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Medical Literature 2022

Turning Evidence into Practice

Mel L. Anderson, MD, MACP

National Program Executive Director, VHA Hospital Medicine

Associate Professor of Medicine, Univ. of CO SOM

COLORADO STATE ACP MEETING 2023



Disclosures

► None



Learning Objectives

1. **Describe** the primary conclusions of each study
2. **Identify** changes to your practice
3. **Implement** these practice changes



Journals Reviewed

Jan 2022 – Dec 2022

- ▶ N Engl J Med
- ▶ JAMA; JAMA Intern Med
- ▶ J Gen Intern Med
- ▶ J Hospit Med, J Am Coll Cardiol
- ▶ Ann Intern Med + ACP J Club
- ▶ Lancet, Am J Med, Circulation, BMJ
- ▶ ACP Plus, BMJ Online update, J Watch



Acknowledgements

- ▶ **Jeffrey J. Glasheen, MD**
University of Colorado School of Medicine
- ▶ **Dan Heppe, MD**
University of Colorado School of Medicine
- ▶ **Joseph Li, MD**
Harvard Medical School
- ▶ **Cason Pierce, MD**
University of Colorado School of Medicine
- **Anneliese Schleyer, MD**
University of Washington School of Medicine
- ▶ **Brad Sharpe, MD**
UCSF School of Medicine



Notable in 2022

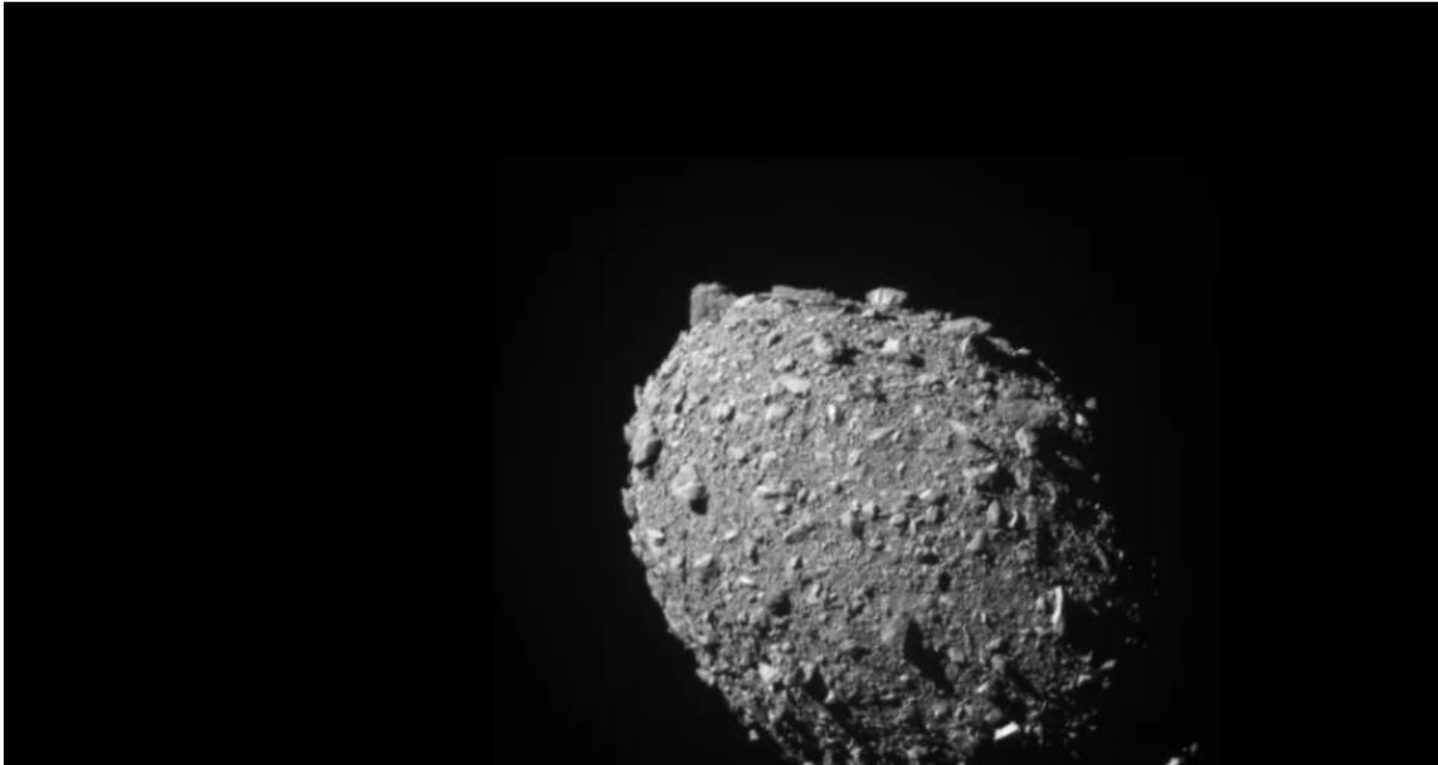


RAMIN SKIBBA

SCIENCE OCT 11, 2022 2:52 PM

Bam! NASA Says DART Really Clocked That Asteroid

Two weeks after the spacecraft collided with Dimorphos, researchers determined that it knocked the space rock 32 minutes off its old orbit.



TRAVEL |

Ger
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Mark Hallam

08/24/2022

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Roadmap for our Journey Today

Case 1: Heart Failure



Case 2: Suicidality



Case 3: Clinic pt HTN, claudication



Short Takes



Practice summary

Case 1

64 y/o woman presents with worsening dyspnea, orthopnea, and LE edema bilat.

BPPV, HTN, OA, GERD, OSA

146/74, 132, 18, Afeb. JVP 15, bibasilar rales, irreg tachy S3, LE edema to knees

EKG Tachy A fib; CXR interstitial, bilat eff.

ECHO LVEF 30%



Which of the following are true?

