Updates in Outpatient Medicine

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Hypertension guidelines
Influenza vaccine
Prostate cancer screening
Hypertension
Case #1

A 72 yo Caucasian man with HTN, COPD, BPH and a history of prostate cancer s/p radical prostatectomy presents for routine f/u. He feels well except for SOB with heavy exertion that responds to his albuterol inhaler. His BP is 148/78. He is currently on albuterol MDI prn, Lisinopril 10 mg qday, and HCTZ 12.5 mg qday. His labs are unremarkable. What should you do with his hypertensive regimen?
It depends on who you listen to
JNC HISTORY

- JNC 1: published 1976
- JNC 2: published 1980
- JNC 3: published 1984
- JNC 4: published 1988
- JNC 5: published 1992
- JNC 6: published 1997
- JNC 7: published 2003
- JNC LATE
JNC 8 Simplified

- Over 60 without CKD or DM, goal 150/90
- Everyone else, goal 140/90
- Can use thiazide, CCB, ACE or ARB
  - If CKD, use ACE or ARB
  - In black population w/o CKD, use thiazide or CCB
Not everyone agrees

"Objection, Your Honor. Counsel is leading the witness."
Dissention within JNC 8

- 5 members voiced exception to the recommendation to increase the target SBP from 140 to 150 mm Hg in patients over age 60

- "The majority of the JNC 8 panel embraced the view that in the absence of definitive evidence, increasing the SBP goal was the optimum approach in patients 60 or older. We, the panel minority, believed that evidence was insufficient to increase the SBP goal from its current level of less than 140 mm Hg because of concern that increasing the goal may cause harm by increasing the risk for CVD and partially undoing the remarkable progress in reducing cardiovascular mortality in Americans older than 60 years."
Cochrane Review: The other side of the coin

[Intervention Review]

Pharmacotherapy for mild hypertension

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Antihypertensive drugs used in the treatment of adults (primary prevention) with mild hypertension (systolic BP 140-159 mmHg and/or diastolic BP 90-99 mmHg) have not been shown to reduce mortality or morbidity in RCTs. Treatment caused 9% of patients to discontinue treatment due to adverse effects. More RCTs are needed in this prevalent population to know whether the benefits of treatment exceed the harms.
Switching Gears from JNC 8 Marathon to SPRINT
Systolic Blood Pressure Intervention Trial (SPRINT)

- 9361 patients ≥50 yo with SBP of 130-180 mm Hg and high CV risk
  - known symptomatic or asymptomatic CV disease
  - CKD with GFR 20–59 mL/minute/1.73 m²
  - 10-year Framingham CV risk ≥15%
  - or age ≥75
- Patients with diabetes, obesity, CHF, h/o orthostasis, and stroke were excluded
Systolic Blood Pressure Intervention Trial (SPRINT)

- Randomized to either intensive or standard treatment (SBP targets, 120 or 140 mm Hg)
- The protocol included general guidelines for choice of antihypertensive agents, but researchers were permitted discretion in choosing drug regimens.
- Diuretics, angiotensin-converting–enzyme inhibitors or angiotensin-receptor blockers, calcium-channel blockers, and β-blockers were used extensively.
- During the trial, intensive and standard treatment patients required averages of three and two drugs, respectively.
Systolic Blood Pressure Intervention Trial (SPRINT)

- Trial was stopped early after median f/u of 3.3 years
- Average SBPs were 121.5 mm Hg (intensive) and 134.6 mm Hg (standard)
- The primary composite outcome (MI, non-MI ACS, stroke, heart failure, or CV-related death) occurred in 5.2% of intensive-treatment patients and 6.8% of standard-treatment patients (P<0.001).
- Relative reductions in this outcome were similar in subgroups of patients with CKD and of patients >75.
- Two components of the composite outcome were significantly lower with intensive treatment — heart failure (1.3% vs. 2.1%) and CV-related death (0.8% vs. 1.4%).
- All-cause mortality also was significantly lower with intensive treatment (3.3% vs. 4.5%).
Systolic Blood Pressure Intervention Trial (SPRINT)

- Several serious adverse events were significantly more common with intensive than with standard treatment:
  - Incidences of hypotension, syncope, and electrolyte abnormalities were each about 1% higher,
  - Incidence of acute kidney injury was about 2% higher.
- Among patients without CKD at baseline, the incidence of a >30% decline in GFR was significantly greater with intensive treatment (3.8% vs. 1.1%).
Let’s look at the numbers a bit differently (Annals editorial)

- On the basis of the SPRINT results, we estimate that for 1000 persons treated over 3.2 years to a systolic BP goal less than 120 mm Hg compared with less than 140 mm Hg, an average of 16 persons will benefit, 22 persons will be harmed, and 962 will not experience benefits or harms.

