Outpatient Updates 2025

Chris Knight and Gena Lenti

ACP®
American College of Physicians
Leading Internal Medicine, Improving Lives

Disclosure of Financial Relationships

Nothing to disclose for either of us.

Women's Health

Gena Lenti

Question

Your patient presents at a visit for vaginal discharge. Workup reveals a vaginal pH of 5, a positive amine test and clue cells on microscopy consistent with bacterial vaginosis (BV) . This is her third recurrence of BV this year. She is monogamous with one male partner. She asks about the most effective treatment for recurrent BV. What do you recommend?

A. Patient treatment with PO metronidazole 400 mg BID for 7 days

B. Patient treatment with intravaginal metronidazole gel for 5 days

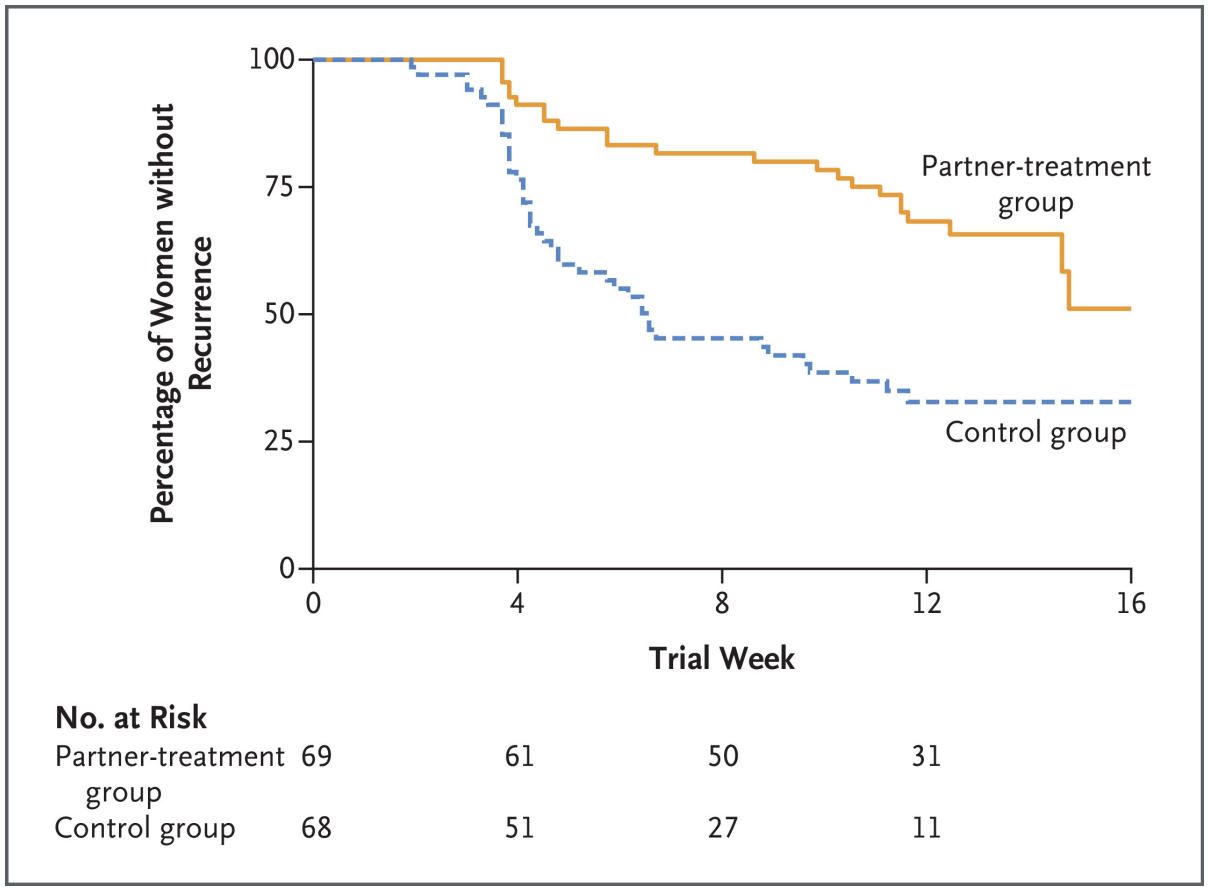
C. Patient and partner treatment with PO metronidazole 400 mg BID for 7 days

D. Patient and partner treatment with PO metronidazole 400 mg BID + partner treatment with topical clindamycin cream applied to penile skin BID for 7 days

E. Patient and partner treatment with PO metronidazole 400 mg BID + patient treatment with topical clindamycin cream applied to vagina BID for 7 days

Bacterial Vaginosis Male Partner Treatment

- Open label RCT; 164 couples
- Population: women with BV + monogamous male partner
- Intervention:
  - Woman + partner treatment vs woman treatment alone
  - Partner Tx: metronidazole 400 mg BID + topical 2% clindamycin to penile skin for 7 days
- Measure: Recurrent BV at 12 weeks
- Results: BV recurred in 35% of women in the woman + partner treatment arm vs 63% in the woman only arm



https://pmid.us/40043236

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C. Patient and partner treatment with PO metronidazole 400 mg BID for 7 days

D. Patient and partner treatment with PO metronidazole 400 mg BID + partner treatment with topical clindamycin cream applied to penile skin BID for 7 days

E. Patient and partner treatment with PO metronidazole 400 mg BID + patient treatment with topical clindamycin cream applied to vagina BID for 7 days

Practice Changing Update

Recommend treating male partners of women with recurrent, symptomatic bacterial vaginosis.

