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AL/MS ACP 2024
Updates in Hospital Medicine

Presented by:

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Disclosures

- none

Objectives

- **MAUD Trial** – medications for alcohol use disorder
- **VA HTN Trial** – treatment of hypertension in older hospitalized patients
- **PERFECT Trial** – timing for appendicectomy
- **STEP HFpEF Trial** – GLP-1 Agonist use for HFpEF treatment

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JAMA Network Open™

Original Investigation | Substance Use and Addiction

Outcomes After Initiation of Medications for Alcohol Use Disorder at Hospital Discharge

Eden Y. Bernstein, MD; Travis P. Baggett, MD, MPH; Shrunjal Trivedi, MPH; Shoshana J. Herzig, MD, MPH; Timothy S. Anderson, MD, MAS

March 2024

MAUD Trial - Methods

- Retrospective cohort study
- Used 20% of national sample of CMS administrative and pharmacy claims from 2015-2017

Inclusion Criteria

- Acute care AUD hospitalizations in 2016 (more than one admission counted)
- Filled MAUD within 2 days of discharge

Exclusion Criteria

- Pharmacy claim for Naltrexone, Acamprosate, or Disulfiram within 90d prior to admission
- Liver disease or renal failure
- Patients readmitted within 2 days of hospital discharge

MAUD Trial – End Points

Primary End Point

- Composite all cause mortality
- Return to hospital within 30d

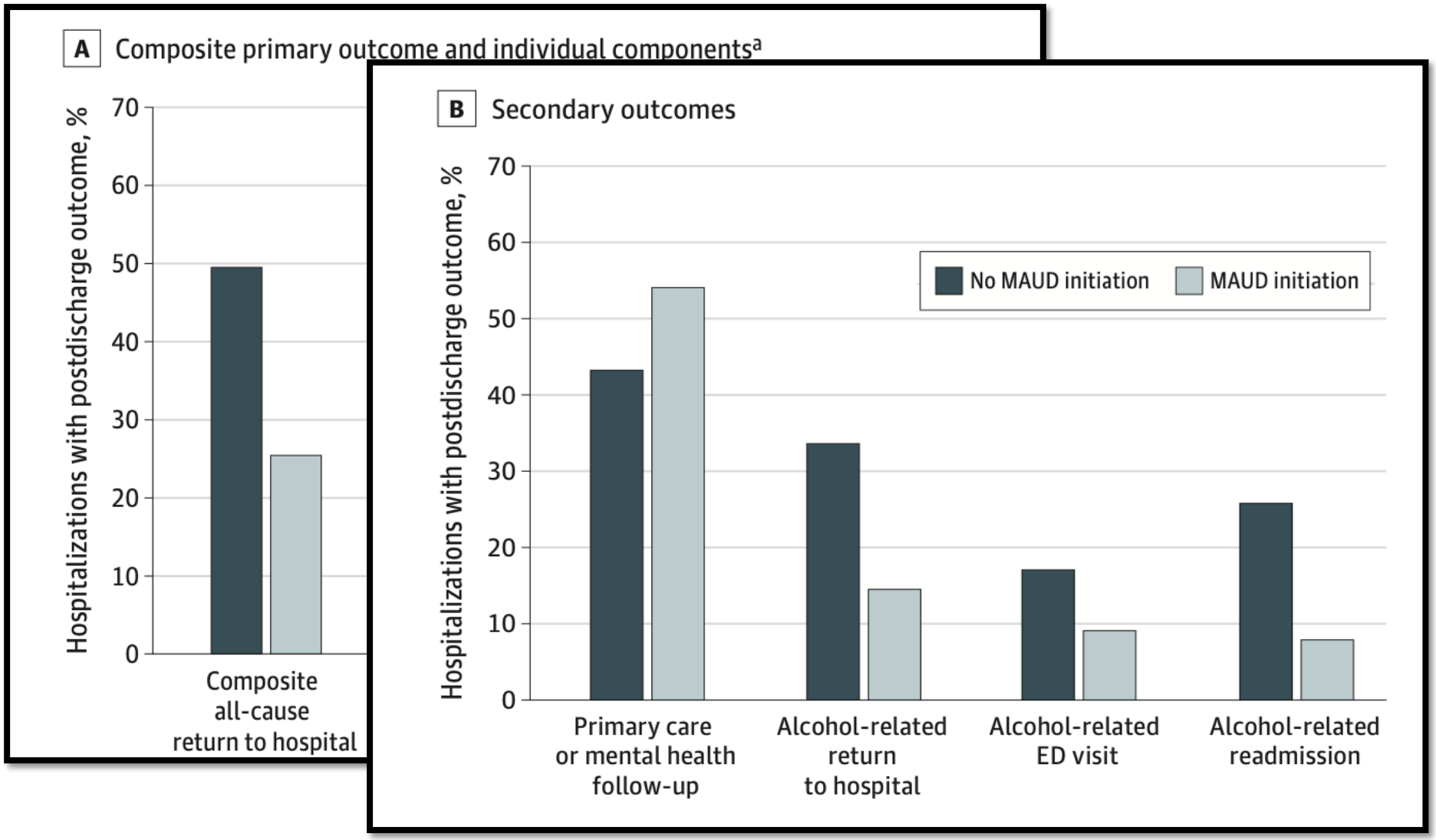
Secondary End Point

- Individual components of all cause mortality
- Alcohol-related return to hospital
- Outpatient Primary care or mental health follow up

MAUD Trial - Results

- ~9800 alcohol related hospitalizations → ~6800 patients
- Only 192 hospitalizations resulted in discharge with MAUD initiation (Naltrexone 58%, Acamprosate 27%, Disulfiram 16%)

Figure 1. Unadjusted Posthospitalization Care Patterns After Alcohol-Related Hospitalizations at 30 d



MAUD Trial - Conclusion

- MAUD initiation on discharge is associated with:
  - Decreased alcohol-related and non alcohol related return to hospital
  - Increased outpatient primary care or mental health follow up

- Limitations:
  - Inherent limitations of this observational study design, including unmeasured confounding (i.e. psychosocial factors)
  - Unable to determine severity using diagnosis codes
  - Results may not be generalizable to patients who are younger, do not have disabilities, or are Medicare Advantage beneficiaries
  - Unable to identify use of nonpharmacologic treatment (i.e. 12-step facilitation or behavioral interventions)

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Research

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Clinical Outcomes of Intensive Inpatient Blood Pressure Management in Hospitalized Older Adults

Timothy S. Anderson, MD, MAS; Shoshana J. Herzig, MD, MPH; Bocheng Jing, MS; W. John Boscardin, PhD; Kathy Fung, MS; Edward R. Marcantonio, MD, SM; Michael A. Steinman, MD

May 2023

VA HTN Trial - Methods

- Retrospective cohort study
- Used inpatient and outpatient clinical and pharmacy data from the VHA Corporate Data Warehouse linked to VHA and Medicare administrative claims from 2013 through 2018

Inclusion Criteria

- >65yo, Hospitalized between Oct 2015-Dec 2017
- 2 or more elevated BPs w/in 48hr of hospitalization

Exclusion Criteria

- Admission for cardiovascular disease or hypertensive emergency

VA HTN Trial - Methods

- Started with ~114,000 patients ➔ ~66,000 patients had multiple elevated BPs within 48hr

- **Exposed/Intensive Treatment Group-** received 1 or more IV antihypertensive doses of any class or oral doses of antihypertensive classes that were NOT filled prior to hospitalization
- Male- 97.5% / Female 2.6%

VA HTN Trial - End Points

Primary End Point

Composite of:

- Inpatient mortality
- AKI
- Stroke
- Myocardial injury
- BNP elevation
- ICU transfer

Secondary End Point

- Each component of the composite outcome
- Hypotensive episode
- Length of stay
- Discharge disposition