- A. Acetazolamide improves clinical congestion by day 3**
- B. SGLT2 Inhibitors lower rates of hypokalemia**
- C. IV iron improves long-term clinical outcomes**
- D. All of the above are true**
- E. None of the above are true**
- F. “Mmmmmm. Floor pie...”**



ORIGINAL ARTICLE

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, K. Tartaglia, F. Chenot, S. Moubayed, R. Dierckx, P. Blouard, P. Troisfontaines, D. Derthoo, W. Smolders, L. Bruckers, W. Droogne, J.M. Ter Maaten, K. Damman, J. Lassus, A. Mebazaa, G. Filippatos, F. Ruschitzka, and M. Dupont, for the ADVOR Study Group*

N Engl J Med 2022;387:1185-95



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Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, K. Tartaglia, F. Chenot, S. Moubayed, R. Dierckx, P. Blouard, P. Troisfontaines, D. Derthoo, W. Smolders, L. Bruckers, W. Droogne, J.M. Ter Maaten, K. Damman, J. Lassus, A. Mebazaa, G. Filippatos, F. Ruschitzka, and M. Dupont, for the ADVOR Study Group*

Patients: 519 adults, acute decompensated HF

Intervention: Acetazolamide 500mg IV daily x 3 days

Comparison: Placebo

Outcomes: Decongestion by day 3 / no need to augment diuresis; LOS; death, rehospitalization

N Engl J Med 2022;387:1185-95



ADVOR

	Placebo	Acetaz.	Abs.	NNT	P value
Primary	30.5%	42.2%	11.7%	9	<0.001
LOS	9.9 days	8.8 days	1.1 d	0.89	0.81-0.98
M/3mHHF	27.8%	29.7%	1.9%	NS	NS

N Engl J Med 2022;387:1185-95

ADVOR

	Placebo	Acetaz.	Abs.	NNT	P value
Met acid.	0%	0%	0%	NS	NS
HypoK+	3.9%	5.5%	1.6%	NS	NS
Renal SE	0.8%	2.7%	1.9%	NS	NS

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, K. Tartaglia, F. Chenot, S. Moubayed, R. Dierckx, P. Blouard, P. Troisfontaines, D. Derthoo, W. Smolders, L. Bruckers, W. Droogne, J.M. Ter Maaten, K. Damman, J. Lassus, A. Mebazaa, G. Filippatos, F. Ruschitzka, and M. Dupont, for the ADVOR Study Group*



Patients: 519 adults, acute decompensated HF

Intervention: Acetazolamide 500mg IV daily x 3 days

Comparison: Placebo

Outcomes: Decongestion by day 3 / no need to augment diuresis; LOS; death, rehospitalization

Conclusion: Acetazolamide improves decongestion at 3d

SGLT2 Inhibitor CORNER



Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, B. Claggett, R.A. de Boer, D. DeMets, A.F. Hernandez, S.E. Inzucchi, M.N. Kosiborod, C.S.P. Lam, F. Martinez, S.J. Shah, A.S. Desai, P.S. Jhund, J. Belohlavek, C.-E. Chiang, C.J.W. Borleffs, J. Comin-Colet, D. Dobreanu, J. Drozd, J.C. Fang, M.A. Alcocer-Gamba, W. Al Habeeb, Y. Han, J.W. Cabrera Honorio, S.P. Janssens, T. Katova, M. Kitakaze, B. Merkely, E. O'Meara, J.F.K. Saraiva, S.N. Tereshchenko, J. Thierer, M. Vaduganathan, O. Vardeny, S. Verma, V.N. Pham, U. Wilderäng, N. Zaozerska, E. Bachus, D. Lindholm, M. Petersson, and A.M. Langkilde, for the DELIVER Trial Committees and Investigators*

N Engl J Med 2022;387:1089-99



SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

Muthiah Vaduganathan, Kieran F Docherty*, Brian L Claggett, Pardeep S Jhund, Rudolf A de Boer, Adrian F Hernandez, Silvio E Inzucchi, Mikhail N Kosiborod, Carolyn S P Lam, Felipe Martinez, Sanjiv J Shah, Akshay S Desai, John J V McMurray†, Scott D Solomon†*

