Updates in Primary Care

Addie H McClintock, MD *ahearst@uw.edu, @McClintockMD*
Chris Knight, MD, FACP *cknight@uw.edu, @clknight*

SGLT2-inhibitors

Empagliflozin

- **We already know:**
- Empagliflozin reduces hospitalization for heart failure and cardiovascular death in people with heart failure with ***reduced*** EF with or without diabetes.
- Packer, 2020

Empagliflozin

- **New this year:**
- Reduces hospitalization for heart failure and cardiovascular death in people with heart failure with ***preserved*** EF (>40%)
- Improves health-related quality of life
- Reduces all cause mortality

EMPEROR-Preserved Trial

- 5,988 patients with:
  - Class II-IV Heart failure
  - EF >40%
- Randomized to 10 mg Empagliflozin vs Placebo
- Primary outcome:
  - composite of cardiovascular death or hospitalization for heart failure
- Secondary outcomes:
  - Number of hospitalizations for heart failure (including first and recurrent)
  - Rate of decline of eGFR

https://pmid.us/34449189/

EMPEROR-Preserved Trial- Primary Outcome

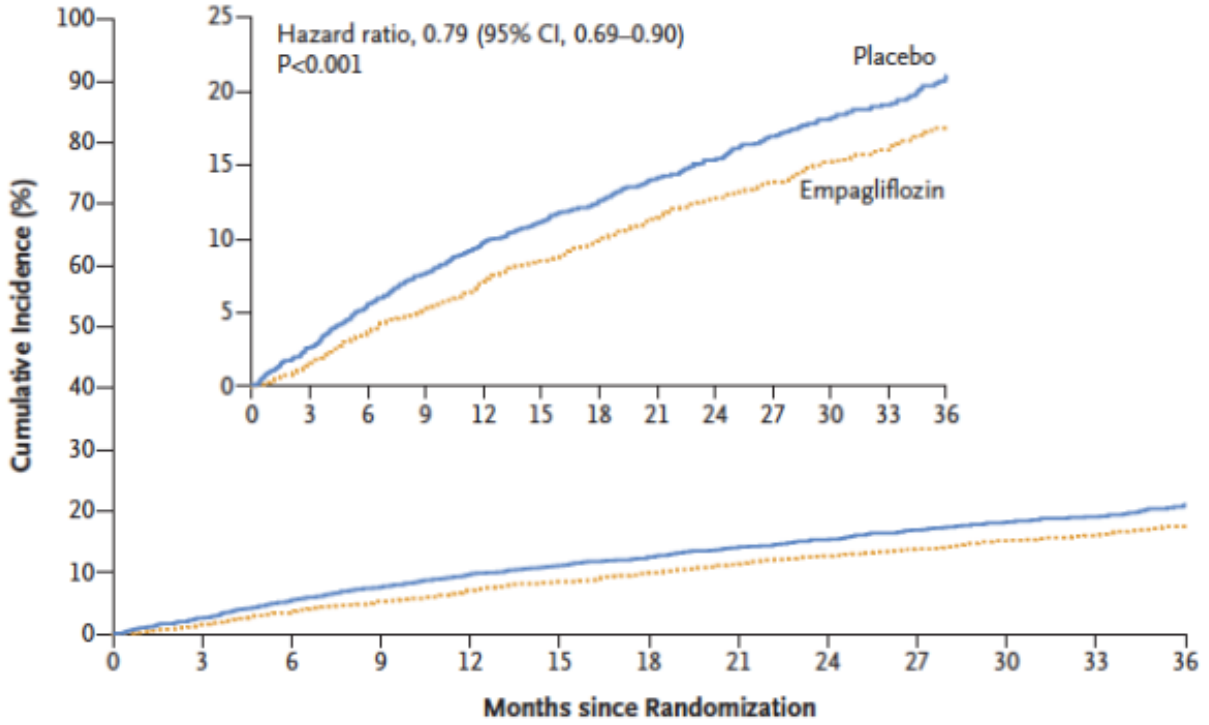

Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.

The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the same data on an expanded y axis.

- Events occurred in:
  - 415 (13.8%) patients in empagliflozin group
  - 511 Placebo group (17.1%)
- Effect driven largely by reduction in hospitalizations
- Effect seen in patients with and without DMII

EMPEROR-Preserved Trial

Table 2. Primary and Secondary Cardiovascular Outcomes.*

Variable	Empagliflozin (N=2997)		Placebo (N=2991)		Hazard Ratio or Difference (95% CI)	P Value
		events per 100 patient-yr		*events per 100 patient-yr*		
Primary composite outcome — no. (%)	415 (13.8)	6.9	511 (17.1)	8.7	0.79 (0.69–0.90)	<0.001
Hospitalization for heart failure	259 (8.6)	4.3	352 (11.8)	6.0	0.71 (0.60–0.83)	
Cardiovascular death	219 (7.3)	3.4	244 (8.2)	3.8	0.91 (0.76–1.09)	

Empagliflozin and Health Related Quality of Life in HFpEF

- EMPEROR-preserved dataset, same methods
- Research questions:
  - Evaluate the efficacy of empagliflozin of health-related quality of life in patients with HFpEF
  - Whether the clinical benefit varies according to baseline health status
  - Health Related Quality of Life Measure (Kansas City Cardiomyopathy Questionnaire, KCCQ) and baseline and 12, 32 and 52 weeks
  - KCCQ domains:
    - Total Symptom Score, TSS (frequency and burden)
    - Clinical Summary Score, CSS (physical limitations)
    - Overall Summary Score, OSS (CSS + social limitations)

https://pmid.us/33420498/

Empagliflozin reduced CV death or HF hospitalization across the range of baseline HRQoL

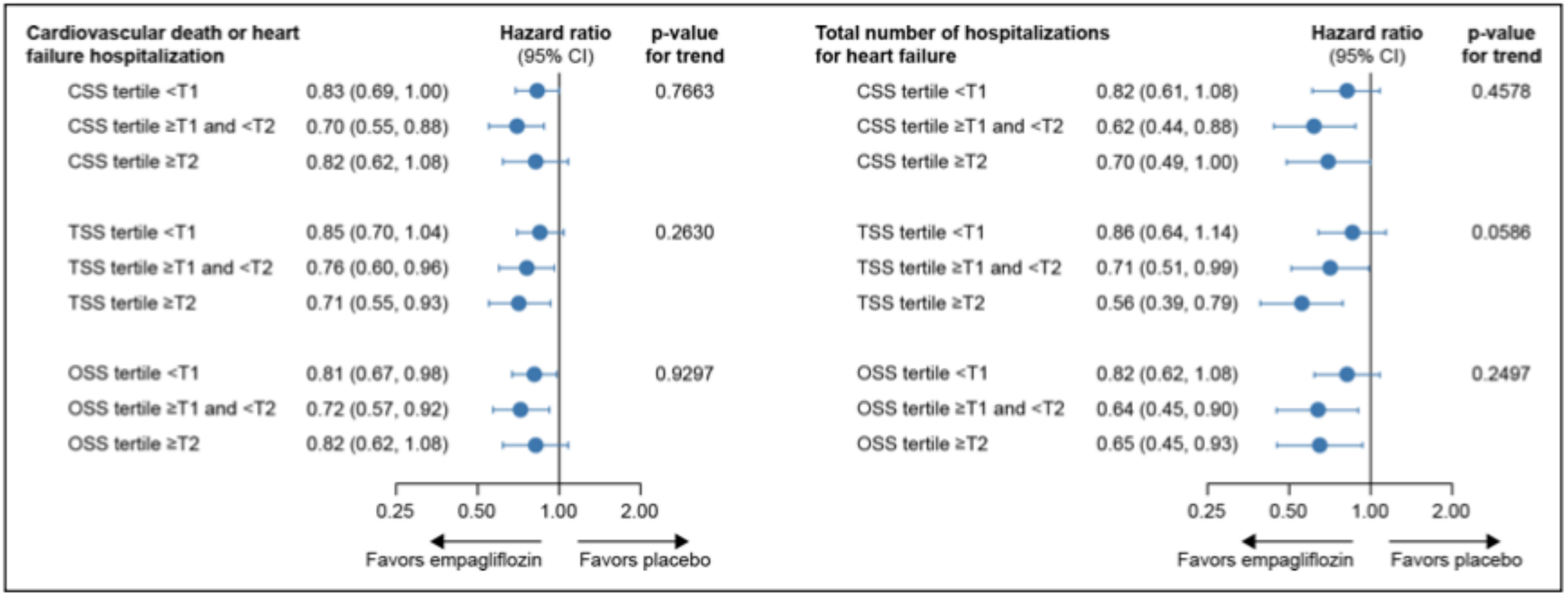

Figure 1. Effect of empagliflozin on outcomes by baseline KCCQ tertiles.

CSS indicates Clinical Summary Score; KCCQ, Kansas City Cardiomyopathy Questionnaire; OSS, Overall Summary Score; and TSS, total symptom score. *P value from trend test assuming ordering of the KCCQ tertiles