Figure 2. Clinical Outcomes of Intensive Inpatient Antihypertensive Treatment

	Intensively treated, No. (%) (n = 14 064)	Not intensively treated, No. (%) (n = 52 076)	OR (95% CI)
Primary outcome			
Composite	1220 (8.7)	3570 (6.9)	1.28 (1.18-1.39)
Clinical outcome			
Death	156 (1.1)	573 (1.1)	1.11 (0.91-1.37)
ICU transfer	408 (2.9)	1322 (2.5)	1.20 (1.05-1.37)
AKI			
Any stage	769 (5.5)	2031 (3.9)	1.43 (1.29-1.58)
Stage 2 or 3	165 (1.2)	440 (0.8)	1.34 (1.08-1.66)
Stroke	21 (0.2)	43 (0.1)	1.46 (0.77-2.78)
BNP elevation	38 (0.3)	95 (0.2)	1.81 (1.16-2.82)
Troponin elevation	227 (1.6)	710 (1.4)	1.20 (1.00-1.43)
Hypotension	2078 (14.5)	7283 (14.0)	1.22 (1.15-1.30)
Disposition			
SNF discharge	1714 (12.2)	5239 (10.1)	1.12 (1.04-1.20)
Home	11 936 (84.9)	45 372 (87.1)	0.89 (0.83-0.94)

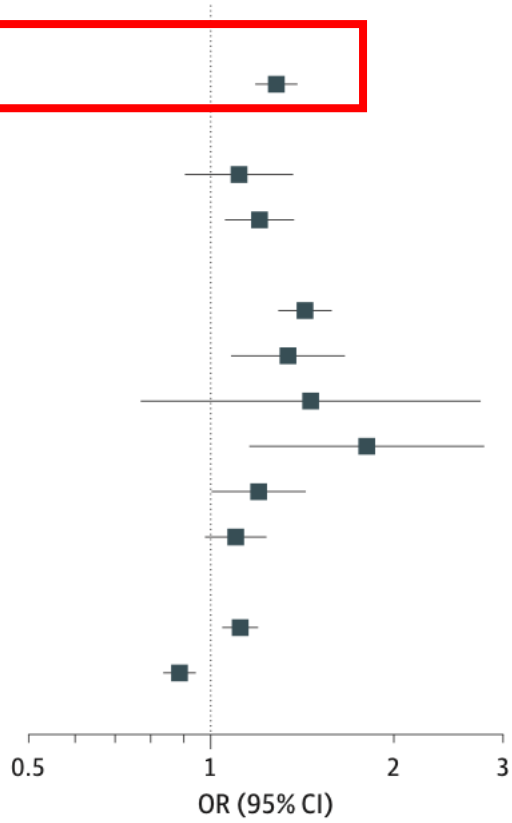

Table 2. Clinical Outcomes of Intensive Inpatient Antihypertensive Treatment by Use of Intravenous vs Oral Antihypertensives

	OR (95% CI)			
		Route of antihypertensive administration		*P* value for interaction
	Overall	Oral only	Any intravenous	
No. of patients exposed to intensive BP treatment	14 064	11 560	2504	NA
Primary outcome				
Composite[a]	1.28 (1.18-1.39)	1.15 (1.05-1.26)	1.90 (1.65-2.19)	<.001
Clinical outcome				
Death	1.11 (0.91-1.37)	0.96 (0.76-1.21)	1.79 (1.26-2.53)	.008
ICU transfer	1.23 (1.09-1.39)	0.92 (0.79-1.07)	2.54 (2.08-3.11)	<.001
AKI, any stage	1.43 (1.29-1.58)	1.38 (1.23-1.54)	1.63 (1.34-1.97)	.14
AKI, stage 2 or 3	1.34 (1.08-1.66)	1.30 (1.03-1.64)	1.53 (1.02-2.28)	.47
Stroke	1.46 (0.77-2.78)	1.19 (0.58-2.44)	2.67 (1.02-7.04)	.23
BNP elevation	1.81 (1.16-2.82)	1.88 (1.18-2.99)	1.47 (0.54-4.10)	.62
Troponin elevation	1.20 (1.00-1.43)	1.09 (0.90-1.33)	1.67 (1.22-2.31)	.03
Hypotension (systolic BP <100 mm Hg)	1.22 (1.15-1.30)	1.21 (1.13-1.29)	1.27 (1.12-1.44)	.48
Disposition				
SNF discharge	1.12 (1.04-1.20)	1.13 (1.05-1.21)	1.06 (0.92-1.22)	.40
Home	0.89 (0.83-0.94)	0.90 (0.84-0.96)	0.83 (0.73-0.94)	.25