Lancet 2022;400:757-67

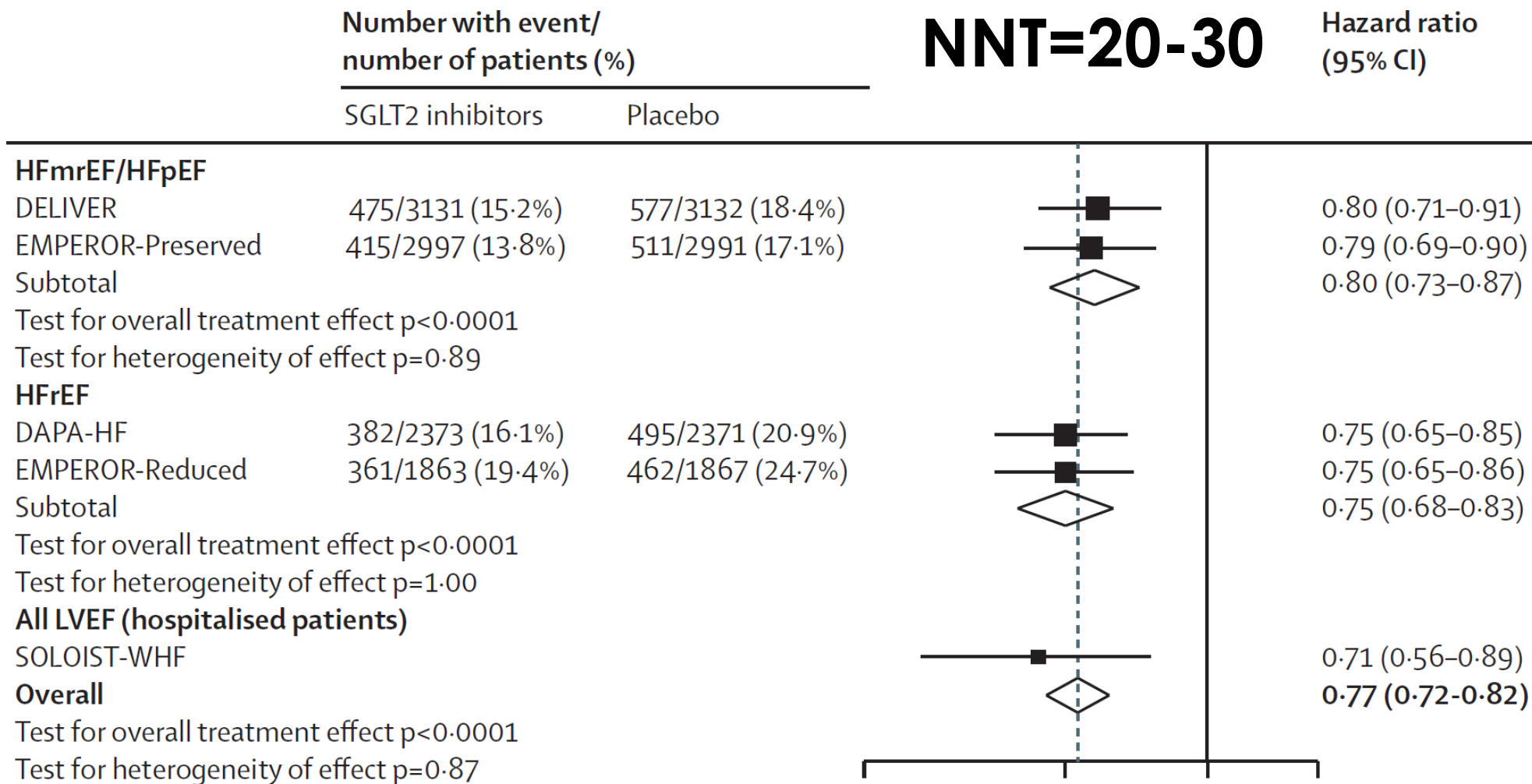


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Cardiovascular death or heart failure hospitalisation

NNT=20-30

Hazard ratio (95% CI)



Dapagliflozin in Patients Recently Hospitalized With Heart Failure and Mildly Reduced or Preserved Ejection Fraction

J Am Coll Cardiol 2022;80:1302-1310

ORIGINAL RESEARCH ARTICLE



Effects of Early Empagliflozin Initiation on Diuresis and Kidney Function in Patients With Acute Decompensated Heart Failure (EMPAG-HF)

P. Christian Schulze^{id}, MD, PhD; Jürgen Bogoviku, MD; Julian Westphal^{id}, MD; Pawel Aftanski, MD; Franz Haertel, MD; Sissy Grund, MS; Stephan von Haehling, MD, PhD; Ulrike Schumacher, PhD; Sven Möbius-Winkler^{id}, MD, PhD; Martin Busch, MD

Circulation 2022;146:289-298



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Impact of empagliflozin on decongestion in acute heart failure: the EMPULSE trial

Jan Biegus ^{1*}, Adriaan A. Voors², Sean P. Collins^{3,4}, Mikhail N. Kosiborod^{5,6}, John R. Teerlink ⁷, Christiane E. Angermann ⁸, Jasper Tromp ⁹, Joao Pedro Ferreira^{10,11}, Michael E. Nassif¹², Mitchell A. Psotka ¹³, Martina Brueckmann ^{14,15}, Afshin Salsali ^{16,17}, Jonathan P. Blatchford ¹⁸, and Piotr Ponikowski ¹

Eur Heart J 2022;44:41-50

In non-CV shock decompensated heart failure:

- Safe and effective
- Augment diuresis
- Kind to the kidneys





Sodium-Glucose Cotransporter 2 Inhibitors and Risk of Hyperkalemia in People With Type 2 Diabetes: A Meta-Analysis of Individual Participant Data From Randomized, Controlled Trials

Brendon L. Neuen^{ID}, MBBS, MSc; Megumi Oshima, MD, PhD; Rajiv Agarwal^{ID}, MD, MS; Clare Arnott^{ID}, MBBS, PhD; David Z. Cherney^{ID}, MD, PhD; Robert Edwards, MPH; Anna Maria Langkilde, MD, PhD; Kenneth W. Mahaffey, MD; Darren K. McGuire^{ID}, MD, MHSc; Bruce Neal^{ID}, MBChB, PhD; Vlado Perkovic^{ID}, MBBS, PhD; Annpey Pong, PhD; Marc S. Sabatine^{ID}, MD, MPH; Itamar Raz^{ID}, MD; Tadashi Toyama^{ID}, MD, PhD; Christoph Wanner, MD; David C. Wheeler^{ID}, MD; Stephen D. Wiviott^{ID}, MD; Bernard Zinman, MD; Hidde J.L. Heerspink^{ID}, PharmD, PhD

Across 6 RCT's enrolling 49,875 patients

Risk of $K \geq 6.0$ mEq/L dec by 16% RRR (NNT 76)

Circulation 2022;145:1460-1470



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Estimated Long-Term Benefit of Dapagliflozin in Patients With Heart Failure



24

Muthiah Vaduganathan, MD, MPH,^{a,*} Brian L. Claggett, PhD,^{a,*} Pardeep Jhund, MD, PhD,^b Rudolf A. de Boer, MD,^c Adrian F. Hernandez, MD,^d Silvio E. Inzucchi, MD,^e Mikhail N. Kosiborod, MD,^f Carolyn S.P. Lam, MD,^g Felipe Martinez, MD,^h Sanjiv J. Shah, MD,ⁱ Akshay S. Desai, MD,^a Daniel Lindholm, MD, PhD,^j Magnus Petersson, MD, PhD,^j Anna Maria Langkilde, MD,^j John J.V. McMurray,^b Scott D. Solomon, MD^a

DELIVER trial (HFpEF):

For a 65 y/o participant at randomization, estimated 2.3 year improvement in event-free survival (p=0.002)

J Am Coll Cardiol 2022;80:1775-1784



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SGLT2 Inhibitor CORNER



JAMA Internal Medicine | **Original Investigation**

Cost-effectiveness of Empagliflozin in Patients With Heart Failure With Preserved Ejection Fraction

Jimmy Zheng, BS; Justin T. Parizo, MD; John A. Spertus, MD, MPH; Paul A. Heidenreich, MD, MS;
Alexander T. Sandhu, MD, MS

JAMA Intern Med 2022;182(12):1278-1288



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Cost-effectiveness of Empagliflozin in Patients With Heart Failure With Preserved Ejection Fraction

Jimmy Zheng, BS; Justin T. Parizo, MD; John A. Spertus, MD, MPH; Paul A. Heidenreich, MD, MS;
Alexander T. Sandhu, MD, MS

Cost-effectiveness Markov analysis EMPEROR-Preserved
5988 Patients

Empagliflozin or standard of care without empa.