*American College of Gynecology recommends shared decision-making regarding partner treatment in patients with same sex partners and in patients with first occurrence of bacterial vaginosis.

Question

Your 55-year-old female patient presents for a visit following DEXA scan. DEXA was obtained given strong family history of osteoporosis (mother and two sisters).

Her T-scores were –1.5, -1.7, and -1.5 at the lumbar spine, hip and femoral neck, respectively. Her FRAX score was 1.3% at the hip and 9% for major osteoporotic fracture. Given her family history, she is very concerned about her fracture risk. You provide recommendations on vitamin D and calcium intake and offer...

A. No other treatment; continue current management and follow up DEXA in about 5 years

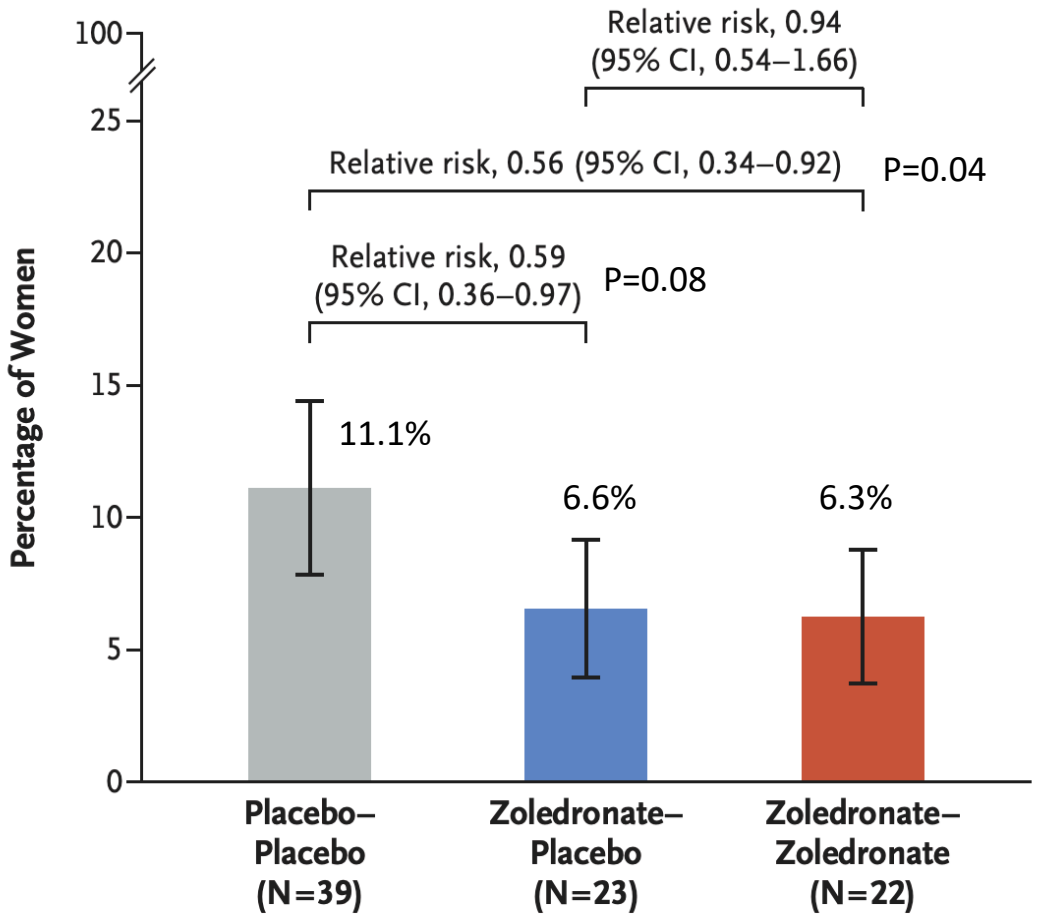
B. Start oral alendronate and plan to continue for 3-5 years

C. One dose of zolendronic acid now and repeat DEXA in 5 years

D. One dose of zolendronic acid now and again in 5 years

Fracture Prevention with Infrequent Zolendronate

Risk of Morphometric Vertebral Fracture



Prospective double blind RCT; Randomized 1054 50-60 y/o women without osteoporosis (BMD 0-(-2.5))

Intervention (baseline & 5 years):

1. Zolendronate-zolendronate (ZZ)
2. Zolendronate-placebo (ZP)
3. Placebo-placebo (PP)

Endpoints at 10 years:

1. **Morphometric vertebral fracture**
2. Other fractures

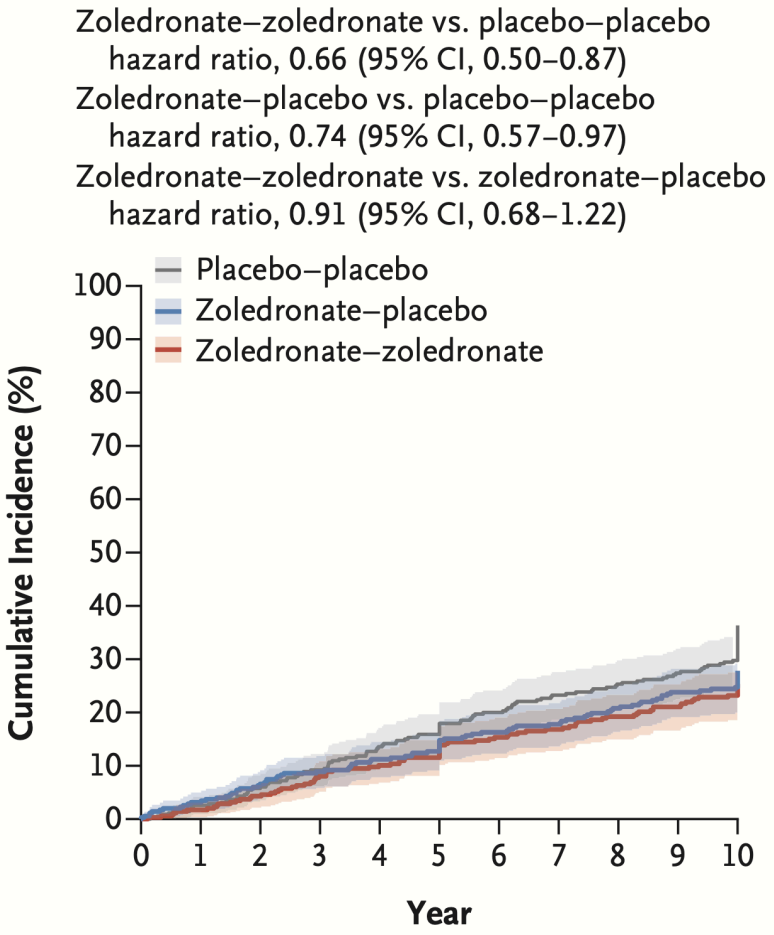
Primary outcome:

- Morphometric fracture in 6.3% (ZZ), 6.6% (ZP), and 11.1% (PP)
- NNT to prevent one woman from having a new morphometric vertebral fracture was 21 for ZZ group and 22 for ZP group

https://pmid.us/39813642

Fracture Prevention with Infrequent Zolendronate

Risk of Any Fracture at 10 Years



No. at Risk											
Placebo–placebo	351	341	326	314	298	287	272	260	253	245	235
Zoledronate–placebo	351	339	325	314	303	293	280	274	263	250	242
Zoledronate–Zoledronate	352	344	333	319	309	303	287	279	268	259	250

Intervention (baseline & 5 years):

1. Zolendronate-zolendronate (ZZ)
2. Zolendronate-placebo (ZP)
3. Placebo-placebo (PP)

Endpoints at 10 years:

1. Morphometric vertebral fracture
2. **Fragility fracture (FF), any fracture (AF), and major osteoporotic fracture (MOF)**

Secondary outcomes:

- There was a lower risk of all fracture types when comparing ZZ to PP
- There was a lower risk of major osteoporotic and any fracture when comparing ZP to PP

Limitations: Clinical relevance of morphometric fracture?

https://pmid.us/39813642

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A. **No other treatment; continue current management and follow up DEXA in about 5 years**

B. Start oral alendronate and plan to continue for 3-5 years

C. **One dose of zolendronic acid now and repeat DEXA in 5 years** ?

D. **One dose of zolendronic acid now and again in 5 years**

Practice Changing Update

Consider using one dose of zolendronate for fracture prevention in early postmenopausal women, particularly those who have risk factors for osteoporosis and want to reduce fracture risk...

...although we likely need more data before this is approved by insurance.

Question

You are discussing cervical cancer screening (CCS) with a 31-year-old transgender male patient. The patient has a vagina and cervix, though has not had prior cervical cancer screening. They are currently sexually active with one female partner; they have had vaginal intercourse with male partners in the past. They prefer to avoid pelvic exams due to a history of trauma.

What do you recommend?

A. Defer cervical cancer screening given preference to avoid pelvic exams and patient being generally low risk

B. HPV self swab; if negative, follow up CCS in 3 years

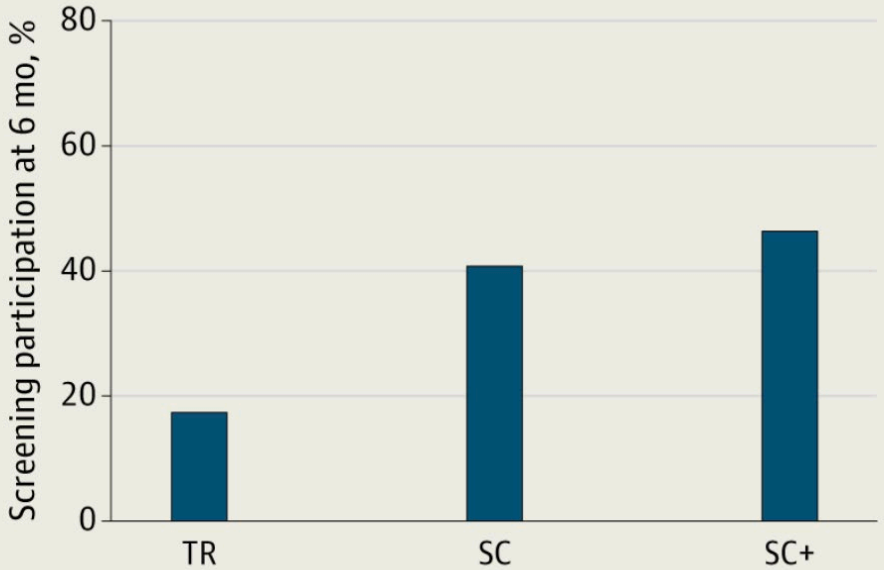
C. HPV self swab; if negative, follow up CCS in 5 years