VA HTN Trial - Methods

- In hospitalized older adults who received additional antihypertensives for elevated BPs, receipt of intensive treatment was associated with a greater odds of adverse clinical outcomes (including cardiac injury, AKI, and ICU transfer)

- Limitations
  - VA based study; older male predominant population (97% male)
  - Excluded patients admitted for a hypertensive emergency, more subjective symptoms may not have been identified (i.e. hypertensive encephalopathy)
  - Cannot exclude the possibility of unmeasured confounding

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THE LANCET

Role of preoperative in-hospital delay on appendiceal perforation while awaiting appendicectomy (PERFECT): a Nordic, pragmatic, open-label, multicentre, non-inferiority, randomised controlled trial

Sept 2023

Karoliina Jalava, Ville Sallinen, Hanna Lampela, Hanna Malmi, Ingeborg Steinholt, Knut Magne Augestad, Ari Leppäniemi, Panu Mentula

PERFECT Trial - Methods

- A pragmatic, open-label, multicenter, non-inferiority, parallel, randomized controlled trial
- Location: Finland and Norway, academic teaching hospitals
- Compared appendectomies scheduled within 8h and 24h in adult patients with predicted uncomplicated acute appendicitis
- Enrolled 1822 patients

PERFECT Trial - Methods

Inclusion Criteria

- Acute appendicitis
- Diagnosed clinically or via imaging (nearly all were eventually imaged to rule out complications)

Exclusion Criteria

- Pregnancy
- Suspicion of complications (perforation, peritonitis, > CRP, fever)

PERFECT Trial – End Points

Primary End Point

- Complicated appendicitis (assess intraoperatively)

Secondary End Point

- Length of stay
- Surgical site infection
- Bacteremia
- All post-op complications
- Patient reported pain
- Rate of conversion to open surgery

PERFECT Trial - Results

- Surgery was performed within 8h in 574 of 907 (63%) patients in the red group and within 24h in 792 of 896 (88%) patients in the orange group.

	Red group, <8 h (n=574)	Orange group, 8–24 h (n=578)	p value	Effect size (95% CI)
Primary outcomes				
Perforated appendicitis (AAST 3–5)	43 (7%)	61 (11%)	0·070*	Difference 3·1% (−0·2 to 6·4)
AAST 0—normal appendix	12 (2%)	12 (2%)	NA	NA
AAST 1—acutely inflamed appendix, intact	445 (78%)	429 (74%)	NA	NA
AAST 2—gangrenous appendix, intact	74 (13%)	76 (13%)	NA	NA
AAST 3—perforated, local contamination	23 (4%)	21 (4%)	NA	NA
AAST 4—perforated with peri-appendiceal phlegmon or abscess	12 (2%)	23 (4%)	NA	NA
AAST 5—perforated with generalised peritonitis	8 (1%)	17 (3%)	NA	NA