Outcomes: HHF, quality-adjusted life years, lifetime
incremental cost-effectiveness

JAMA Intern Med 2022;182(12):1278-1288



JAMA Internal Medicine | [Original Investigation](#)

Cost-effectiveness of Empagliflozin in Patients With Heart Failure With Preserved Ejection Fraction

Jimmy Zheng, BS; Justin T. Parizo, MD; John A. Spertus, MD, MPH; Paul A. Heidenreich, MD, MS;
Alexander T. Sandhu, MD, MS

< \$60,000 / QALY “high value”

\$60,000 -- \$180,000 / QALY “intermediate value”

> \$180,000 / QALY “low value”

JAMA Intern Med 2022;182(12):1278-1288



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Cost-effectiveness of Empagliflozin in Patients With Heart Failure With Preserved Ejection Fraction

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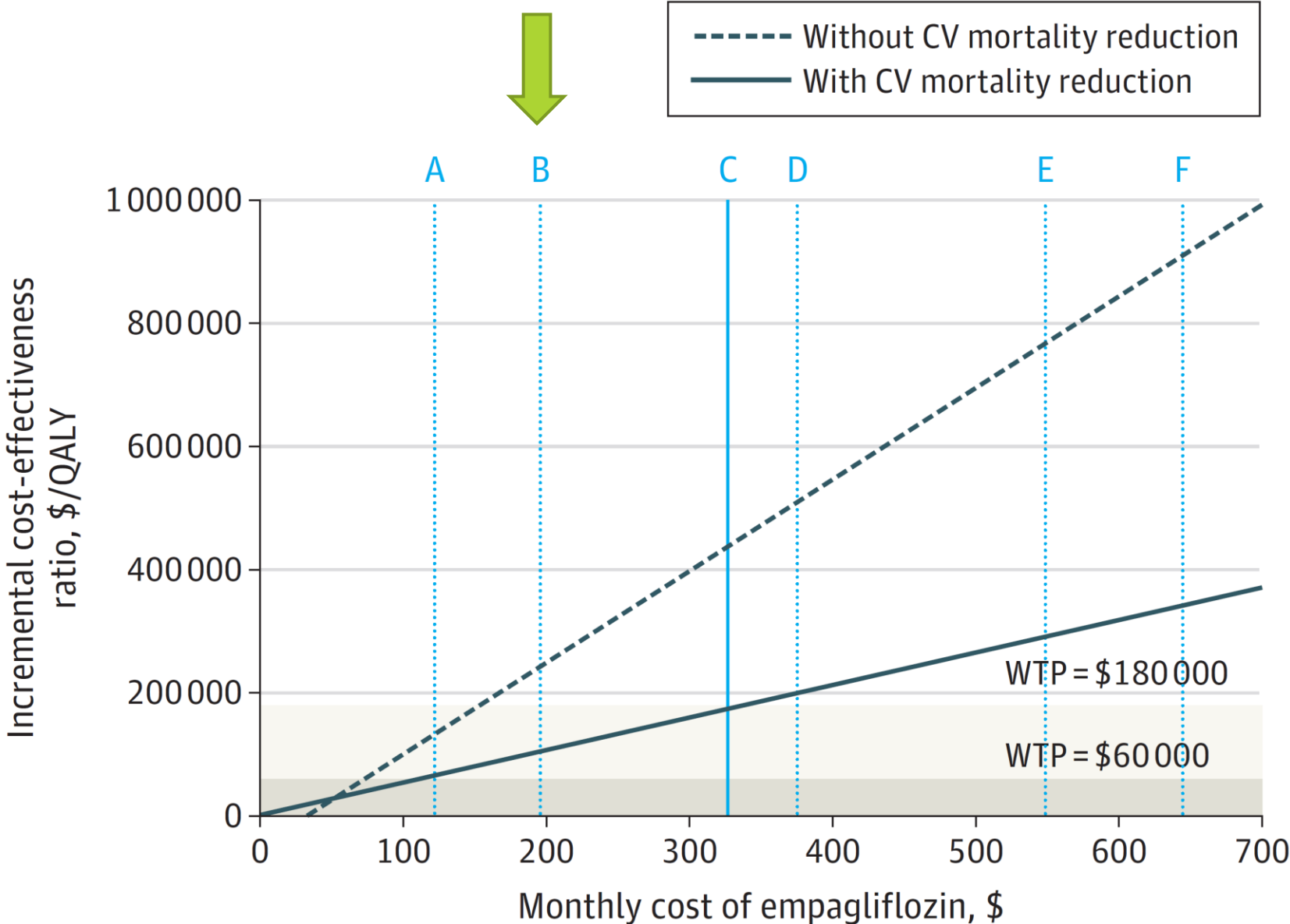
At Federal Supply Schedule price of \$327 / month...
\$437,422 / QALY

At Medicare Part D price \$375 after rebates / \$511 before
\$509,636 / QALY or \$710,825

JAMA Intern Med 2022;182(12):1278-1288



Figure 1. Cost-effectiveness Based on the Monthly Price of Empagliflozin



The incremental cost-effectiveness ratio is plotted across a broad range of price points for empagliflozin in 2021 dollars. Scenarios with and without treatment effect on cardiovascular mortality are shown. Light shaded and darker shaded regions indicate intermediate and high value of treatment, respectively. Vertical lines are plotted at different monthly costs associated with empagliflozin: A, Medicaid price of \$121.86; B, VA price of \$195.69; C, base case of \$326.69; D, Medicare Part D price of \$375.24 after mean rebate (26.5%); E, wholesale acquisition cost of \$548.54; F, retail pharmacy price of \$644.50. CV indicates cardiovascular; QALY, quality-adjusted life-year; VA, Department of Veterans



Medicare Coverage and Out-of-Pocket Costs of Quadruple Drug Therapy for Heart Failure

Kamil F. Faridi, MD, MSc,^{a,b,*} Elias J. Dayoub, MD, MPP,^{c,*} Joseph S. Ross, MD, MHS,^{b,d,e}
Sanket S. Dhruva, MD, MHS,^f Tariq Ahmad, MD, MPH,^{a,b} Nihar R. Desai, MD, MPH^{a,b}

Median annual OOP costs

- 4x therapy \$2217
- 3x therapy (no SGLT2 Inh) \$1319
- 4x therapy (ACEI for ARNI) \$1322

J Am Coll Cardiol 2022;79:2516-2525



SGLT2 Inhibitor CORNER



- **Good for heart failure across LVEF's**
- **Early use safe / beneficial**
- **Ensure dx is solid – circulatory overload clearly present**
- **Cost is an issue in the U.S.**



Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Sliwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkiene, Gad Cotter

Lancet 2022;400:1938-52



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Patients: 1078 adults, HHF, not yet on full doses GDMT

Intervention: Up-titration to 100% in 2 weeks after D/C; 4 visits over 2 months after D/C