Empagliflozin improved HRQoL, sustained at least 1 year

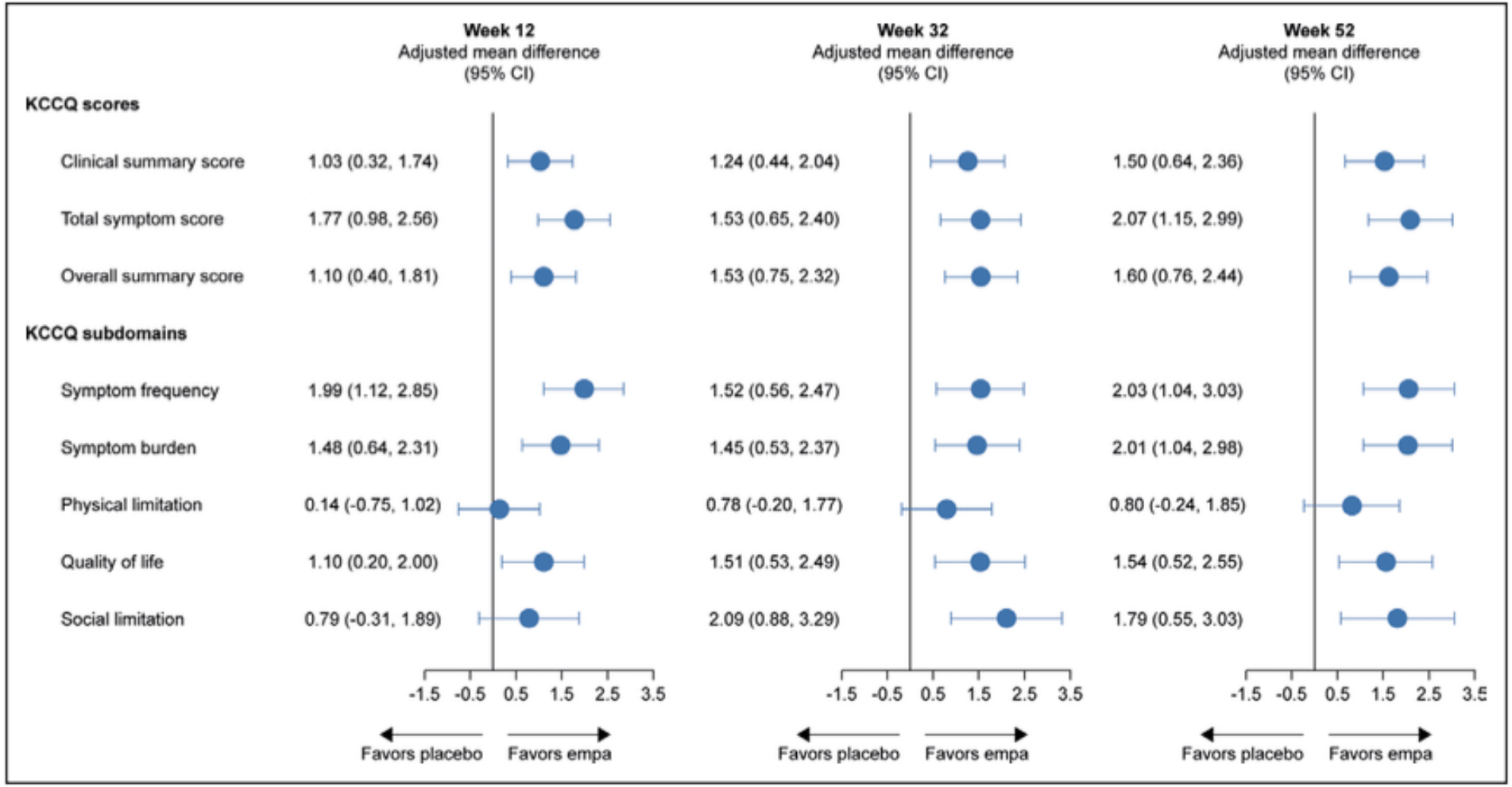

Figure 3. Adjusted mean difference in KCCQ-CSS, TSS, OSS, and subdomains for empagliflozin versus placebo at 12, 32, and 52 weeks.

CSS indicates Clinical Summary Score; empa, empagliflozin; KCCQ, Kansas City Cardiomyopathy Questionnaire; OSS, Overall Summary Score; and TSS, Total Symptom Score.

SGLT2 inhibitors and all cause mortality

- Meta-analysis including 21 trials
- Selection criteria
  - Randomized trials
  - >100 patients enrolled in each arm
  - 52 weeks duration of treatment (minimum)
  - Comparing SGLT2-inhibitor with placebo OR any other non SGLT2-inhibitor drug

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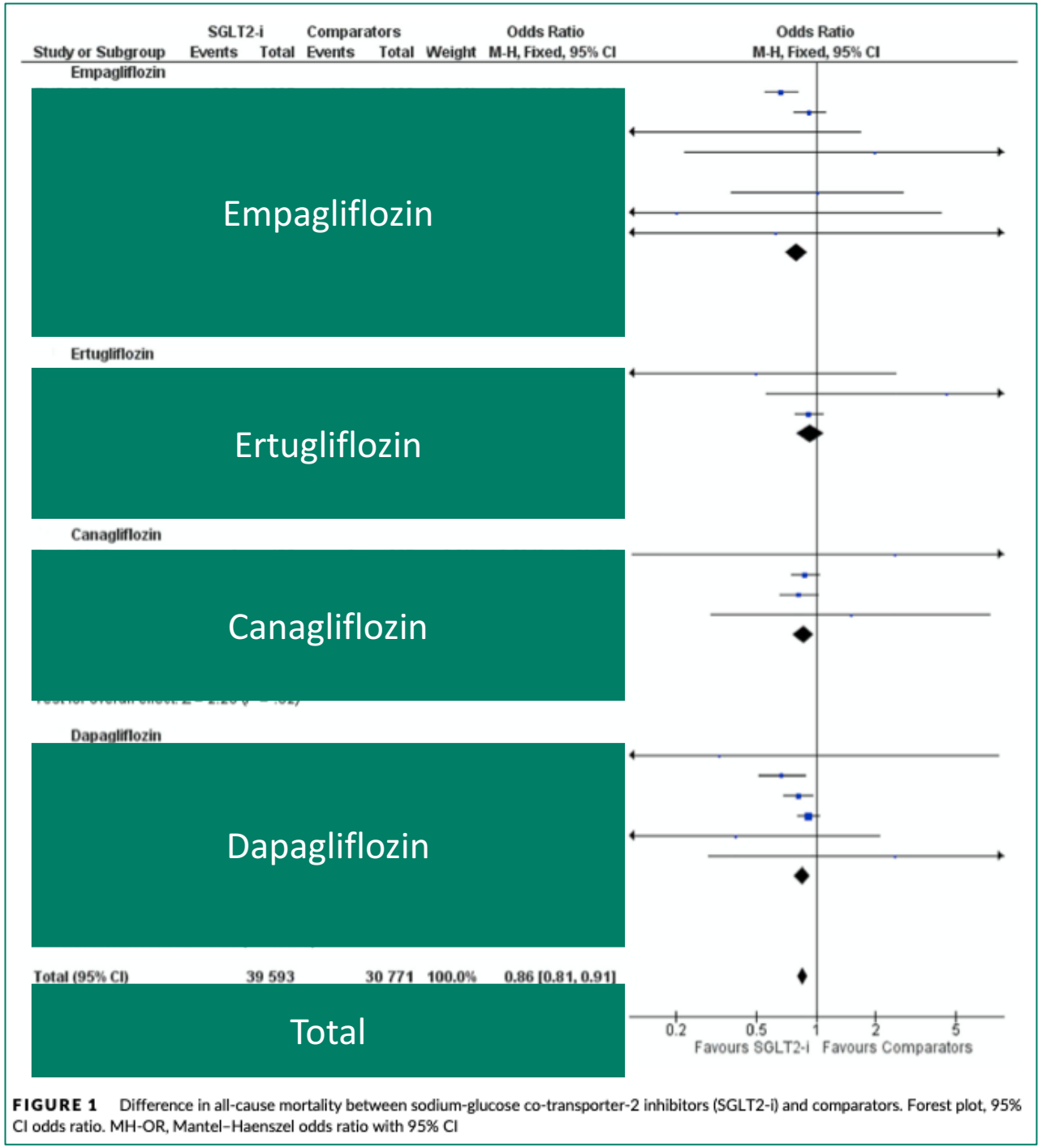


FIGURE 1 Difference in all-cause mortality between sodium-glucose co-transporter-2 inhibitors (SGLT2-i) and comparators. Forest plot, 95% CI odds ratio. MH-OR, Mantel–Haenszel odds ratio with 95% CI

- Effect on all cause mortality statistically significant for empagliflozin, canagliflozin, dapagliflozin
- NOT significant for Ertugliflozin

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

- Recommendations to use SGLT 2 inhibitors for HF, regardless of degree of EF impairment.

PMID: 35363499

Empagliflozin- Recap

- **Take home points:**
- Reduces hospitalization for heart failure and cardiovascular death in people with heart failure with ***preserved*** EF (>40%)
- Improves health-related quality of life in people with HFpEF (with and without DMII)
- Reduces all cause mortality
- Should be used in patients with heart failure, regardless of whether their EF is reduced or whether they have diabetes

Discontinuing Statins in people over 75 years old

Statin discontinuation

- **Background:**
  - As health status and goals of care change in older persons, there is little evidence to guide a decision about whether to stop or continue a statin.
- **New this year:**
  - Statin discontinuation in adults 75 years old and older is associated with a higher rate of MI, stroke, TIA, revascularization, or death due to MI/CVA

Statin discontinuation

- **Population:**
  - Adults 75 years or older who had been on a statin for at least 5 years as of Jan 2011
  - N= 67,418 long term statin users

- **Study design:**
  - Cohort study in Denmark
  - Followed for up to 6 years
  - Outcome: rate of occurrence of: MI, stroke, TIA, coronary revascularization and death from MI or CVA
  - Separate analysis for primary (47%) and secondary prevention (59%)

Figure 1. Cumulative Incidence Curve for the Outcome of Major Adverse Cardiovascular Events in the Primary Prevention Cohort

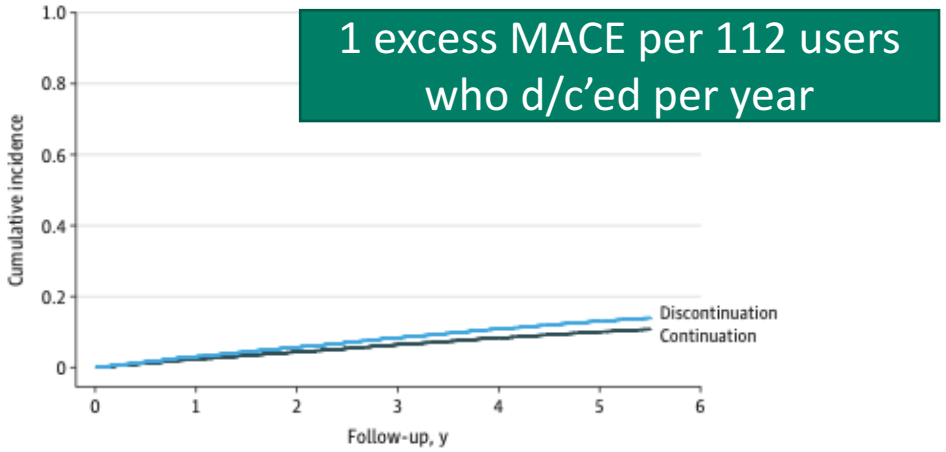
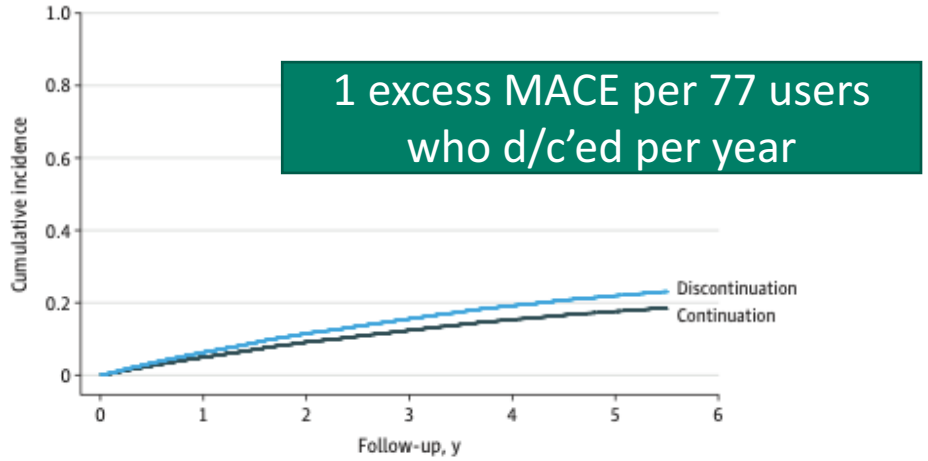