- Patients may believe that it is worthwhile to aim for lower BPs if they hear that receiving 3 drugs every day for more than 3 years might reduce their risk for cardiovascular events by 25%. However, after learning that their likelihood of absolute benefit is only 1.6%, with a greater likelihood of serious harm, their enthusiasm for more medications may diminish.
Who were the patients?

- 1 in 12 or 17 million Americans would have been eligible for study.
- 90% were already on anti-hypertensive meds so this study is not compelling evidence to initiate anti-hypertensive meds in high risk patients with SBP<140.
- 1 in 6 of Americans currently treated for HTN would have been eligible (finding not relevant for 5 of 6).
- Diabetics excluded. This trial mirrors ACCORD trial in which same intervention did not show significant benefit of intensive BP lowering.
How was BP measured?

- Blood pressure was measured in SPRINT using an automated oscillometric blood pressure (AOBP) device.
- It was measured “unattended” (The white coat was out of the room).
- This is not the way clinicians measure BP.
- What is 120 in our clinics?
- Some argue that SBP should be adjusted up by 10-20 mm Hg (~140).
What does the ACP say?

- The ACP and AAFP released a joint practice guideline in January 2017 on systolic blood pressure targets for people aged 60 years and older with hypertension.

- Start treatment for patients who have persistent SBP ≥150 mm Hg to achieve a target ≤150 mm Hg to reduce risk for stroke, cardiac events, and death (strong evidence).

- Patients with a history of stroke or TIA or have high cardiovascular risk, consider starting or increasing drug therapy to achieve systolic blood pressure ≤140 mm Hg to reduce risk for stroke and cardiac events (weak evidence).
What is clear

- Many Americans have hypertension and many are undiagnosed
- Patients with very elevated blood pressure will derive the most benefit from anti-hypertensive therapy
- Shared medical decision making
Influenza vaccine 2017-8
Case #2

It is a beautiful October day and a 72 yo healthy man on no medications comes in for routine follow up. He states he feels well and wants to stay that way. His golfing buddies told him he should get the shingles shot. He doesn’t want the flu shot since he gets sick when he takes it.
Background

- Acute respiratory illness caused by influenza A or B viruses
- The high rate of mutation of influenza virus results in compromised ability of immune system to protect against new variants
- New vaccines are produced each year to match the circulating viruses
- Protective efficacy of the vaccine depends on match between the strains in the vaccine and the circulating viruses
Influenza viruses

- Influenza A frequently undergoes changes in antigenic characteristics of envelope glycoproteins hemagglutinins (H) and neuraminidases (N)
  - Antigen drift- minor antigenic changes (typical epidemic)
  - Antigenic shift- major antigenic changes (risk for pandemic)
- Influenza B less frequently undergoes changes in antigenic characteristics and only antigenic drifts in hemagluttanins have been described
What is the vaccine this year?

- A/Michigan/45/2015 (H1N1) pdm09-like virus (different than last year)
- A/Hong Kong/4801/2014 (H3N2)-like virus
- B/Brisbane/60/2008-like virus
- B/Phuket/3073/2013-like virus (only in quadrivalent vaccine)
Indications

- ACIP recommends annual influenza for all individuals age 6 months and older
- High priority groups
  - Pregnant women
  - Immunocompromised patients
  - Health care workers and their household contacts
Major vaccine formulations

- Standard dose trivalent and quadrivalent inactivated vaccine
  - Given IM to adults of any age

- High dose trivalent inactivated vaccine (Fluzone high dose)
  - Approved for age ≥ 65 (and preferred if available)
  - Given IM
  - Contains 60 mcg of each virus antigen rather than 15 mcg

- Other formulations
  - Intradermal (needle phobia if < 65 yo)
  - Intranasal (not recommended)
Vaccine administration

- Preferably administered before the end of October, but continue to give later
Vaccine manufacturers have projected that as many as 151 to 166 million doses of injectable flu vaccine will be available for the 2017-2018 season.

- Can co-administer inactivated vaccine with other vaccines since it does not interfere with immune response to other vaccines.

- Studies have shown repeatedly that a healthcare provider's recommendation plays a critical role in a patient's decision to get a seasonal influenza vaccine.
Prostate cancer screening
Case #3

A 59 yo man with HTN and BPH comes in for routine follow up. His medications are chlorthalidone 12.5 mg qd, tamsulosin 0.4 mg qd, and finasteride 5 mg. His labs show Na 143, K 4.1, Cl 101, CO2 28, BUN 22, creatinine 0.88, Ca 10.1, PSA 2.5, WBC 7.8, Hgb 16.4, Hct 41.8, Plt 285.
**Background**

- **Men have**
  - 16% lifetime risk of developing prostate cancer
  - 2.9% lifetime risk of dying of prostate cancer
- **Many cases of prostate cancer are not clinically evident (autopsy data)**
  - 30% incidence in men age 55
  - 60% incidence in men age 80
- **Prostate cancer survival related to extent of tumor at diagnosis**
  - Localized prostate cancer has 100% 5 year survival rate
  - Metastatic prostate cancer has 29.3% 5 year survival rate
PSA testing history