Comparison: Usual care / local practice

Outcomes: 180-day HF readmission + death

Lancet 2022;400:1938-52



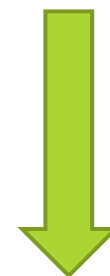
STRONG-HF Results 180 days

	Usual	STRONG	Abs.	NNT	P value
Primary	23.3%	15.2%	8.1%	13	0.0021
Re-HFF	17.1%	9.5%	7.6%	13	0.0011
CV death	10.0%	8.5%	1.5%	NS	NS

Lancet 2022;400:1938-52

STRONG-HF Results 90 days

	Usual	STRONG
RAS Inh	2%	55%
BB	4%	49%
MRA	46%	84%



HR, BP, NYHA Class,
body weight,
& NT-proBNP

Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Sliwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkiene, Gad Cotter

Patients: 1078 adults, HHF, not yet on full doses GDMT

Intervention: Up-titration to 100% in 2 weeks after D/C; 4 visits over 2 months after D/C

Comparison: Usual care / local practice

Outcomes: 180-day HF readmission + death

Conclusion: **Reduced symptoms & HHF; and inc QOL**

Lancet 2022;400:1938-52

Which of the following are true?

- A. Acetazolamide improves clinical congestion by day 3**
- B. SGLT2 Inhibitors lower rates of hypokalemia**
- C. IV iron improves long-term clinical outcomes**
- D. All of the above are true**
- E. None of the above are true**



Short Takes

AHA Heart Failure Guideline: Direct to ARNI; SGLT2 Inh for all EF's. *J Am Coll Cardiol* 2022;79:e263–e421.

IV Iron reduces HHF out to 2.7 years. *Lancet* 2022;400:2199-209.

IV Iron and Anaphylaxis: iron sucrose, ferric carboxymaltose, and ferric gluconate LOW risk; iron dextran and feromoxytol HIGHER risk (avoid). *Ann Intern Med* 2022;175:656-664

Case 2

33 y/o black woman with underlying bipolar affective disease presents with worsening anxiety, SI, and shortness of breath.

Bipolar d/o

129/72, 116, 22, SpO2 94%, Afeb. Anxious appearing.

EKG Sinus tach, nl CBC and Chem

UDS + cannabis; she asks about ketamine



Which of the following are true about IV ketamine?

- A. Increases the rate of full remission of suicidal ideas at day 3**
- B. Affects unipolar and bipolar depression similarly**
- C. Decreases the experience of somatic pain**
- D. Reduces suicidality out to six weeks**
- E. All of the above are true**



Ketamine for the acute treatment of severe suicidal ideation: double blind, randomised placebo controlled trial

Mocrane Abbar,¹ Christophe Demattei,² Wissam El-Hage,³ Pierre-Michel Llorca,⁴ Ludovic Samalin,⁴ Pierre Demaricourt,⁵ Raphael Gaillard,⁵ Philippe Courtet,^{6,7} Guillaume Vaiva,^{8,9} Philip Gorwood,⁵ Pascale Fabbro,² Fabrice Jollant^{1,5,10,11,12}

BMJ 2022;376:e067194



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Ketamine for the acute treatment of severe suicidal ideation: double blind, randomised placebo controlled trial

43

Mocrane Abbar,¹ Christophe Demattei,² Wissam El-Hage,³ Pierre-Michel Llorca,⁴
Ludovic Samalin,⁴ Pierre Demaricourt,⁵ Raphael Gaillard,⁵ Philippe Courtet,^{6,7}
Guillaume Vaiva,^{8,9} Philip Gorwood,⁵ Pascale Fabbro,² Fabrice Jollant^{1,5,10,11,12}

Patients: 156 adults, current SI voluntarily admitted,
excluding psychosis, SUD, contraindication to ketamine

Intervention: IV ketamine 40 min infusion on admit + 24 hrs

Comparison: Placebo (IV saline)