Figure 2. Cumulative Incidence Curve for the Outcome of Major Adverse Cardiovascular Events in the Secondary Prevention Cohort



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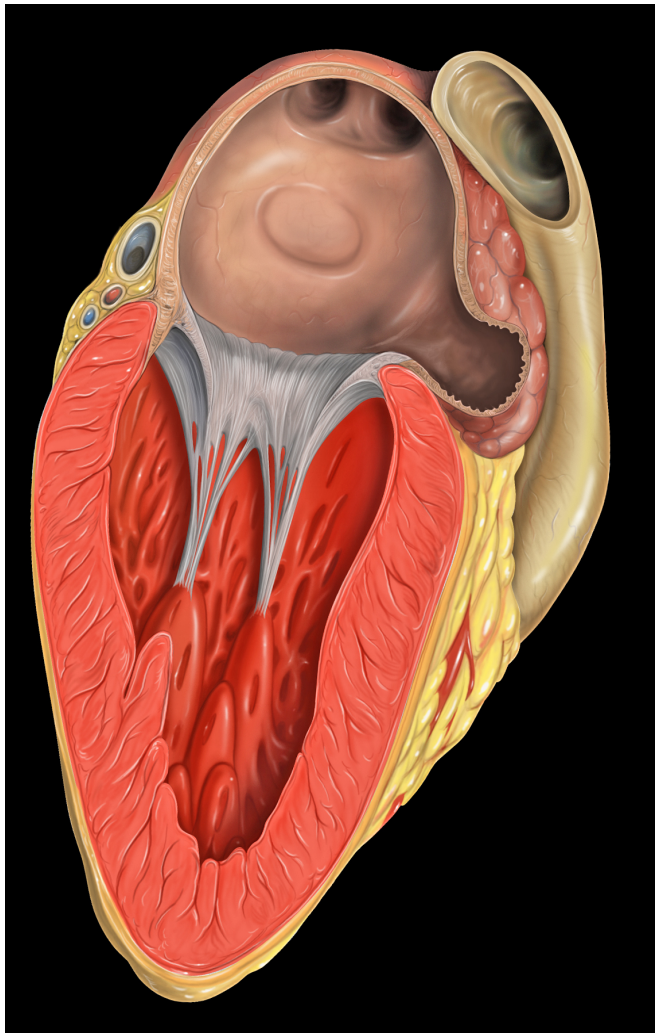
Take home point:

- We should continue statins in older people who aren’t experiencing adverse effects

Interventions for atrial fibrillation

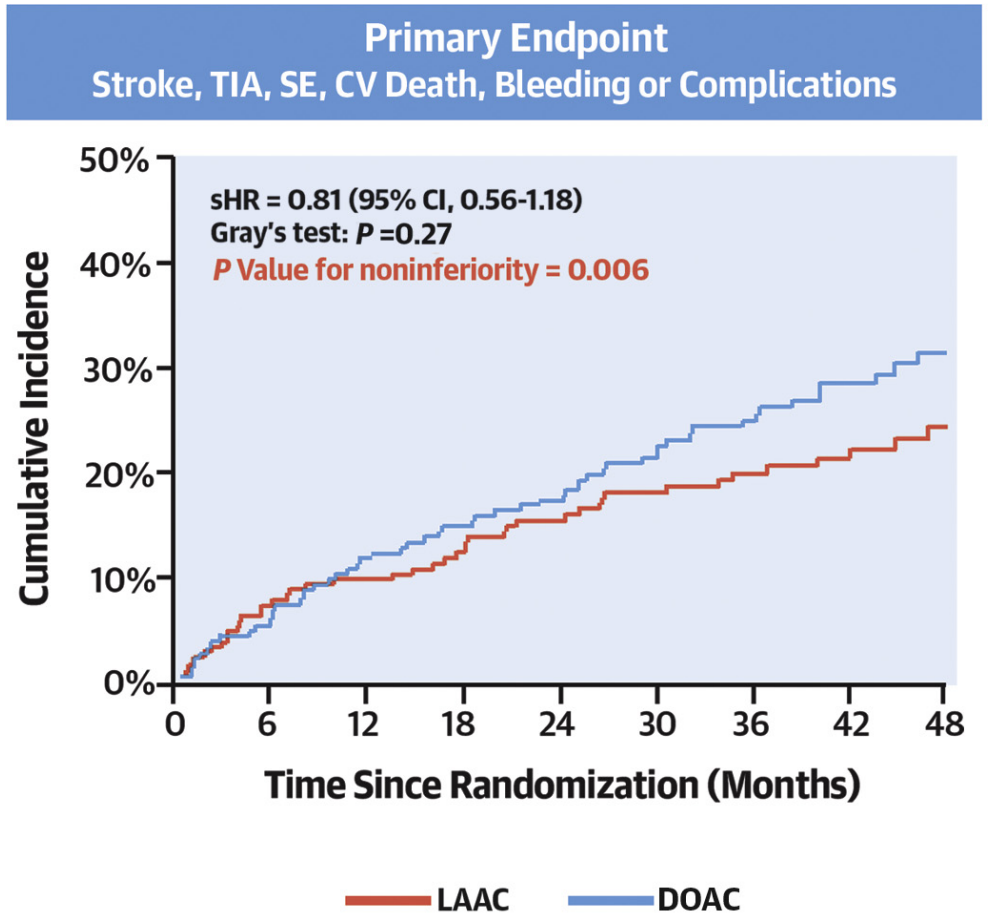
Background



- AFFIRM (2002) established that there was no benefit to rate control vs rhythm control in atrial fibrillation; focus shifted to preventing strokes with anticoagulation
- Technology for rhythm control and stroke prevention has improved significantly in the last 20 years
- Is it time to look again at how we manage atrial fibrillation?

Image: Patrick J. Lynch, Wikipedia; https://creativecommons.org/licenses/by/2.5/

Left atrial appendage closure (LAAC) for stroke prevention in AF



- Question: what are the long-term outcomes of LAA closure devices?
- 4-year follow-up report of open-label randomized trial of LAAC (Watchman or Amulet) vs DOAC in 407 patients (mean age 73, 65% male) with CHADS2-VASc ≥ 3 and HASBLED ≥ 2
- Outcomes: Stroke/TIA/embolism, CV death, bleeding, complications
- Noninferior for stroke/TIA/embolism
- Lower rates of non-procedural bleeding in the LAAC group

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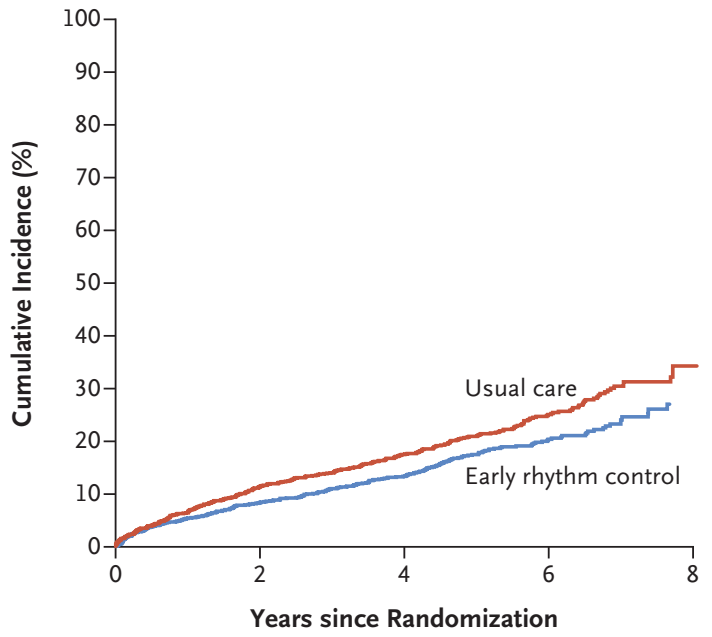
Early rhythm control in AF



No. at Risk					
Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26

Figure 2. Aalen–Johansen Cumulative-Incidence Curves for the First Primary Outcome.

The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome.

- Question: For patients with new AF, is rhythm control better than rate control?
- Open-label RCT of 2789 patients (mean age 70, 54% male) with new onset AF (median 36 days) randomized to rhythm control vs usual care
- Rhythm control patients were monitored with remote ECGs; 54% of patients were in SR at study enrollment
- Most rhythm control pts treated with AADs; ablation rate 19% at 2 yr
- 90% of both groups were anticoagulated for the entire study
- 20% reduction in composite outcome (CV death, stroke, hospitalization for CHF or ACS) for rhythm control arm

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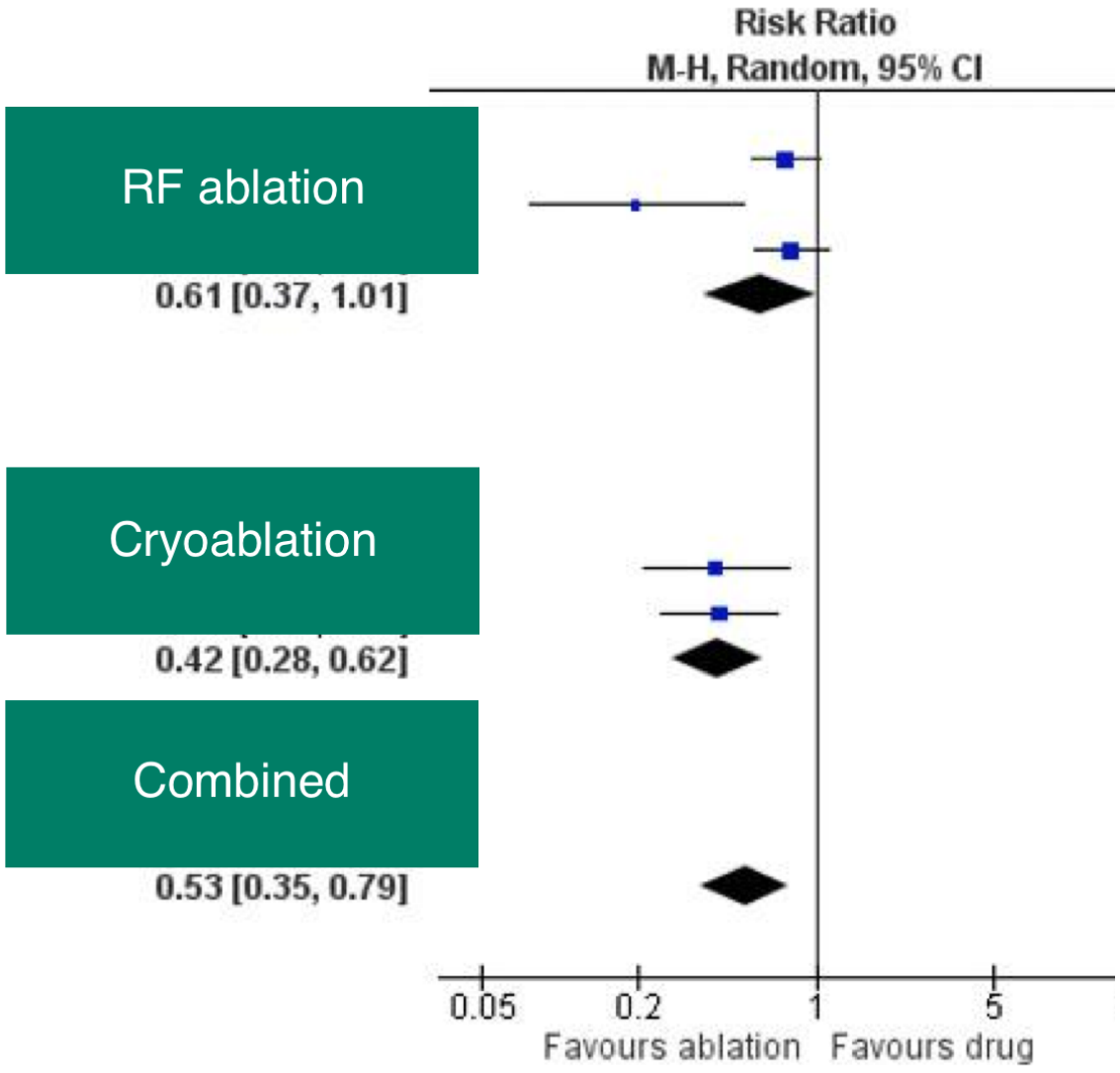
Ablation in symptomatic paroxysmal AF



