuse or dependence. Predictors for abuse or dependence include younger age, chronic opioid use, psychiatric history, abuse of nonopiod substances, alcohol abuse, smoking, use of high morphine doses, receiving prescriptions from more than one source or pharmacy, male gender, and South or Midwest residence.

Most of the risk factors for abuse/dependence identified through this database have been identified and used by earlier established risk screeners. Because this was a retrospective analysis, whether utilizing a risk stratification tool comprised of all 12 risk factors noted in this population would improve risk prediction remains to be determined. ■

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