Outcomes: Remission of suicidality by day 3

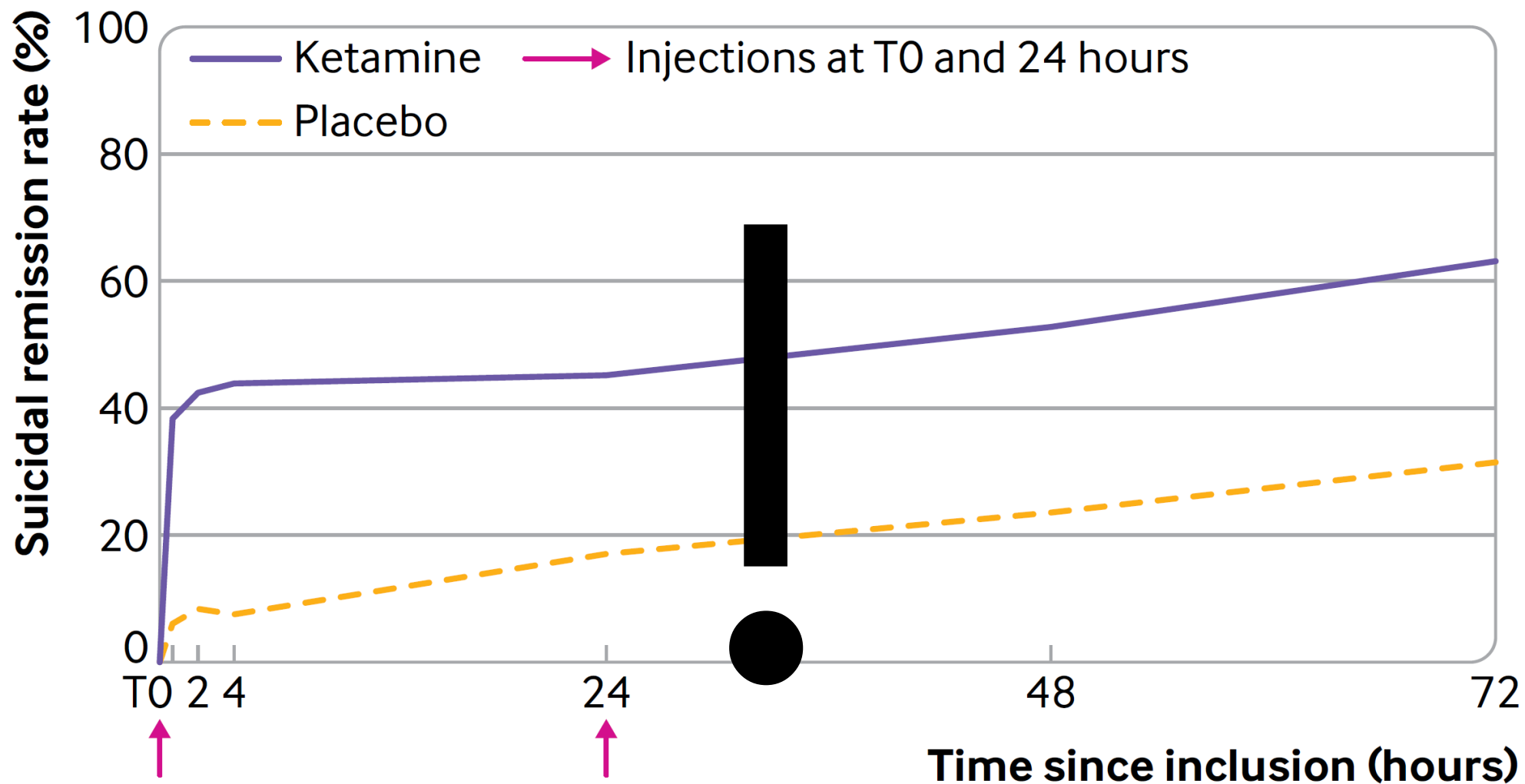
BMJ 2022;376:e067194



IV Ketamine Results

	Saline	Ketamine	Abs.	NNT	P value
No SI 3d	31.6%	63.0%	31.4%	3	<0.001
Unipolar	35.7%	42.3%	6.6%	NS	NS
Bipolar	28.0%	84.6%	56.6%	2	<0.001
No SI 6w	56.3%	69.5%	13.2%	NS	NS

BMJ 2022;376:e067194



Ketamine for the acute treatment of severe suicidal ideation: double blind, randomised placebo controlled trial

46

Mocrane Abbar,¹ Christophe Demattei,² Wissam El-Hage,³ Pierre-Michel Llorca,⁴
Ludovic Samalin,⁴ Pierre Demaricourt,⁵ Raphael Gaillard,⁵ Philippe Courtet,^{6,7}
Guillaume Vaiva,^{8,9} Philip Gorwood,⁵ Pascale Fabbro,² Fabrice Jollant^{1,5,10,11,12}

- **IV ketamine reduced mental pain but not physical pain**
- **No manic or psychotic symptoms seen**
- **Sedation in 11%, depersonalization in 9.6%**
- **NB: this is a potential drug of abuse**

BMJ 2022;376:e067194



Ketamine for the acute treatment of severe suicidal ideation: double blind, randomised placebo controlled trial

47

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Ludovic Samalin,⁴ Pierre Demaricourt,⁵ Raphael Gaillard,⁵ Philippe Courtet,^{6,7}
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excluding psychosis, SUD, contraindication to ketamine

Intervention: IV ketamine 40 min infusion on admit + 24 hrs

Comparison: Placebo (IV saline)

Outcomes: Remission of suicidality by day 3

Conclusion: **Safely and rapidly reduces bipolar suicidality**

Did you notice SpO2 94% in this black woman with + cannabis on UDS?



Assessment of Racial and Ethnic Differences in Oxygen Supplementation Among Patients in the Intensive Care Unit

Eric Raphael Gottlieb, MD, MS; Jennifer Ziegler, MD, MSc; Katharine Morley, MD, MPH;
Barret Rush, MD, MPH; Leo Anthony Celi, MD, MPH

JAMA Intern Med 2022;182:849-858

Racial and Ethnic Discrepancy in Pulse Oximetry and Delayed Identification of Treatment Eligibility Among Patients With COVID-19

Ashraf Fawzy, MD, MPH; Tianshi David Wu, MD, MHS; Kunbo Wang, MS; Matthew L. Robinson, MD; Jad Farha, MD; Amanda Bradke, MD, MA;
Sherita H. Golden, MD, MHS; Yanxun Xu, PhD; Brian T. Garibaldi, MD, MEHP

JAMA Intern Med 2022;182:730-738



Racial bias and reproducibility in pulse oximetry among medical and surgical inpatients in general care in the Veterans Health Administration 2013-19: multicenter, retrospective cohort study

Valeria S M Valbuena,^{1,2,3} Sarah Seelye,² Michael W Sjoding,⁴ Thomas S Valley,^{2,4}
Robert P Dickson,⁴ Steven E Gay,⁴ Dru Claar,⁴ Hallie C Prescott,^{2,4} Theodore J Iwashyna^{2,3,4}

BMJ 2022;378:e069775

Racial Bias in Pulse Oximetry Measurement Among Patients About to Undergo Extracorporeal Membrane Oxygenation in 2019-2020



A Retrospective Cohort Study

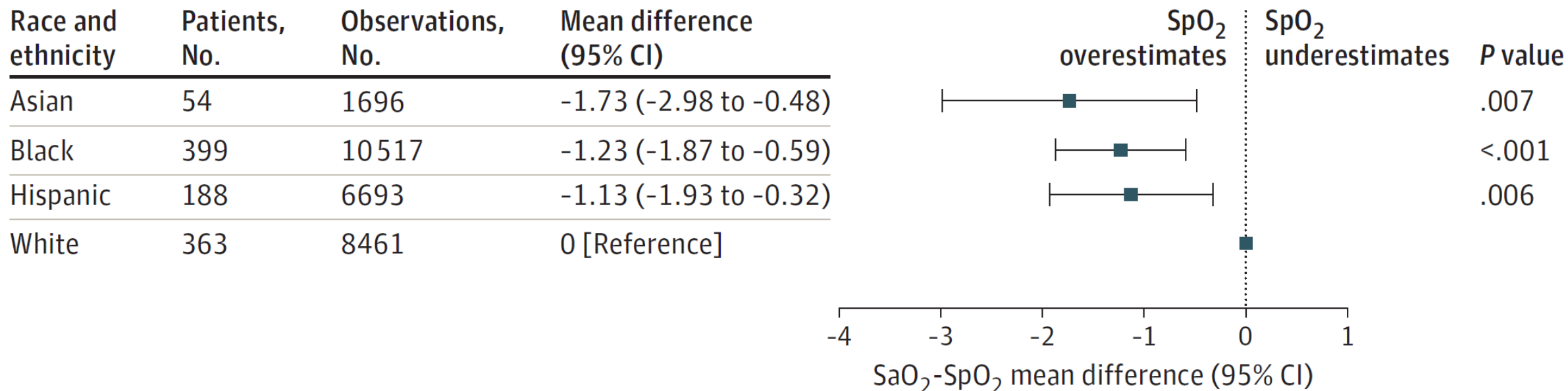
Valeria S. M. Valbuena, MD; Ryan P. Barbaro, MD; Dru Claar, MD; Thomas S. Valley, MD;
Robert P. Dickson, MD; Steven E. Gay, MD; Michael W. Sjoding, MD; and Theodore J. Iwashyna, MD, PhD