- Question: For patients with *symptomatic* PAF, what is the best rhythm control?
- Meta-analysis of 6 open-label RCTs of ablation vs antiarrhythmic drugs (AADs)
- 47% reduction in symptomatic arrhythmia recurrence (NNT 6)
- 35% reduction in health care resource use (NNT 7)
- NS trend toward lower adverse events in ablation group
- Caution: 70% male, mean age 56, few comorbidities (except HTN)

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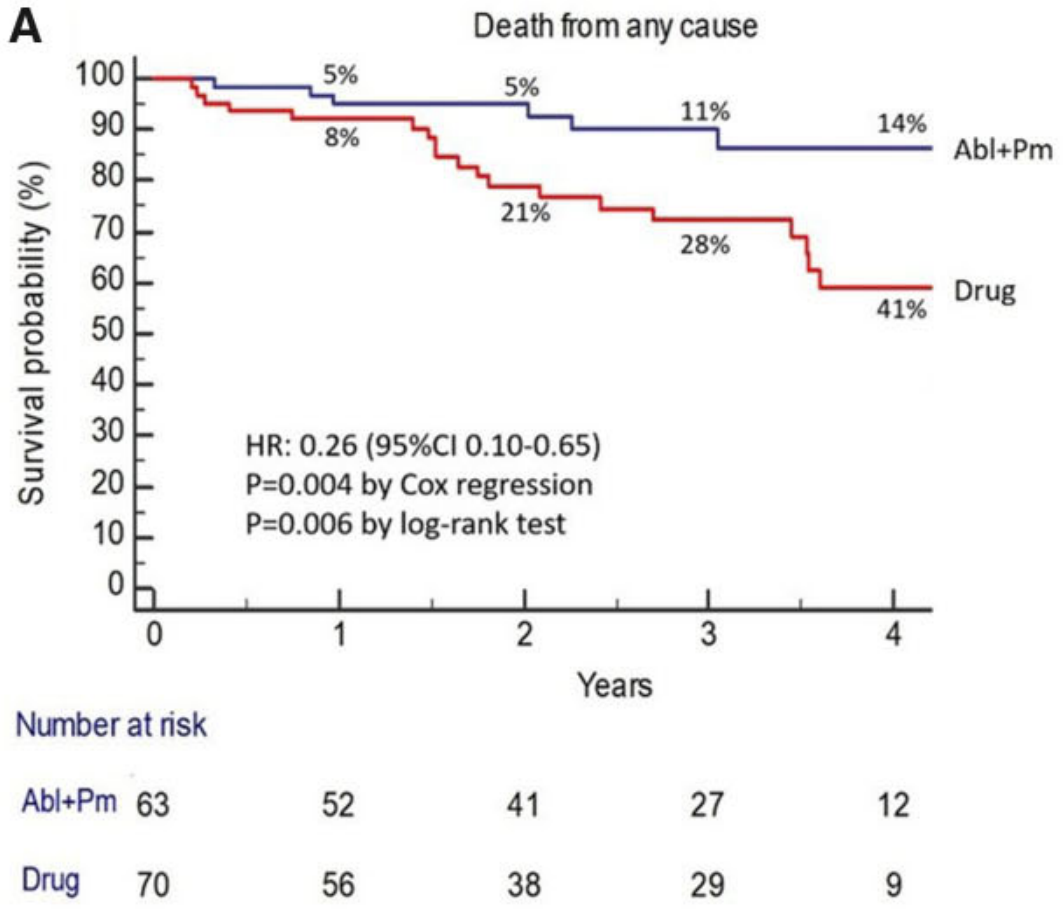
Devices in AF with CHF



- Question: is AV nodal ablation + biventricular pacing helpful in patients with both AF and CHF?
- APAF-CRT: Open label RCT of 133 patients (mean age 73 y/o, 53% male) with symptomatic AF, narrow QRS, prior hospitalization for CHF
- Randomized to AV nodal ablation + BiV pacing vs usual pharmacologic mgmt.
- 71% reduction in all-cause mortality, NNT 5 to prevent one death
- Caution: small trial, few deaths

https://pmid.us/34453840/

Take home points: AF

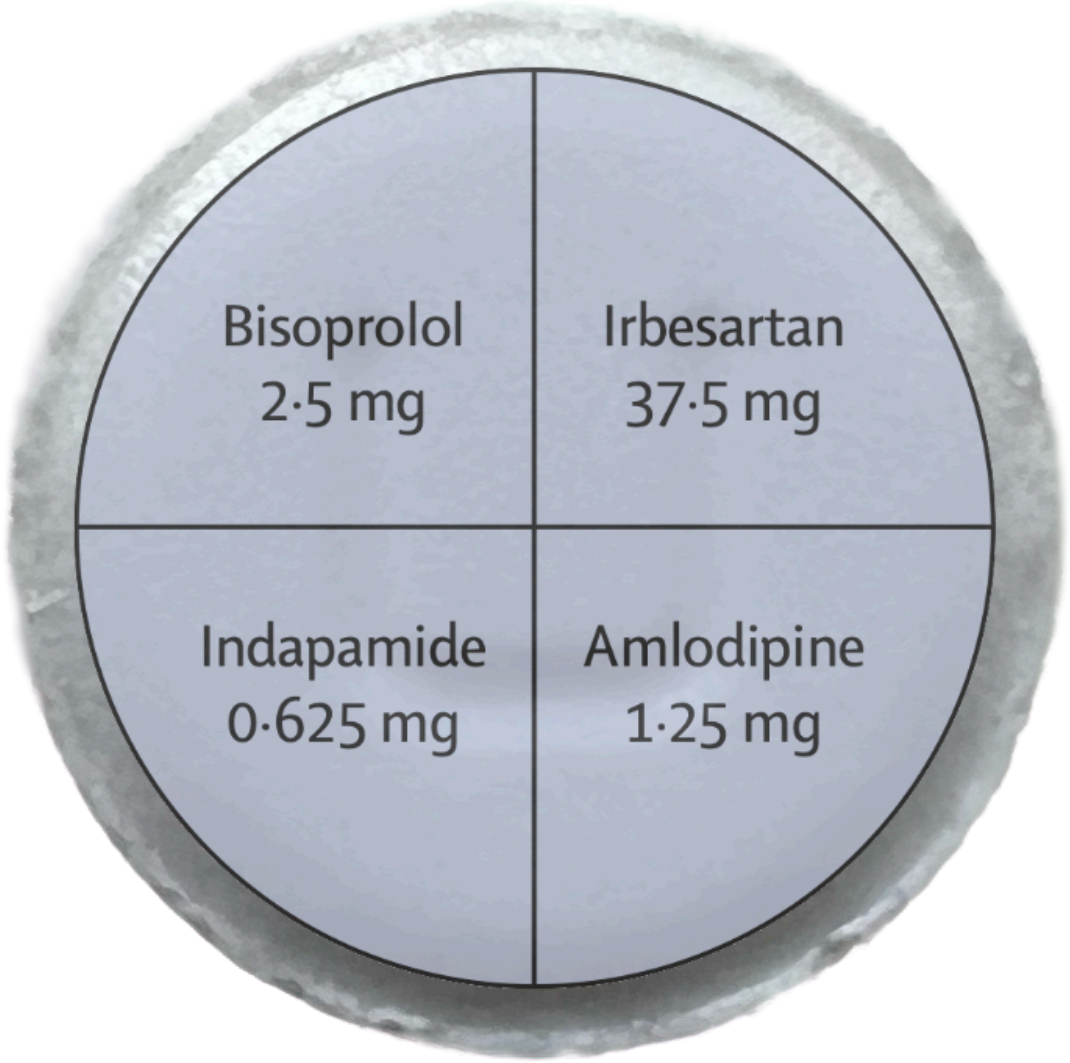
- For patients at high risk of both stroke and bleeding, we should consider left atrial appendage closure devices as an alternative option
- Patients with new (ideally <1 month) AF may benefit from a more aggressive rhythm control strategy
- Interventions are effective for specific subgroups with atrial fibrillation:
  - Symptomatic PAF: Ablation more effective at controlling symptoms and reducing healthcare utilization in a young, healthy, disproportionately male cohort
  - AF with CHF: ablation + pacing = mortality benefit
- **Bottom line: more AF patients now stand to benefit from a proactive cardiologist**

Hypertension: How many meds?