D. Clinician performed pap smear with high risk HPV testing; if negative, follow up CCS in 5 years

Self-Collection for Cervical Cancer Screening (CCS) in a Safety Net Setting

- Pragmatic, single blinded RCT (PRESTIS)
- Safety net hospital setting; 2474 participants in the intention to screen analysis
- System level comparison of:
  1. Telephone reminders (TR) for clinic based CCS
  2. TR with mailed self-collection (SC) kit
  3. TR with mailed SC kit + patient navigation
- Primary outcome: SC was more effective than TR at increasing CCS participation.

  SC+ provided marginal additional benefit.



CCS participation at 6 mo:

TR group, 17.4%
SC group, 41.1%
SC+ group, 46.6%

Relative participation vs TR group:

SC group: 2.36; 95% CI, 1.99-2.80
SC+ group: 2.68; 95% CI, 2.27-3.16

https://pmid.us/40478588

Self-collection Vaginal Specimens for HPV Testing: Enduring Consensus Guidelines 2025

Normal (Negative for high-risk HPV)	Positive for HPV types 16 or 18	Positive for HPV types 45, 33/58, 31, 52, 35/39/68, or 51	Positive for HPV types 56/59/66 alone
Repeat CCS in 3 years	Colposcopy with collection of cytology	Clinician collected cytology	Repeat HPV testing in 1 year

***Clinician-collected preferred following previously abnormal tests.*

https://pmid.us/39982254

Question

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What do you recommend?

A. Defer cervical cancer screening given difficulty with pelvic exams in past and patient being generally low risk

B. HPV self swab; if negative, follow up CCS in 3 years

C. HPV self swab; if negative, follow up CCS in 5 years

D. Clinician performed pap smear with high risk HPV testing; if negative, follow up CCS in 5 years

Practice Changing Updates

Patients who are under-screened for cervical cancer should be offered vaginal HPV self-collection. Systems should consider sending mailed self-collection kits.

New guidelines exist for HPV self-collection; if testing is normal, can repeat screening in 3 years.

Question

Your 68-year-old female patient with depression and a BMI of 32 was recently diagnosed with hypertension. She kept a blood pressure log, and most of her blood pressures are in the 130s-140s/90s. She prefers not to take medication, so you counsel her on lifestyle changes to help bring blood pressure down, including weight loss, dietary changes, and reducing alcohol intake.

She is sedentary at baseline. When counseling about physical activity, you share there was a recent study that showed you can lower your blood pressure slightly by....

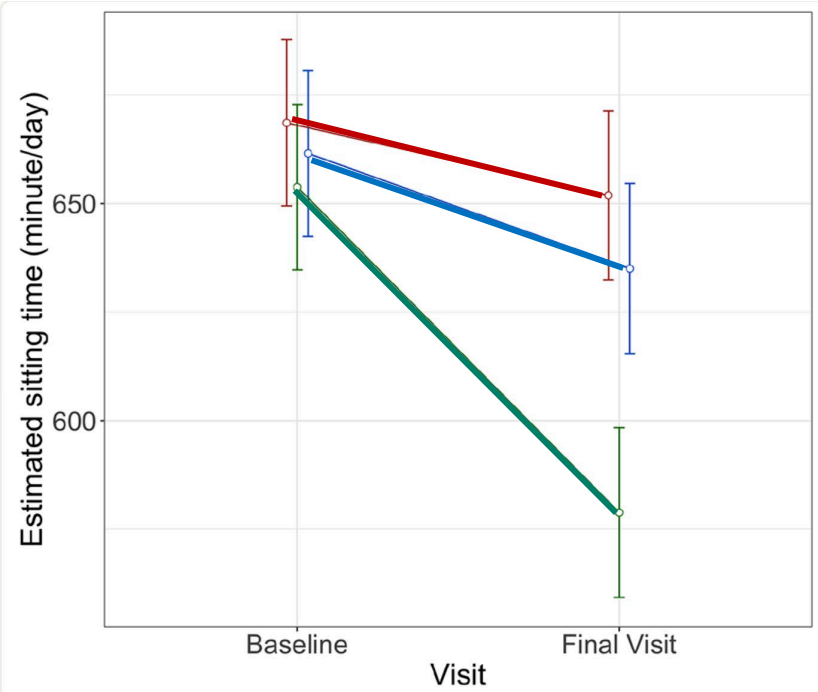
A. Reducing the amount of time you spend sitting down