Chest 2022;161:971-978



Figure 3. Relative Mean Differences With 95% CIs of SaO₂-SpO₂ for Patients of Racial and Ethnic Minority Groups Based on the Adjusted Parsimonious Linear Mixed-Effects Model



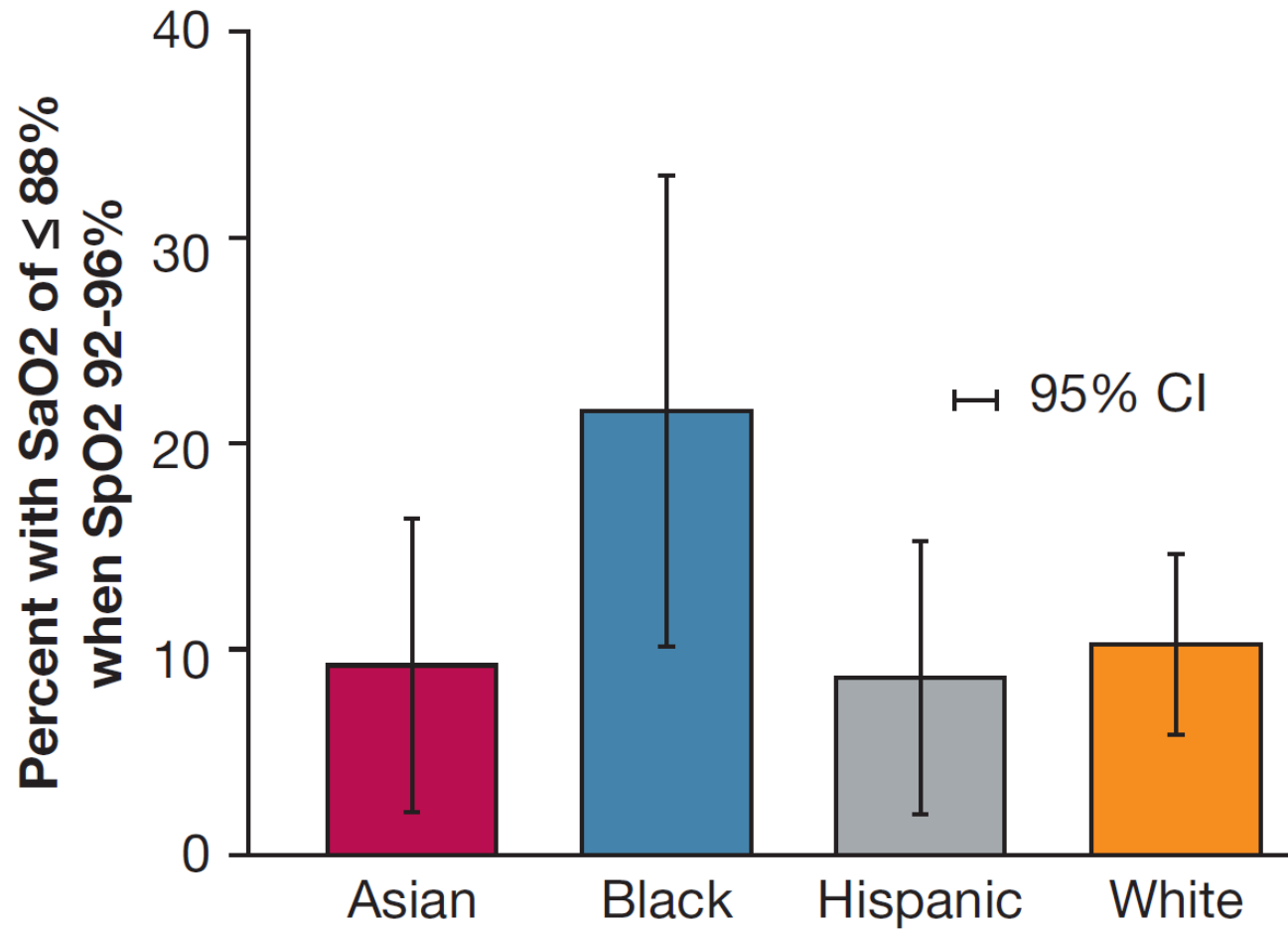


Figure 3 – Prevalence of SaO_2 of $\leq 88\%$ despite SpO_2 of 92% to 96% across different races and ethnicities. SaO_2 = arterial oxygen saturation; SpO_2 = peripheral oxygen saturation.

**With pigmented skin, SpO₂ will
OVERestimate SaO₂ – don't be fooled!**



Which of the following are true about IV ketamine?

- A. Increases the rate of full remission of suicidal ideas at day 3**
- B. Affects unipolar and bipolar depression similarly**
- C. Decreases the experience of somatic pain**
- D. Reduces suicidality out to six weeks**
- E. All of the above are true**



Case 3

**72 y/o man regular clinic follow-up; claudication
HTN, CKD2, BPH, GERD, OA, longstanding tobacco
Meds: HCTZ 25, lisinopril 40, tamsulosin 0.4, omeprazole 20
132/74, 76, 18, dependent rubor, hair loss
He asks about chlorthalidone instead of HCTZ...**



Which of the following are true re: chlorthalidone vs. HCTZ?