Background

- ACC/AHA and ESC/ESH guidelines for treatment of hypertension both advocate starting with combination therapy for most patients
- These recommendations were based on expert opinion (ACC/AHA) and inferences from adherence studies (ESC/ESH) showing that more pills = less adherence
- Direct evidence of clinically relevant differences with combination therapy has been scant

Polypill for hypertension



- Question: Does a combination pill with low doses of multiple antihypertensives outperform a single agent?
- Double-blind RCT randomized 591 patients (mean age 58 y/o, 60% male) to initial therapy with a “quadpill” vs. irbesartan 150 mg alone
- Pts had to be either untreated or on monotherapy at study entry; baseline BP was 153/89 in office, 144/84 on ABPM

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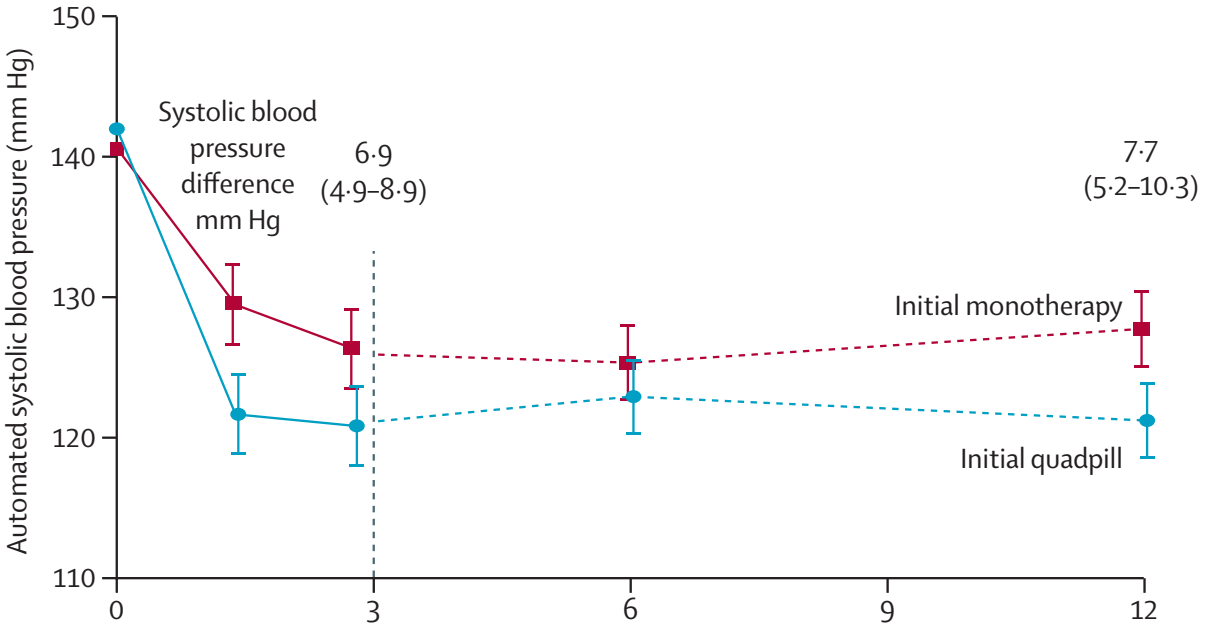
Polypill for hypertension



- At one year 79% of polypill group was on one pill vs. 57% of irbesartan monotherapy group
- BP was 8/6 points lower in polypill group
- 53% of polypill group achieved target of <120/80 vs 25% of monotherapy group
- More dizziness in intervention group (31% vs 25%)
- **Take home**: low dose combination therapy is more effective at lowering BP than monotherapy

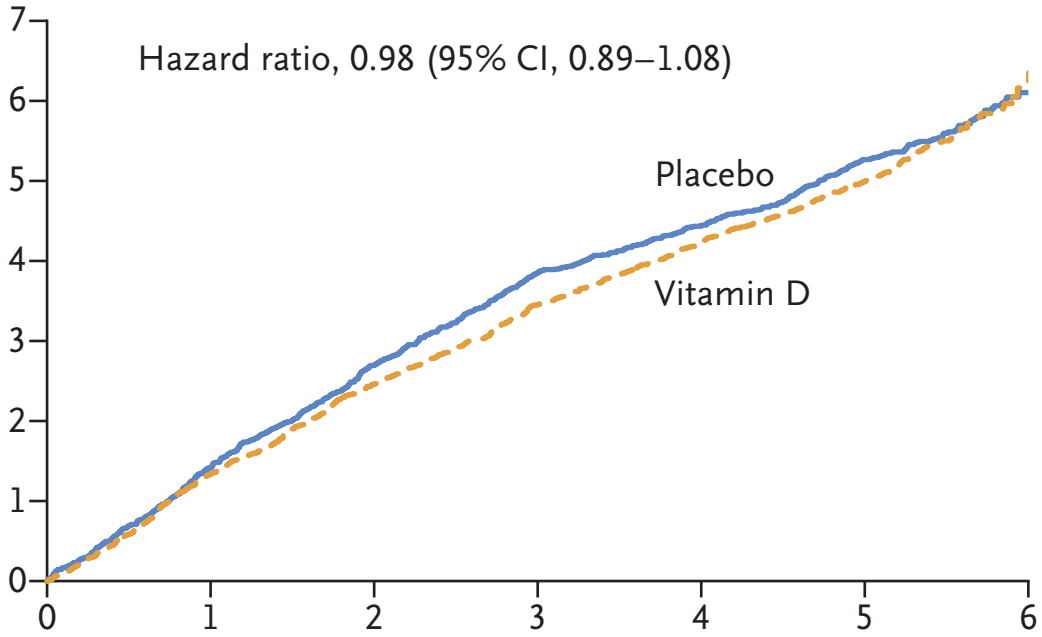
Vitamin D Supplementation

Background

- Meta-analyses of vitamin D supplementation in postmenopausal women with osteoporosis show moderate reductions in non-vertebral fractures, no change in vertebral/hip fractures
- Vitamin D supplementation in patients with low vitamin D levels (< 20 ng/ml) has not been shown to reduce mortality, fracture risk, or fall risk
- Who should be taking vitamin D?

Photo: Wisconsin Historical Museum

Vitamin D supplementation in healthy adults



- Large RCT: 25,871 US participants, included men ≥ 50 y/o and women ≥ 55 y/o; excluded patients with cancer and cardiovascular disease; 50% male, 20% Black
- Randomized to 2000 IU (50 mcg) cholecalciferol daily vs placebo
- No change in fracture risk over 5.3 years of follow-up

https://pmid.us/30907953/

Vitamin D supplementation in healthy adults: Conclusions

- Vitamin D supplementation has only been shown to benefit patients with osteoporosis
- The primary value of treating mild vitamin D deficiency (10-20 ng/ml) is in preventing severe vitamin D deficiency
- We should avoid recommending vitamin D supplements in healthy patients
- **Postscript:** US Preventive Services Task Force found no evidence of meaningful benefit for other vitamin supplements, either

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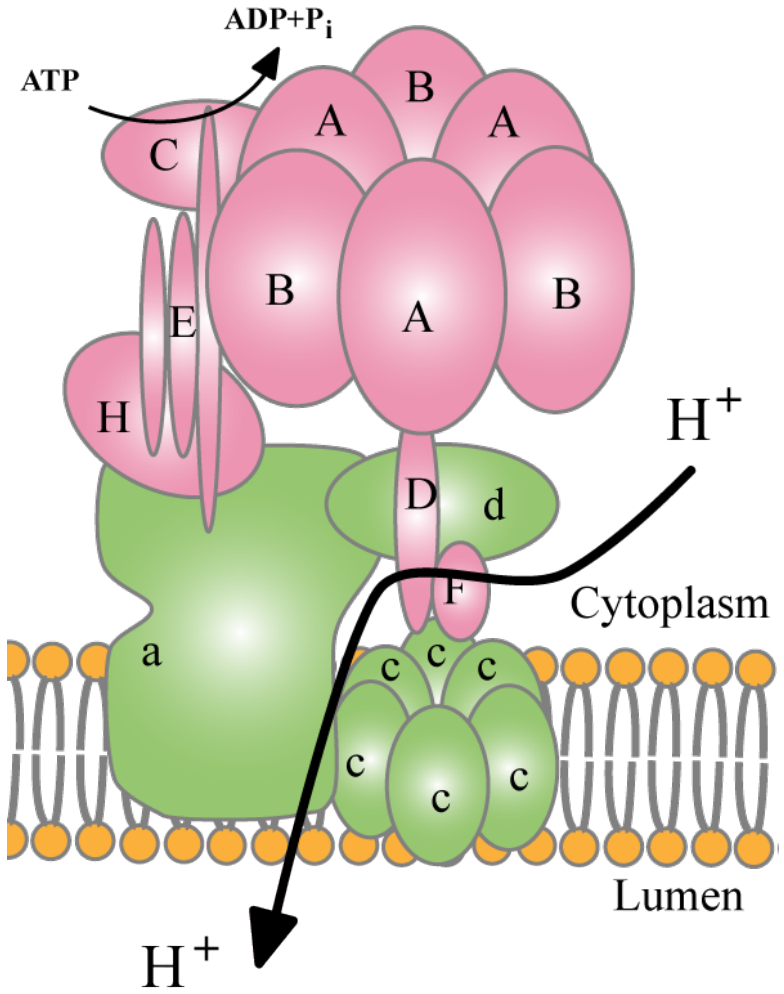
Time to stop PPIs?

Background



- Proton pump inhibitors are extremely commonly used and are available OTC in the United States
- Observational studies have linked PPI use with many adverse effects, including *C. difficile* infection, hypomagnesemia, microscopic colitis, and B12 deficiency, but causality hasn't been established
- Are we overusing PPIs? Are there situations in which we can reduce or stop PPI use?

PPI deprescribing: core principles

- Patients who *don't* need PPIs shouldn't be on them
- Patients who *do* need PPIs shouldn't stop them because of concern for adverse events
- High dose PPIs haven't been studied in chronic conditions: should consider dose reduction in those patients

https://pmid.us/35183361/

PPI deprescribing: specific cases

- **Should continue**
  - Barrett's esophagus
  - Esophageal strictures
  - Significant erosive esophagitis
  - Eosinophilic esophagitis
  - Chronic NSAID/aspirin use in high-risk patients
  - Idiopathic pulmonary fibrosis [weak evidence]
- **Could continue**
  - Symptoms that improve with PPI but recur when they are stopped
- **Could stop**
  - Secondary prevention of peptic ulcer disease in low-risk patients (i.e. no NSAIDs, antiplatelet agents)
- **Should stop**
  - Mild erosive esophagitis
  - Non-ulcer bleeding
  - Steroids without NSAIDs
  - GERD/dyspepsia without trial of deprescribing