B. Increasing the amount of time you go from sitting down to standing up

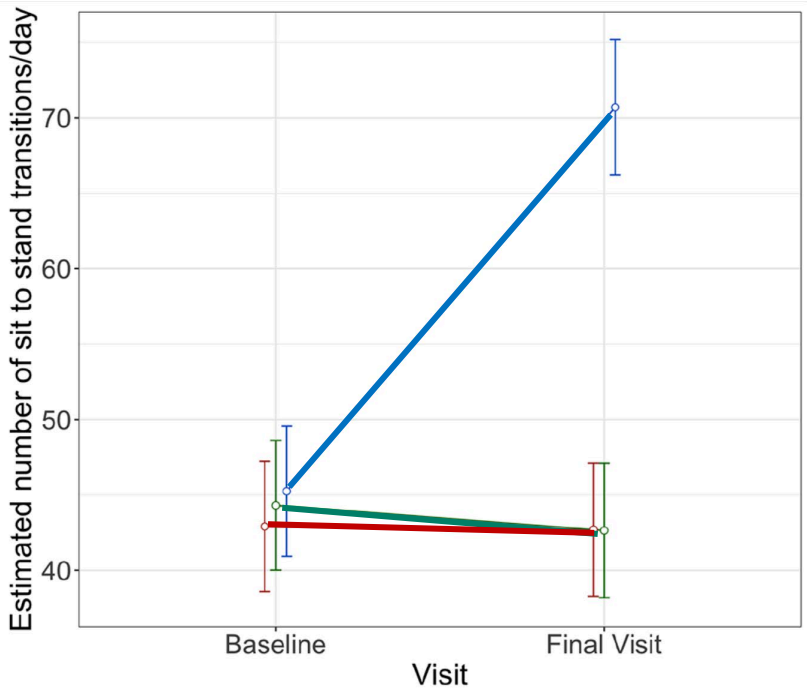
Sit-to-Stand Transitions for Hypertension

- Three-arm RCT of 407 overweight or obese sedentary post-menopausal women
- Measures: changes in blood pressure, glucose regulation, and activity

- Study conditions:
  1. Healthy living (control)
  2. Reduce sitting time (sit less)
  3. Increase sit to stand transitions (sit to stand, STS)



a. Minutes per day of sitting time by study arm at baseline and 3-month Final Visit



b. Number of sit-to-stand transitions per day by study arm at baseline and 3-month Final Visit

Results:

- **STS arm had significant decrease in diastolic BP** (-2.24 mmHg, p=0.02) and non-significant decrease in systolic BP (-3.33 mmHg, p=0.03)
- "Sit less" arm had no significant change in BP
- Neither arm had significant change in glucoregulatory measures

https://pmid.us/40709462

Question

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She is sedentary at baseline. When counseling about physical activity, you share there was a recent study that showed you can lower your blood pressure slightly by....

A. Reducing the amount of time you spend sitting down

B. **Increasing the amount of time you go from sitting down to standing up**

Compared to other lifestyle interventions...

Lifestyle Intervention		Goal	Approximate Impact on SBP
Weight loss	Weight/body fat	Aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	-5 mm Hg
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mm Hg
	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5 to 6 mm Hg
Physical activity	Aerobic	90–150 min/wk 65%–75% heart rate reserve	-5 to 8 mm Hg
	Dynamic resistance	90–150 min/wk 50%–80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set	-4 mm Hg
	Isometric resistance	4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk 8–10 wk	-5 mm Hg
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol to: Men: ≤2 drinks daily Women: ≤1 drink daily	-4 mm Hg

https://pmid.us/33037326

Practice Changing Update

Encouraging your older female patients to increase their sit-to-stand transitions is a low risk, easy intervention to help lower blood pressure (albeit a small amount).

And maybe that standing desk is not as helpful as we thought...

Cardiovascular Disease

Chris Knight

Question

A 72 y/o male patient with BMI of 38 returns for hospital follow-up after a recent admission for HFpEF (EF 63% on inpatient echo). In addition to their prior meds (lisinopril, atorvastatin), they are discharged on empagliflozin and torsemide. On exam they appear euvolemic, BP 118/75, p 78.

What medication change would reduce their chances of being readmitted with HFpEF?

A. Change lisinopril to sacubitril-valsartan

B. Add metoprolol SR

C. Add tirzepatide

D. Add diltiazem

GLP-1's for HFpEF

- GLP-1s have recently been shown to be effective for... oh, never mind.
- 731 pts with HfPEF and BMI > 30 randomized to tirzepatide vs. placebo for 1-2 years
- 5.4% absolute reduction in (CV death + worsening HF) in treatment group over full trial (NNT 30/year)
- Mostly reduced hospitalizations, small reduction in CV death, no change in all-cause mortality
- Improved QoL, six-minute walk
- 2023 semaglutide study had similar findings

https://pmid.us/39555826

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B. Add metoprolol SR

C. **Add tirzepatide**

D. Add diltiazem

Practice Changing Update

GLP1s are effective for HFpEF with obesity; it’s worth going to bat with insurance for these patients.

Question

A 68 y/o female patient comes in for a wellness visit. 14 months ago they were treated for unstable angina with placement of a drug-eluting stent to the LAD. Current medications are aspirin, atorvastatin, candesartan, hydrochlorothiazide, and prasugrel. Exam shows BP 112/68, p 72, otherwise unremarkable.

What should you do with their dual antiplatelet therapy (DAPT)?