Table 3: **Outcomes in the modified per-protocol population**

Secondary outcomes	Red group, <8 h (n=574)	Orange group, 8–24 h (n=578)	p value	Effect size (95% CI)
Geometric mean duration of hospital stay, h	27 (1·7)	44 (1·0)	<0·0001†	Geometric mean ratio 0·6 (0·58 to 0·65)
Laparoscopic procedure	570 (99%)	576 (<100%)	0·45‡	Difference 0·3% (–0·5 to 1·2)
Conversion	4 (1%)	2 (<1%)	0·45‡	Difference –0·4% (–1·2 to 0·5)
SAGS	NA	NA	0·34*	0·3§
0—no appendicitis	12 (2%)	12 (2%)	NA	NA
1—simple appendicitis	433 (75%)	418 (72%)	NA	NA
2 and 3—purulent discharge locally or in four quadrants¶	86 (15%)	87 (15%)	NA	NA
Pathological verification‖	NA	NA	0·19*	0·03§
Non-perforated gangrenous appendix	44 (8%)	43 (7%)	NA	Difference –0·2% (–3·3 to 2·8)
Perforated appendix	43 (7%)	61 (11%)	NA	Difference 3·1% (–0·2 to 6·4)
30 day follow-up**				
Complication rate ≤30 days	43 (7%)	34 (6%)	0·23*	Difference –1·6% (–4·5 to 1·3)
Clavien–Dindo grade 1	8 (1%)	5 (1%)	NA	NA
Clavien–Dindo grade 2	28 (5%)	20 (3%)	NA	NA
Clavien–Dindo grade 3a + b and 4a	7 (1%)	9 (2%)	NA	NA
Surgical site infection	17 (3%)	14 (2%)	0·57*	Difference –0·5% (–2·4 to 1·3)
Superficial and deep incisional infection	6 (1%)	4 (1%)	NA	NA
Intra-abdominal infection	11 (2%)	10 (2%)	NA	NA
Positive blood culture	2 (<1%)	6 (1%)	0·29‡	Difference 0·7% (–0·3 to 1·6)
NRS for pain				
NRS average value per h	4·0 (2·3)	3·8 (2·1)	0·45††	Difference 0·2 (–0·3 to 0·6)
Area under NRS curve	13 (7–24)	55 (32–82)	<0·0001‡‡	–0·6§§
Incompletely filled or unreturned NRS forms	375 (65%)	382 (66%)	NA	NA

Table 3: **Outcomes in the modified per-protocol population**

PERFECT Trial - Conclusion

- In patients presenting with uncomplicated acute appendicitis
  - Scheduling appendicectomy within 24h was non-inferior to scheduling appendicectomy within 8h
  - There no significant increase in complications preop, periop, or postop
    - There is potentially a slight increase in perforation rate if surgery is delayed closer to 24hr (not clinically significant)
  - Benefits of 8hr window was shorter duration of discomfort for the patient and decrease length of stay.

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The NEW ENGLAND JOURNAL of MEDICINE

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Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*

STEP HFpEF Trial - Methods

- Randomized, double blind, placebo-controlled trial
- 96 sites, 13 countries (Asia, Europe, NA, SA)
- Experiment group given Semaglutide 2.4mg for 52 weeks → 5 week follow up

Inclusion Criteria

- EF >45%
- BMI >30
- NYHA Class >2
- KCCQ-CSS <90
- 6min Walk Test >100m
- Confirmation in labs/imaging of HF