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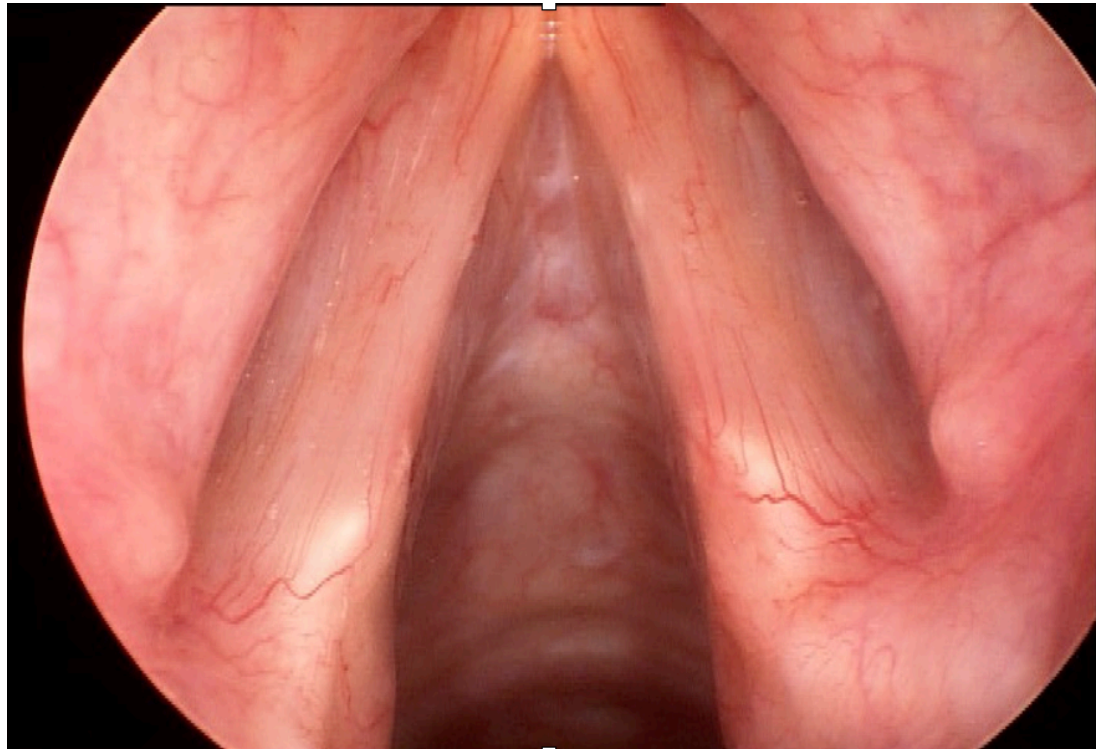
Postscript: laryngeal reflux



- Multiple small RCTs (largely by otolaryngologists) show no benefit to empiric treatment of laryngopharygeal symptoms with PPIs
- But.. most patients had negative laryngoscopy
- Guidelines say that if symptoms clearly improve with PPI and worsen without it, ok to continue

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Tapering Long-Term, High-Dose Opiates

Tapering Opiates

- **We already know:**
  - National prescribing guidelines for long-term opiates for pain management have led to dose tapering, but opiate related mortality continues to rise
  - Taping has been associated with SI, transition to illicit opioids and overdose after tapering

- **Question**:
  - What are the risks of overdose or mental health crisis when opiates are tapered?
  - Are there risks associated with the rate of taper?

Tapering Opiates

- Retrospective medical and pharmacy claims
- 113,618 patients prescribed stable, long-term opiates (no more than 10% adjustments in dose over prior 12 months)
- Individual mean daily dose of at least 50 MME
- Oregon-state commercial and Medicare Advantage plans

Rate of overdose higher with tapering

Table 2. Primary and Secondary Outcomes in a Study of the Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids[a]

Outcome	Tapered[b]		Not tapered[b]		Adjusted incidence rate difference per 100 person-years by tapering status (95% CI)[c,d]	Adjusted incidence rate ratio (95% CI)[c]	*P* value
	No. of events/ total person-years	Adjusted incidence rate per 100 person-years (95% CI)[c]	No. of events/ total person-years	Adjusted incidence rate per 100 person-years (95% CI)[c]			
Overdose[e]							
Entire cohort	2336/22 097	6.3 (5.6-7.0)	10 550/152 194	4.9 (4.7-5.2)	1.4 (0.7-2.1)	1.28 (1.15-1.43)	<.001[f]
Baseline opioid dose, MME/d[g]							.63[h]
50-89	400/5321	4.7 (3.5-5.8)	2699/53 260	3.6 (3.2-3.9)	1.1 (-0.1-2.2)	1.30 (1.01-1.68)	
90-149	489/5524	5.1 (4.1-6.2)	2407/38 994	4.4 (4.0-4.8)	0.7 (-0.4-1.8)	1.43 (1.11-1.75)	
150-299	783/6864	7.8 (6.3-9.3)	3237/38 782	6.1 (5.6-6.6)	1.6 (0.1-3.2)	2.17 (1.70-2.64)	
≥300	664/4388	11.8 (9.9-13.7)	2207/21 159	8.3 (7.5-9.2)	3.4 (1.4-5.5)	3.29 (2.67-3.91)	

https://pmid.us/34342618/

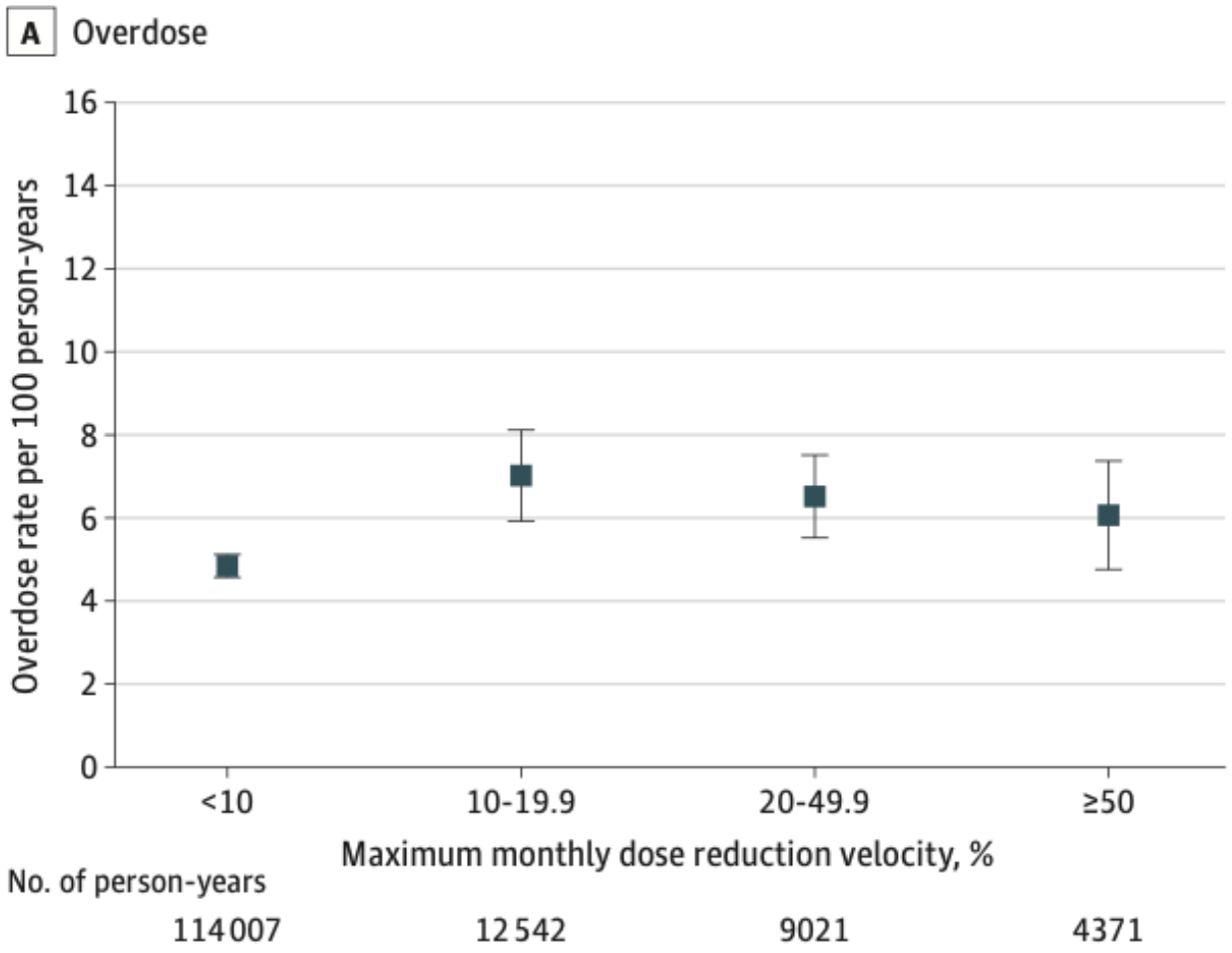
Higher rate of mental health crisis with tapering

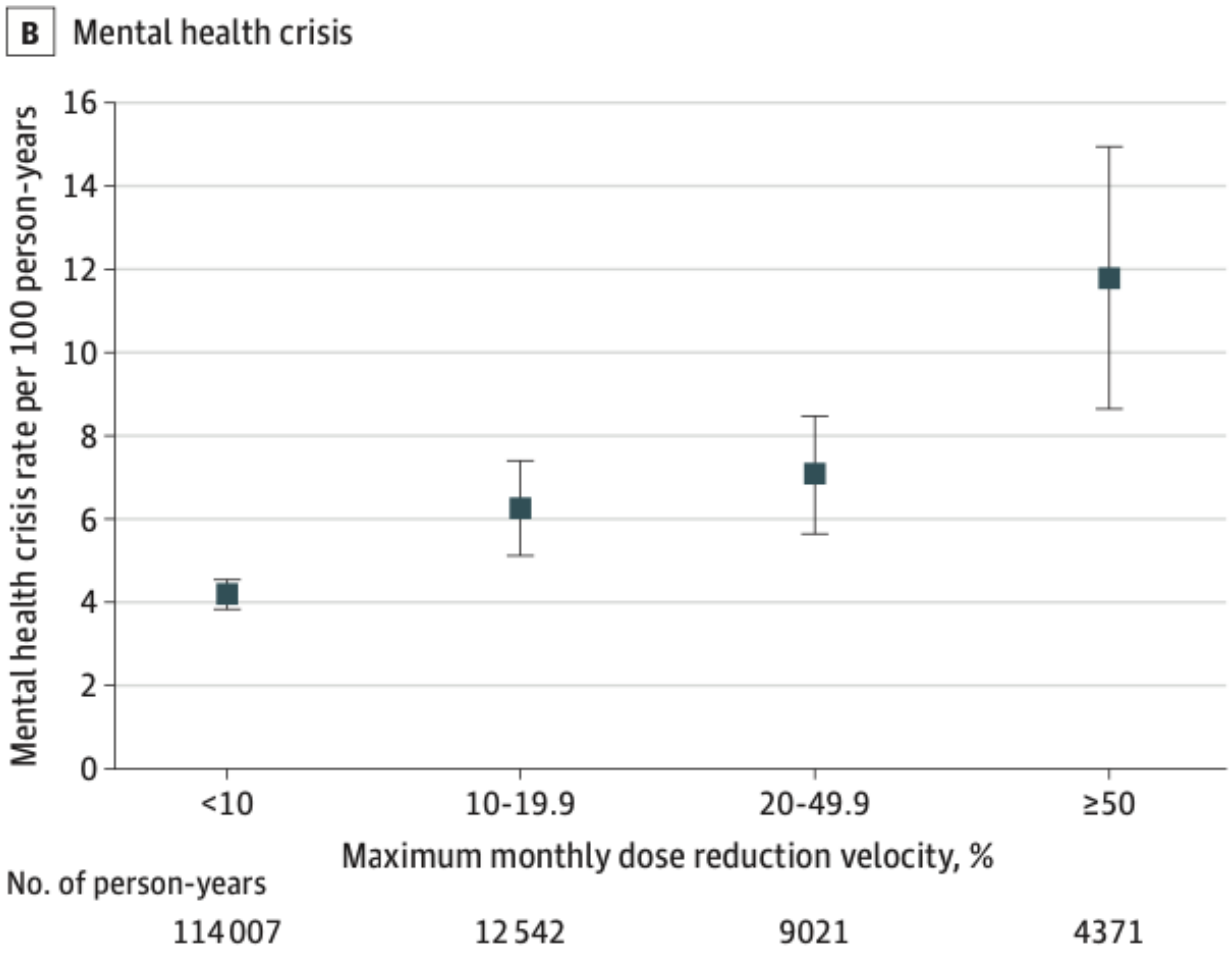
Table 2. Primary and Secondary Outcomes in a Study of the Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids[a]