A. Stop DAPT and continue daily aspirin

B. Stop DAPT and start daily clopidogrel

C. Continue DAPT indefinitely

D. Continue DAPT until they can see their cardiologist

Aspirin for..?

- Post-PCI most pts get P2Y12 inhibitor + ASA for 6-12 months
- 5506 pts ≥ 6 months post PCI (median 17 mos) randomized to clopidogrel 75 mg daily vs ASA 100 mg daily
- 2.2% absolute reduction in (death + MI + CVA) over 3 years (NNT 137/year)
- No difference in bleeding
- Study done in Korea; subgroup analysis of CYP genotype showed high prevalence, no difference in outcome

https://pmid.us/40174599

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C. Continue DAPT indefinitely

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Aspirin for...?

- Vs. clopidogrel post-DAPT for PCI: **No** (SMART-CHOICE3, 2025; HOST-EXAM, 2022)
- Vs. apixaban for subclinical a-fib: **No** (ARTESIA, 2024)
- Vs. P2Y12 for secondary prevention: **No** (JACC meta-analysis, 2023; CAPRIE, 1996)
- Vs. clopidogrel post-DAPT for stroke/TIA: **No** (MATCH, 2004)
- Vs. placebo for primary prevention in older patients: **No, no, no** (ASPREE, 2018; ARRIVE, 2018; ASPREE, 2025)
- Vs. placebo for secondary prevention of colon cancer with PI3K mutations: **Yes!** (ALASCCA, 2025) *[sorry, Alaskans, they're Swedish]*
- For primary prevention in younger patients or those with diagnosed CAD but no prior event: **unclear.**

https://pmid.us/40961426

Practice Changing Update

For most people on aspirin antiplatelet therapy, we should look for a better option. But for some people with colon cancer, it's great!

Question

A 54 y/o male patient with type 2 diabetes comes in for follow-up. Medications include metformin, dapagliflozin, atorvastatin, and losartan 50 mg. Exam shows BP 136/80, p 78, BMI 27. Recent hemoglobin A1C was 5.9%, LDL 60, albumin/creatinine ratio normal.

What do you recommend next?

A. Increase losartan to 100 mg

B. Add tirzepatide

C. Add amlodipine 5 mg

D. Don’t mess with success

BPROAD (HTN in T2DM)

- ACCORD (2010): No benefit with intensive treatment in type 2 DM (4700 pts, 4.7y)
- SPRINT (2015): Intensive treatment helps for high risk but not DM (9361 pts, 3.6 y)
- BPROAD (2025): 12,821 pts > 50 y/o (45% female) with HTN, T2DM + 1 other risk factor randomized to SBP < 120 vs SBP < 140
- 4.2 year f/u: HR for (CV death+ CVA + MI + CHF) 0.79, NNT 227
- Higher rates of symptomatic hypotension (rare) and **hyper**kalemia (common) in intensive treatment arm

https://pmid.us/00000000

Practice Changing Update

There is finally evidence that targeting SBP < 120 is helpful for most patients at high risk of CV disease, *including* those with type 2 diabetes.

Combination drugs for hypertension

- Meta-analysis: 484 trials, 104,176 participants, mean BP 154/100
- Monotherapy: 8.7 mmHg + 1.5 mmHg per doubling of dose
- Combination therapy: 14.9 mmHg + 2.5 mmHg per doubling of dose
- Triple therapy is even more potent

https://pmid.us/40885583

Practice Changing Update

When treating hypertension, it is more effective to use low doses of multiple drugs than escalate a single agent.

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What do you recommend next?

A. Increase losartan to 100 mg

B. Add tirzepatide

C. **Add amlodipine 5 mg**

D. Pat them on the back and don't mess with success

Question

A 47 y/o male patient with prior unprovoked left leg DVT comes in for follow-up. 3 months ago he decided to continue rivaroxaban indefinitely; he has now been on 20 mg daily for six months. He would like to have the best balance of recurrent thrombosis and bleeding risk. Exam shows BP 122/78, p 84, BMI 28. There are no edema or post-phlebitic changes in the left leg.

What do you recommend next?

A. Stop rivaroxaban and start aspirin

B. Decrease rivaroxaban to 10 mg daily

C. Switch to apixaban 2.5 mg bid

D. Continue rivaroxaban 20 mg daily

Dose Reduced Treatment in Unprovoked DVT

- Patients with unprovoked or recurrent DVT are at higher risk of recurrence whenever they stop anticoagulation
- Extending anticoagulation reduces DVT risk at the cost of increased bleeding risk
- Open label RCT of 2768 pts at high risk of recurrence already on full-dose anticoagulation for 6-24 months
- Randomized to low-dose (apixaban 2.5 bid/rivaroxaban 10 qd) vs full-dose DOAC
- Slight increase in VTE (2.2 vs 1.8%, NNH 250) but larger decrease in bleeding (9.9 vs. 15.2%, NNT 19)
- Sibling study in cancer patients had similar results

https://pmid.us/40023651, https://pmid.us/40162636

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What do you recommend next?