Exclusion Criteria

- Change in body weight >5kg in 90d
- Diabetic patients

STEP HFpEF Trial - Endpoints

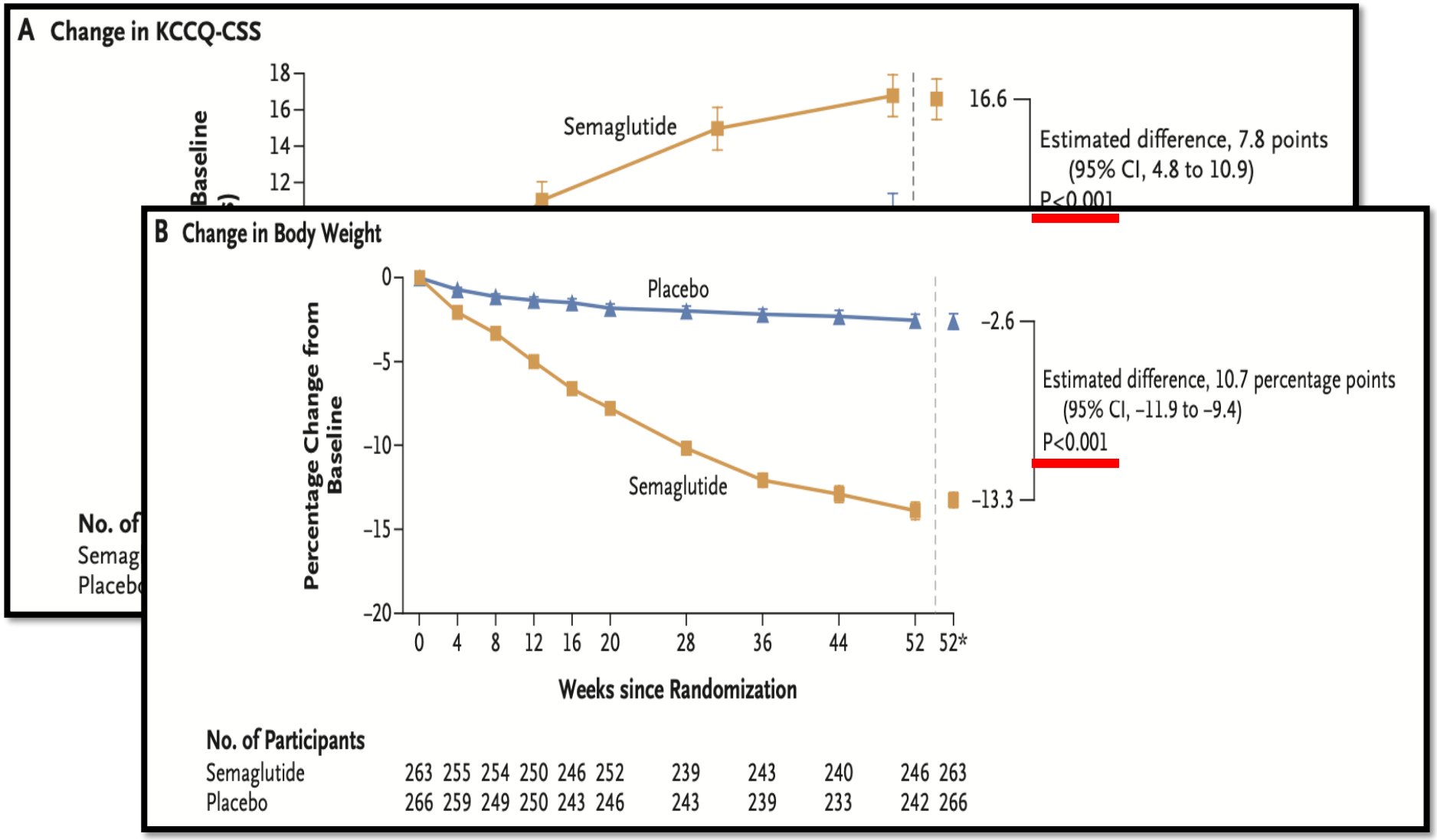
Primary End Point

- Change in KCCQ-CSS
- Percentage of body weight