Outcome	Tapered[b]		Not tapered[b]		Adjusted incidence rate difference per 100 person-years by tapering status (95% CI)[c,d]	Adjusted incidence rate ratio (95% CI)[c]	*P* value
	No. of events/ total person-years	Adjusted incidence rate per 100 person-years (95% CI)[c]	No. of events/ total person-years	Adjusted incidence rate per 100 person-years (95% CI)[c]			
Mental health crisis[i]							
Entire cohort	3117/22 097	7.4 (6.4-8.4)	10,672/152 194	4.3 (3.9-4.6)	3.1 (2.1-4.1)	1.74 (1.50-2.01)	<.001[f]
Baseline opioid dose, MME/d[g]							.005[h]
50-89	525/5321	5.2 (3.8-6.5)	3,392/53 260	4.1 (3.6-4.6)	1.1 (-0.3-2.4)	1.26 (0.96-1.66)	
90-149	615/5524	5.8 (4.3-7.2)	2676/38 994	4.2 (3.6-4.7)	1.6 (0.1-3.2)	1.41 (1.01-1.80)	
150-299	1080/6864	8.7 (6.5-10.8)	2971/38 782	4.3 (3.8-4.8)	4.4 (2.2-6.6)	2.12 (1.53-2.70)	
≥300	897/4388	11.7 (8.7-14.7)	1687/21 159	4.8 (3.9-5.7)	6.9 (3.8-10.0)	2.86 (2.04-3.67)	
Secondary mental health end points[j]							
Depression	2485/22 097	5.4 (4.5-6.3)	8032/152 194	2.9 (2.6-3.2)	2.5 (1.6-3.4)	1.86 (1.57-2.21)	<.001[f]
Anxiety	505/22 097	1.4 (1.2-1.7)	2192/152 194	1.0 (0.9-1.1)	0.4 (0.1-0.7)	1.39 (1.16-1.67)	<.001[f]
Suicide attempt	127/22 097	0.3 (0.2-0.5)	448/152 194	0.1 (0.1-0.2)	0.2 (0.1-0.3)	2.38 (1.57-3.58)	<.001[f]

Rate of Taper >10% dose reduction associated with higher rates of adverse events

Figure 2. Adjusted Event Rates for Overdose and Mental Health Crisis Events





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Medications for Opioid Use Disorder (MOUD) and Suicide Mortality

- Retrospective cohort study
- 60,000 Department of Veterans Affairs (VA) patients receiving MOUD from 2003 to 2017.
  - 92% male, average age 46.5 (SD 13.1)
- Data sources: the VA Corporate Data Warehouse, Centers for Medicare and Medicaid Services Claims Data, and the VA-Department of Defense Mortality Data Repository.
- The exposure of interest was MOUD, including:
  - Starting periods (first 14 days on treatment)
  - Stopping periods (first 14 days off treatment)
  - Stable time on treatment (no change in 14 days)
  - Stable time off treatment (reference category).
- Main outcome: suicide mortality, external-cause mortality, and all-cause mortality in the 5 years following initiation of MOUD.

PMID: 35360916

More than a 50% decrease in risk of suicide mortality during stable treatment periods, persists for external and all-cause mortality

TABLE 2. Crude and adjusted hazard ratios for suicide mortality, external-cause mortality, and all-cause mortality in the MOUD cohort[a]

	Unadjusted		Adjusted for Age, Gender, and Race		Further Adjusted for Medical and Psychiatric Comorbidities		Further Adjusted for Health Care Utilization	
Measure and Period	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Suicide mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.54	0.24, 1.19	0.54	0.24, 1.20	0.54	0.24, 1.21	0.55	0.25, 1.21
Stable on MOUD	0.45	0.32, 0.63	0.42	0.30, 0.59	0.44	0.31, 0.61	0.45	0.32, 0.63
Stopping MOUD	1.38	0.82, 2.34	1.41	0.83, 2.38	1.41	0.83, 2.39	1.47	0.86, 2.51
External-cause mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.56	0.42, 0.76	0.56	0.42, 0.76	0.57	0.42, 0.77	0.57	0.42, 0.78
Stable on MOUD	0.35	0.31, 0.40	0.33	0.29, 0.38	0.35	0.30, 0.40	0.35	0.31, 0.40
Stopping MOUD	1.19	0.98, 1.46	1.21	0.99, 1.48	1.21	0.99, 1.48	1.24	1.01, 1.52
All-cause mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.58	0.48, 0.71	0.58	0.48, 0.71	0.59	0.49, 0.72	0.59	0.49, 0.72
Stable on MOUD	0.33	0.30, 0.36	0.33	0.30, 0.36	0.34	0.31, 0.37	0.34	0.31, 0.37
Stopping MOUD	1.20	1.05, 1.37	1.17	1.03, 1.34	1.16	1.02, 1.33	1.14	1.00, 1.30

[a] MOUD=medications for opioid use disorder.

Increased risk associated with stopping MOUD

TABLE 2. Crude and adjusted hazard ratios for suicide mortality, external-cause mortality, and all-cause mortality in the MOUD cohort[a]

	Unadjusted		Adjusted for Age, Gender, and Race		Further Adjusted for Medical and Psychiatric Comorbidities		Further Adjusted for Health Care Utilization	
Measure and Period	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Suicide mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.54	0.24, 1.19	0.54	0.24, 1.20	0.54	0.24, 1.21	0.55	0.25, 1.21
Stable on MOUD	0.45	0.32, 0.63	0.42	0.30, 0.59	0.44	0.31, 0.61	0.45	0.32, 0.63
Stopping MOUD	1.38	0.82, 2.34	1.41	0.83, 2.38	1.41	0.83, 2.39	1.47	0.86, 2.51
External-cause mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.56	0.42, 0.76	0.56	0.42, 0.76	0.57	0.42, 0.77	0.57	0.42, 0.78
Stable on MOUD	0.35	0.31, 0.40	0.33	0.29, 0.38	0.35	0.30, 0.40	0.35	0.31, 0.40
Stopping MOUD	1.19	0.98, 1.46	1.21	0.99, 1.48	1.21	0.99, 1.48	1.24	1.01, 1.52
All-cause mortality								
Stable off MOUD	Reference		Reference		Reference		Reference	
Starting MOUD	0.58	0.48, 0.71	0.58	0.48, 0.71	0.59	0.49, 0.72	0.59	0.49, 0.72
Stable on MOUD	0.33	0.30, 0.36	0.33	0.30, 0.36	0.34	0.31, 0.37	0.34	0.31, 0.37
Stopping MOUD	1.20	1.05, 1.37	1.17	1.03, 1.34	1.16	1.02, 1.33	1.14	1.00, 1.30

[a] MOUD=medications for opioid use disorder.

Buprenorphine most effective

TABLE 3. Crude and adjusted hazard ratios for suicide mortality, external-cause mortality, and all-cause mortality for each MOUD agent[a]

	Unadjusted		Adjusted for Age, Gender, and Race		Further Adjusted for Medical and Psychiatric Comorbidities		Further Adjusted for Health Care Utilization	
Measure and Agent	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Suicide mortality								
Buprenorphine	0.37	0.24, 0.56	0.33	0.22, 0.49	0.34	0.22, 0.51	0.34	0.23, 0.52
Methadone	0.38	0.17, 0.85	0.43	0.19, 0.95	0.47	0.21, 1.06	0.47	0.21, 1.08
Naltrexone	1.45	0.77, 2.76	1.38	0.73, 2.63	1.30	0.68, 2.48	1.28	0.67, 2.44
External-cause mortality								
Buprenorphine	0.27	0.23, 0.32	0.25	0.21, 0.29	0.26	0.22, 0.31	0.27	0.23, 0.31
Methadone	0.45	0.34, 0.59	0.49	0.37, 0.64	0.53	0.40, 0.71	0.53	0.40, 0.71
Naltrexone	0.98	0.75, 1.28	0.96	0.73, 1.25	0.90	0.69, 1.18	0.88	0.67, 1.15
All-cause mortality								
Buprenorphine	0.25	0.23, 0.28	0.26	0.23, 0.29	0.27	0.24, 0.30	0.27	0.24, 0.30
Methadone	0.51	0.43, 0.60	0.49	0.42, 0.58	0.52	0.44, 0.61	0.51	0.43, 0.60
Naltrexone	0.71	0.58, 0.88	0.67	0.55, 0.83	0.64	0.52, 0.79	0.64	0.52, 0.79

[a] MOUD=medications for opioid use disorder. Reference period is off MOUD.