A. Stop rivaroxaban and start aspirin

B. **Decrease rivaroxaban to 10 mg daily**

C. Switch to apixaban 2.5 mg bid

D. Continue rivaroxaban 20 mg daily

Practice Changing Update

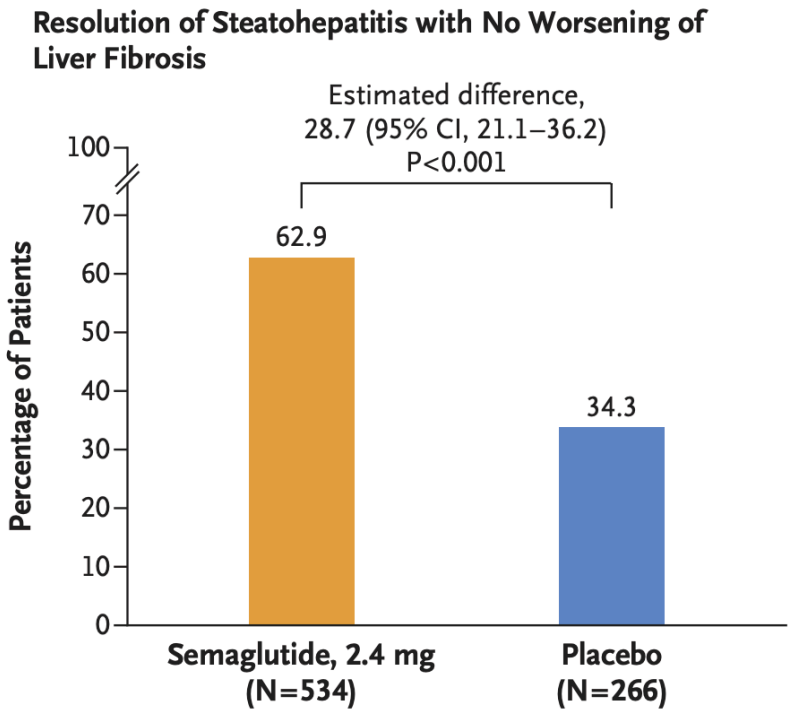
For patients with unprovoked VTE or ongoing risk factors, low-dose DOACs after six months provide a good balance of VTE prevention and bleeding risk.

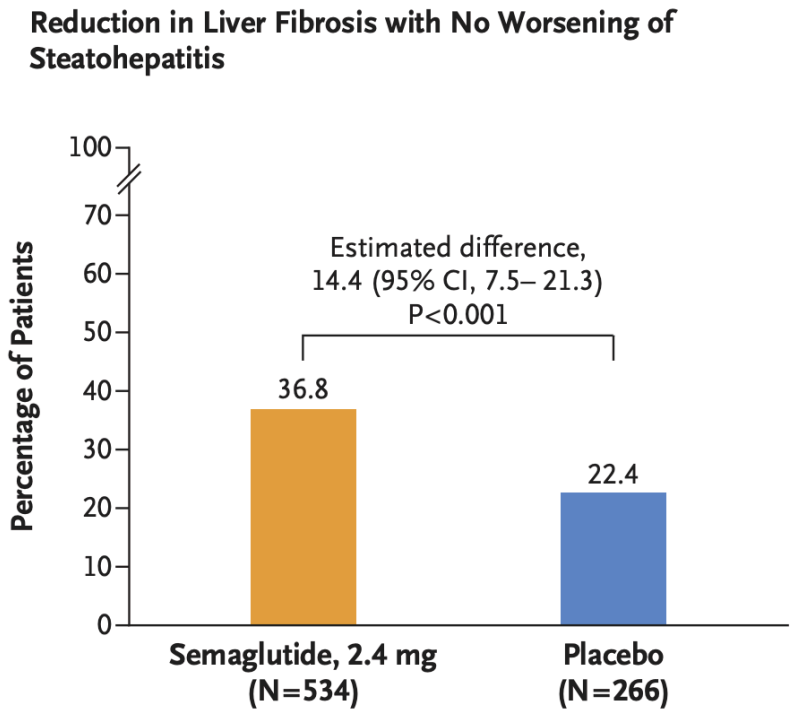
Anything else...?

A few points on MASH...

Semaglutide for Metabolic Dysfunction Associated Steatohepatitis

- Phase 3 multicenter placebo controlled double blind RCT
- Population: 800 patients with biopsy-defined MASH and fibrosis stage 2-3
- Intervention: Weekly SQ semaglutide (SG) at 2.4 mg vs placebo (P) for 72 weeks
- Measures: resolution of steatohepatitis and reduction in liver fibrosis





Results:

Resolution of steatohepatitis with no worsening of liver fibrosis
62.9% (SG) vs. 34.3% (P) (P<0.001)