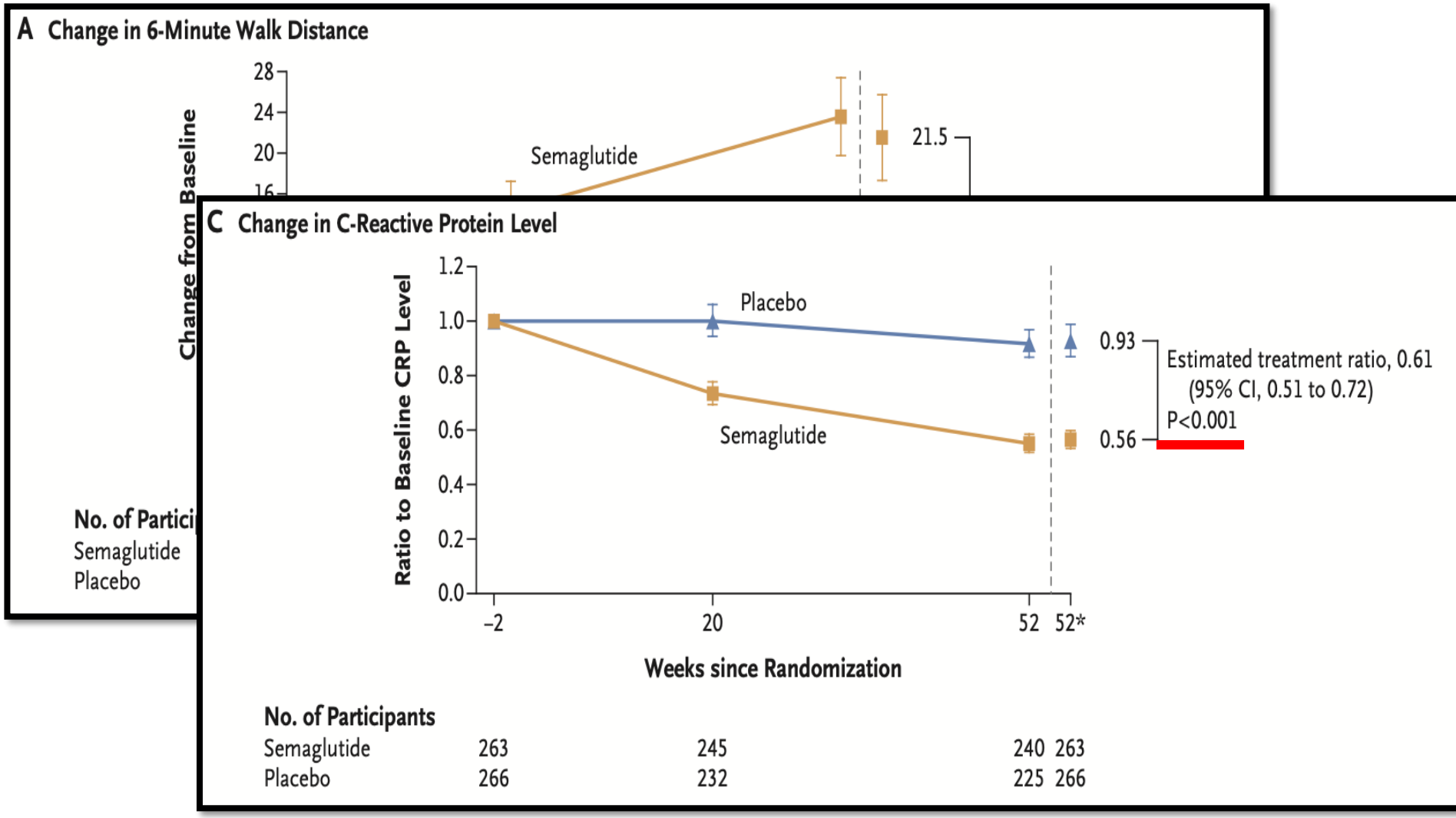
Secondary End Point

- Change in 6min Walk Test
- Hierarchical Composite End Point (All cause death, # HF events, change in KCCQ-CSS, and change in Walk Test)
- Change in CRP