- Originally used as a tumor marker to detect cancer recurrence and disease progression after treatment
- Adopted for cancer screening in the early 1990’s
  - Dramatic increase in prostate cancer incidence
  - Majority of these cancers were localized
  - Increase in radical prostatectomy and radiation therapy
PSA

- Glycoprotein produced by prostate epithelial cells
- PSA levels may be elevated in men with prostate cancer
- PSA elevations may proceed clinical disease by 5-10 years
- PSA may also be elevated in benign conditions
  - BPH
  - prostatitis
  - DRE
  - Ejaculation
  - Prostate biopsy
  - Urinary retention
- PSA lowered by about 50% by 5 alpha reductase inhibitors
  - Double PSA if on finasteride or dutasteride
Effectiveness of prostate cancer screening

- United States Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial
  - Cancer detection in the screening group was significantly higher than in the control group (2820 versus 2322, rate ratio 1.22, CI 1.16-1.29)
  - No reduction in the primary outcome of prostate cancer mortality (50 versus 44 deaths in the screening and control groups)

- European Randomized Study of Screening for Prostate Cancer (ERSPC)
  - Prostate cancer was diagnosed more frequently in the screening group (9.6 versus 6.2 cases per 1000 person-years)
  - All-cause mortality in the core group was not reduced with screening (18.6 versus 18.9 deaths per 1000 person-years; rate ratio 1.00, CI 0.98-1.02)
  - Prostate cancer mortality was reduced in the entire cohort of men ages 50 to 74 (rate ratio 0.83, CI 0.73-0.94).
Harms of screening

- Risk of biopsy (bleeding, infections, pain, anxiety)
- Risks of therapy
  - operative mortality rate ranges from 0.1-0.5 %
  - urinary incontinence (15-50% radical prostatectomy, 2-16% radiation)
  - Sexual dysfunction (20-70 %radical prostatectomy, 20-45% radiation)
- Overdiagnosis
  - detection by screening of conditions that would not have become clinically significant
  - most men with screening-detected prostate cancers have early-stage disease and will be offered aggressive treatment
Approach to screening

- Although screening for prostate cancer with PSA can reduce mortality from prostate cancer, the absolute risk reduction is very small.
- There remain important concerns about whether the benefits of screening outweigh the potential harms.
- Shared medical decision making beginning at age 50 (earlier if high risk).
- If patient elects screening, it should be performed every two to four years with PSA alone and stop at age 69 or when life expectancy <10 years.
Urology referral

- May depend on your urologist
- High PSA levels require immediate referral
- Many urologists request repeat testing for low level elevations or have age based guidelines
Concerns about current prostate cancer screening practices

- Provider knowledge (ever-changing guidelines)
  - Most PCP are not aware of the need to double the PSA level for patients taking finasteride
  - Most providers are not aware of GU’s age-adjusted criteria for continued annual screening, repeating PSA, and referral to GU
  - Currently, most providers refer only for PSA >4 regardless of age or finasteride use

- No current systematic mechanism for:
  - Instructing patients on activities to avoid before getting a PSA drawn
  - Capturing patients who had PSA ordered, but did not complete the test
  - Ensuring that patients with elevated age-adjusted PSA levels are referred to GU
  - Identifying patients who were referred to GU clinic, but were not seen

- Puts patients, PCP, and institutions at risk for bad outcomes
Novel approach to PSA screening at Albuquerque VA

- At the Albuquerque VA, we have developed a PSA registry for prostate cancer screening
- We are able to query the VA data warehouses to look at labs, pharmacy, biopsy results etc.
- Registry is run monthly
- Not yet ready for prime time, but getting closer
Automated PSA Management System: Screening

- Systematically captures all age-appropriate men who have not had a PSA within one year.
- Automatically generates a letter asking them if they want to opt out of the PSA protocol.
- When a patient who has not elected to opt out is due for PSA testing, an automated letter is sent to the patient with instructions to go to the lab and activities to avoid.
- A second letter is automatically generated if the patient does not get their PSA done in a timely manner.
- If the PSA is not done after the second letter, the patient receives a direct phone call.
Automated PSA Management System: Action

- For all patients on finasteride, the PSA level is doubled automatically.
- Based on age-adjusted PSA levels, patients either
  - go back to the routine annual screening
  - are asked to get a repeat PSA
  - referred directly to GU
- Track all patient who are referred to GU to make sure that they are properly evaluated in GU clinic.
Automated PSA Management System Benefits

- Assists PCP in prostate cancer screening
- Occurs independent of visits
- Automatically makes adjustments for finasteride use
- Automatically determines the course of action for age-adjusted PSA levels
- Has automated safeguards to limit the number of patients who do not get their PSA done or are not appropriately evaluated by GU.