Reduction in liver fibrosis with no worsening steatohepatitis
36.8% (SG) vs. 22.4% (P)(P<0.001)

https://pmid.us/40305708

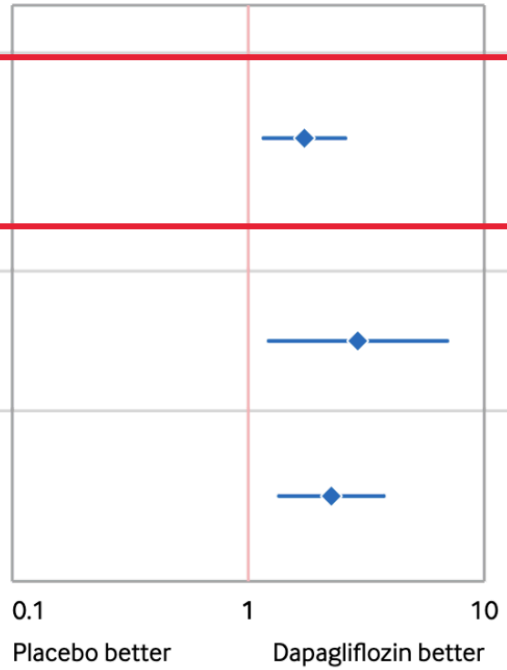
Practice Changing Update

Recommend using semaglutide *(or tirzepatide, NEJM 2024)* for management of metabolic associated steatohepatitis in patients with fibrosis stage 2-3

Dapagliflozin for Metabolic Dysfunction Associated Steatohepatitis

- Multicenter placebo controlled double blind RCT
- Setting: six tertiary hospitals in China
- Population: 154 adults with biopsy diagnosed MASH (with or without T2DM)
- Intervention: Daily 10 mg oral dapagliflozin (DG) vs placebo (P) for 48 weeks
- **Primary measure**: MASH improvement without worsening fibrosis. Improvement defined using non-alcoholic fatty liver disease activity (NAS) score

Endpoint	Responses in placebo group (%)	Responses in dapagliflozin group (%)	Risk ratio	Risk ratio (95% CI)	P value
Primary endpoint					
MASH improvement without worsening of fibrosis	23 (30)	41 (53)		1.73 (1.16 to 2.58)	0.006
Comfirmatory secondary endpoints					
MASH resolution without worsening of fibrosis	6 (8)	18 (23)		2.91 (1.22 to 6.97)	0.01
Fibrosis improvement without worsening of MASH	15 (20)	35 (45)		2.25 (1.35 to 3.75)	0.001



Results:

MASH improvement without worsening of fibrosis 53% (DG) vs. 30% (P) (P<0.006)

https://pmid.us/40467095

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- Population: 154 adults with biopsy diagnosed MASH (with or without T2DM)
- Intervention: Daily 10 mg oral dapagliflozin (DG) vs placebo (P) for 48 weeks
- **Secondary measures**: 1) MASH **<u>resolution</u>** without worsening of fibrosis, 2) Fibrosis improvement without worsening MASH

Endpoint	Responses in placebo group (%)	Responses in dapagliflozin group (%)	Risk ratio (95% CI)	P value
Primary endpoint				
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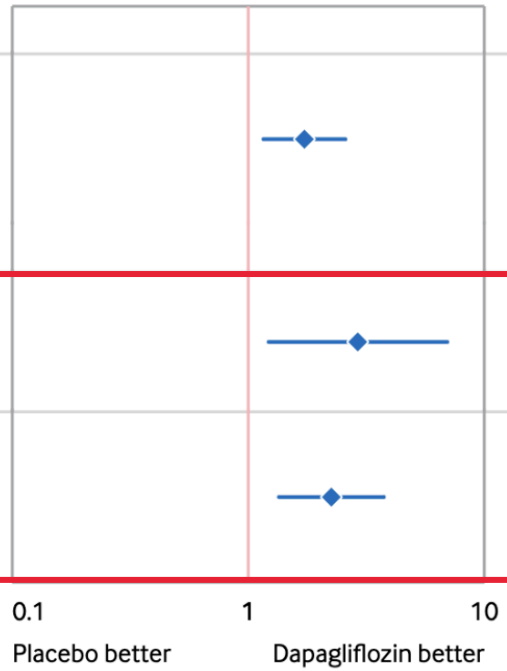

Results:

MASH resolution without worsening of fibrosis 23% (DG) vs. 8% (P) (P<0.01)

Fibrosis improvement without worsening MASH 45% (DG) vs. 20% (P)(P<0.001)

https://pmid.us/40467095

Practice Changing Update

Consider using dapagliflozin for management of metabolic associated steatohepatitis, even in patients without type 2 diabetes...

...Although you may consider using GLP-1s first

Injectable PrEP

- Lencapavir is an injectable HIV capsid inhibitor dosed subcutaneously every 6 mos
- Trial of 3265 cis-men, trans and non-binary people ≥ 16 y/o who have condomless receptive anal sex (global study, 20% US and wide ethnic distribution)
- 1 year of f/u: 2 HIV infections in intervention group vs. 9 in F/TDF control (89% risk reduction, NNT 120)
- Also works in cis-women but data lower quality
- The catch: $20-40K per year
- Once-yearly dosing being studied

https://pmid.us/00000000

Practice Changing Update

Injectable PreP is **a lot** more effective than oral—it's worth trying to get it for high-risk patients

Blood test for Alzheimer's

- Which patients with MCI need further workup for Alzheimer’s?
- Study of 512 patients with a mix of dementia, MCI, and intact cognition
- Compared blood test to PET results as gold standard
- Using two-cutoff approach, sensitivity/specificity both around 95%, but 10-20% of results indeterminate
- FDA approved in May; beware devilish details, especially eGFR < 45

https://pmid.us/40156286

Practice Changing Update

A blood test for p-tau217/amyloid-ß42 may help identify which patients with cognitive impairment should have further testing for Alzheimer’s.

Thanks!

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