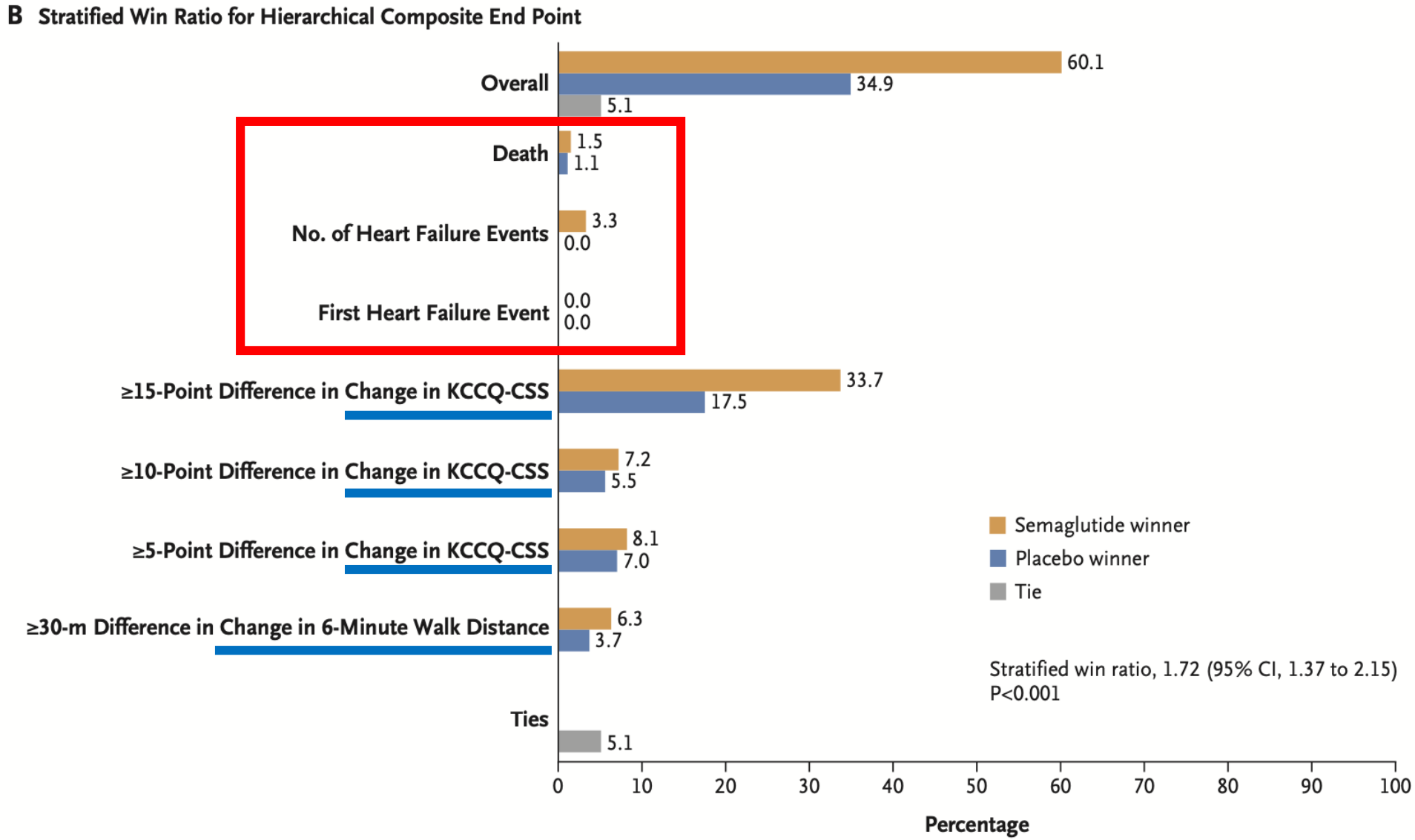
STEP HFpEF Trial - Results



STEP HFpEF Trial - Results



STEP HFpEF Trial - Results



STEP HFpEF Trial - Conclusion

- Patients with HFpEF and obesity on treatment with weekly Semaglutide compared to placebo led to:
  - Larger reductions in heart failure related symptoms and physical limitations
  - Greater improvement in exercise function
  - Greater weight loss
  - Larger reduction of inflammatory markers

- Limitations:
  - Non-white participation was low; US participants were 23% AA
  - Was not adequately powered to evaluate clinical events such as hospitalizations for heart failure and urgent visits.
  - The duration of follow-up was limited to 1 year

Take Aways

- MAUD Trial
  - Medications for AUD on discharge is associated with decreased alcohol-related and non alcohol-related return to hospital and increased outpatient primary care or mental health follow up.
- VA HTN Trial
  - Receipt of intensive treatment was associated with a greater odds of adverse clinical outcomes (including cardiac injury, AKI, and ICU transfer).
- PERFECT Trial
  - Scheduling appendicectomy within 24h was non-inferior to scheduling appendicectomy within 8h.
- STEP HFpEF Trial
  - Patients with HFpEF and obesity on semaglutide QWeek led to larger reductions in heart failure related symptoms and physical limitations and greater improvement in exercise function.

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Questions

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Thank you!