CDC guidelines out for comment in Feb 2022

Tapering:

- ***Unless there are indications of a life-threatening issue****, such as warning signs of impending overdose, e.g., confusion, sedation, or slurred speech,* ***opioid therapy should not be discontinued abruptly, and clinicians should not abruptly or rapidly reduce opioid dosages from higher dosages*** *(recommendation category: B, evidence type: 4).*

- *T****apers of 10% per month or slower*** *are likely to be* ***better tolerated*** *than more rapid tapers, particularly when* ***patients have been taking opioids for longer durations*** *(e.g., for a year or longer).*

https://www.federalregister.gov/documents/2022/02/10/2022-02802/proposed-2022-cdc-clinical-practice-guideline-for-prescribing-opioids

Opiate therapy tapering and medications for OUD take home points:

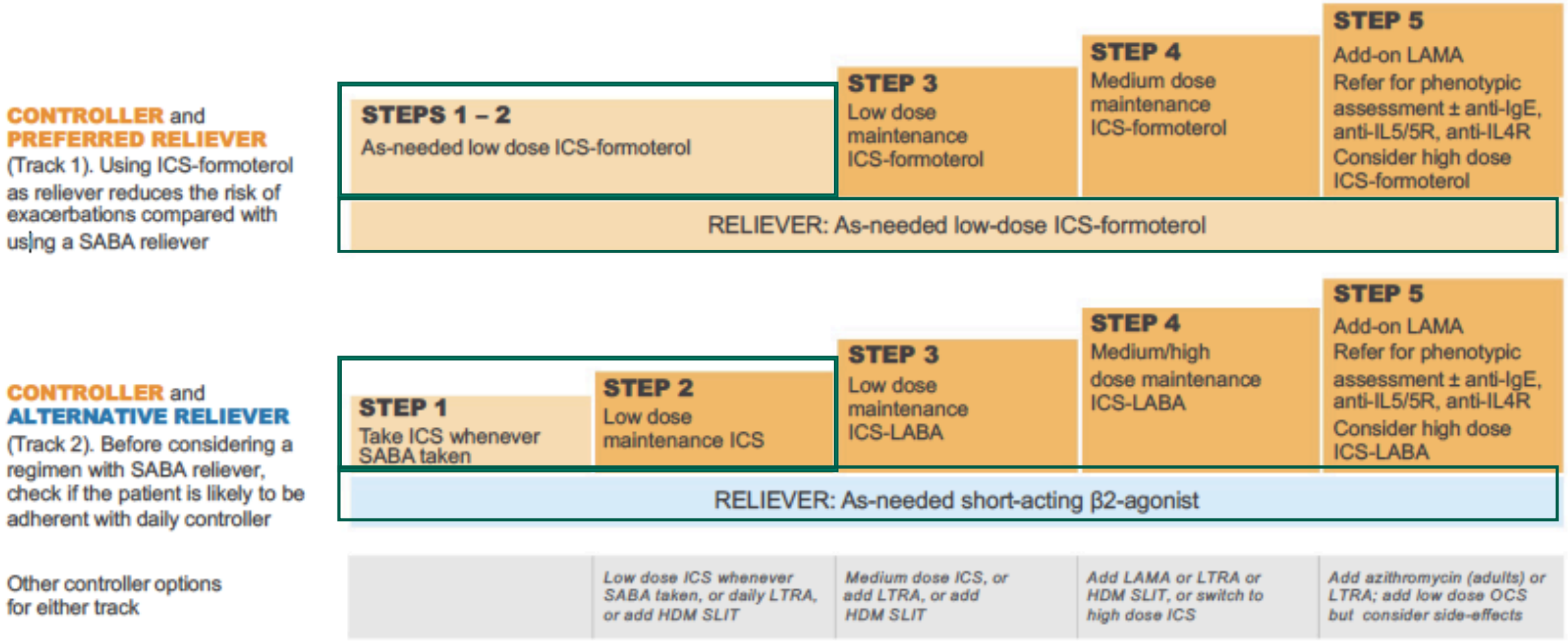
- Dose reductions can be associated with adverse outcomes including
  - Mental Health Crisis
  - Overdose
- Rate of taper >10% per month places patients at higher risk of adverse outcomes

- Medication for opioid use disorder WORKS to reduce mortality from suicide.
- Buprenorphine is the most effective, methadone less so, naltrexone likely is not effective for this purpose

New and Updated Guidelines

Asthma, NASH/NAFLD, Treatment of Diverticulitis

Global Initiative for Asthma (GINA) guidelines



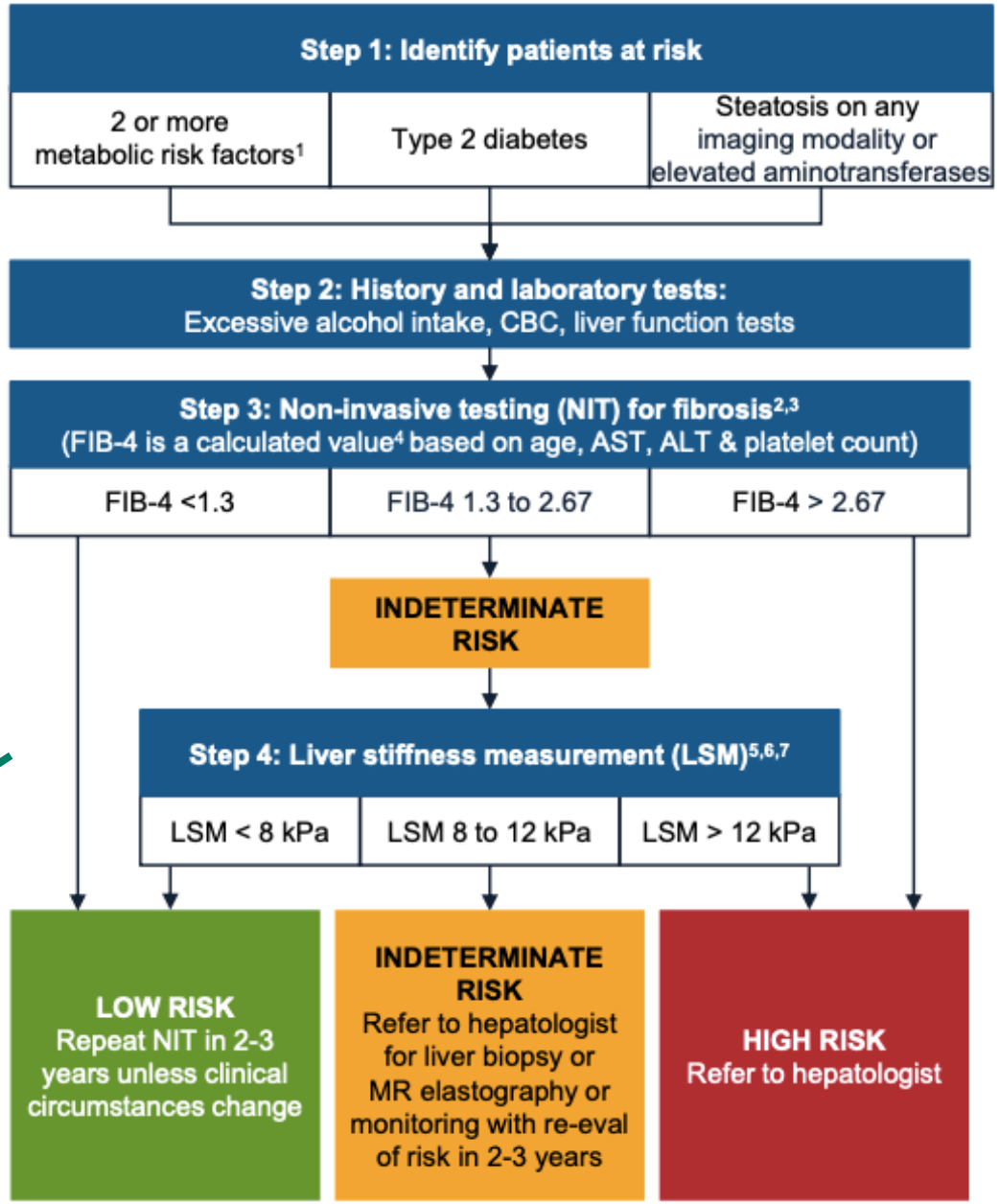
https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf

American Gastroenterological Association: NASH/NAFLD Screening and Dx

- Type II DM
- Central Obesity
- High TGs
- HDL <40 (M) or 50 (F)
- HTN

Online calculator

FibroScan (vibration controlled transient elastography)



https://pmid.us/33307021/

American Gastroenterological Association: NASH/NAFLD Management

- No FDA approved medications for NASH/NAFLD
- In patients with DM, pioglitzaone and GLP 1 RAs (esp semaglutide) have been associated with histological improvement
- Statins can be used for CV benefit unless pt has decompensated cirrhosis

	LOW RISK FIB-4 < 1.3 or LSM < 8 kPa or liver biopsy F0-F1	**INDETERMINATE RISK** FIB-4 1.3 - 2.67 and/or LSM 8 - 12 kPa and liver biopsy not available	**HIGH RISK**[1] FIB-4 > 2.67 or LSM > 12 kPa or liver biopsy F2-F4
	Management by PCP, dietician, endocrinologist, cardiologist, others	Management by hepatologist with multidisciplinary team (PCP, dietician, endocrinologist, cardiologist, others)	
Lifestyle intervention[2]	Yes	Yes	Yes
Weight loss recommended if overweight or obese[3]	Yes May benefit from structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Greater need for structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Strong need for structured weight loss programs, anti-obesity medications, bariatric surgery
Pharmacotherapy for NASH	Not recommended	Yes[4, 5, 6]	Yes[4, 5, 6, 7]
CVD risk reduction[8]	Yes	Yes	Yes
Diabetes care	Standard of care	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)

https://pmid.us/33307021/

AGA and ACP guidelines for Diverticulitis
Use of imaging

- AGA Best Practice Advice 1: Computed tomography should be considered to confirm the diagnosis of diverticulitis in patients without a prior imaging- confirmed diagnosis and to evaluate for potential complications in patients with severe presentations. Imaging should also be considered in those who fail to improve with therapy, are immunocompromised, or who have multiple recurrences

- Recommendation 1: ACP suggests that clinicians use abdominal CT imaging when there is diagnostic uncertainty in a patient with suspected acute left-sided colonic diverticulitis (conditional recommendation; low-certainty evidence).

AGA Treatment and Antibiotics

- Best Practice Advice 5: **A clear liquid diet is advised during the acute phase** of uncomplicated diverticulitis. Diet should advance as symptoms improve.
- Best Practice Advice 6: **Antibiotic treatment can be used selectively, rather than routinely**, in immunocompetent patients with mild uncomplicated diverticulitis.
- Best Practice Advice 7: **Antibiotic treatment is advised in patients with uncomplicated diverticulitis who have comorbidities or are frail, who present with refractory symptoms or vomiting, or who have a C- reactive protein >140 mg/L or baseline white blood cell count > 15** . Antibiotic treatment is advised in patients with **complicated diverticulitis** or uncomplicated diverticulitis with **a fluid collection or longer segment of inflammation on CT scan**.

https://pmid.us/33279517/

ACP treatment and antibiotics

- Recommendation 2: ACP suggests that clinicians **manage most patients** with acute uncomplicated left-sided colonic diverticulitis in **an outpatient setting** (conditional recommendation; low-certainty evidence).

- Recommendation 3: ACP suggests that clinicians initially **manage select patients with acute uncomplicated left-sided colonic diverticulitis without antibiotics** (conditional recommendation; low-certainty evidence).

https://pmid.us/35038273/

Take home points for diverticulitis

- Abdominal CT should only be used if:
  - Uncertain about a diagnosis
  - Evaluating immunocompromised individuals
  - Severe presentations concerning for complicated diverticulitis
  - Failure to improve
- Treat uncomplicated diverticulitis as an outpatient with a clear liquid diet when:
  - Immunocompetent, no SIRS response, not frail, pt can follow up
- Only use antibiotics when:
  - Patients have comorbidities
  - Are frail,
  - Present with refractory symptoms or vomiting
  - Have a C- reactive protein >140 mg/L or baseline white blood cell count > 15

Thanks!

Questions?

Addie H McClintock, MD *ahearst@uw.edu, @McClintockMD*
Chris Knight, MD, FACP *cknight@uw.edu, @clknight*