- A. Improves blood pressure control**
- B. Lowers rates of major adverse cardiac outcomes**
- C. Lowers risk of hospitalization for acute kidney injury**
- D. Increases the risk of hypokalemia**
- E. All of the above are true**



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DECEMBER 29, 2022

VOL. 387 NO. 26

Chlorthalidone vs. Hydrochlorothiazide for Hypertension— Cardiovascular Events

Areef Ishani, M.D., William C. Cushman, M.D., Sarah M. Leatherman, Ph.D., Robert A. Lew, Ph.D., Patricia Woods, M.S.N., R.N., Peter A. Glassman, M.B., B.S., Addison A. Taylor, M.D., Cynthia Hau, M.P.H., Alison Klint, M.S., Grant D. Huang, Ph.D., M.P.H., Mary T. Brophy, M.D., M.P.H., Louis D. Fiore, M.D., M.P.H., and Ryan E. Ferguson, Sc.D., M.P.H., for the Diuretic Comparison Project Writing Group*

N Engl J Med 2022;387:2401-10



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Patients: 13,523 U.S. Veterans ≥ 65 y/o on HCTZ 25-50mg

Intervention: Switch to chlorthalidone 12.5-25mg

Comparison: Stay on HCTZ

Outcomes: Composite non-fatal MI, stroke, HHF, urgent cath for unstable angina, and non-cancer death



Diuretic Comp. Results @ 5 yrs

	HCTZ	Chlorth.	Abs.	NNT/H	P value
Primary	10.0%	10.4%	0.4%	NS	NS
SBPmmHg	139.5	138.4	1.1	NS	NS
Death	6.6%	6.6%	0%	NS	NS
HypoK+	4.4%	6.0%	1.6%	63	<0.001

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Conclusion: Chlorthalidone no better than HCTX, more  K+

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VOL. 387 NO. 25

Surgery or Endovascular Therapy for Chronic Limb- Threatening Ischemia

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Patients: 1830 adults infra-inguinal CLI

Intervention: Surgery (1) if SV conduit OK or (2) if not

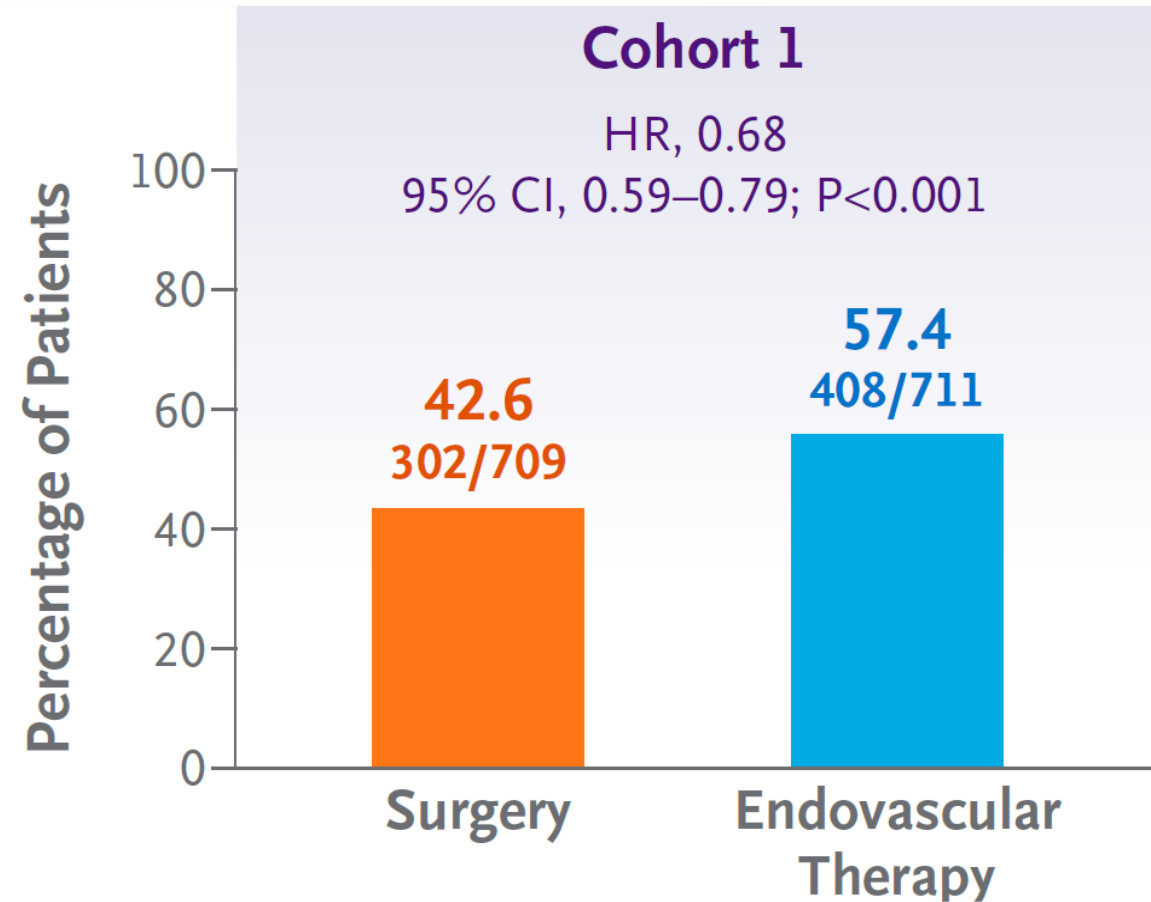
Comparison: Endovascular therapy

Outcomes: Major limb re-intervention + death @ 2.7 yrs



Major Adverse Limb Event or Death from Any Cause

63



ARR 14.8%, NNT = 8

N Engl J Med 2022;387:2305-16



Which of the following are true re: chlorthalidone vs. HCTZ?

- A. Improves blood pressure control
- B. Lowers rates of major adverse cardiac outcomes
- C. Lowers risk of hospitalization for acute kidney injury
- D. Increases the risk of hypokalemia
- E. All of the above are true



Short Takes

USPSTF Primary Prevention ASA – small benefit 40-59 y/o with $\geq$ 10% 10-yr risk. *JAMA* 2022;327:1577-1584.

AHA Heart Failure Guideline: Direct to ARNI; SGLT2 Inh for all EF's. *J Am Coll Cardiol* 2022;79:e263–e421.

Canadian Syncope Score validated in international cohort. *Ann Intern Med* 2022;175:783-794.

Short Takes

Endovascular rx + lytics beneficial for **large territory** ischemic strokes, NNT=5. *N Engl J Med* 2022;386:1303-13.

And for **basilar artery** stroke, NNT=4. *N Engl J Med* 2022;387:1361-72.

Early rhythm control for AF associated w/ better outcomes in **low-risk** pts, effect size small. *Ann Intern Med* 2022;175:1356-1365.

Practice Summary

Things to Do:

1. **SGLT2 Inhibitors in HF any EF; mind the \$**
2. **Intensive GDMT titration after HHF**
3. **Recommend IV ketamine for bipolar suicidality**
4. **Incorporate skin color into SpO2 interpretation**
5. **Release the belief that chlorthalidone >> HCTZ**
6. **Refer CLI patients to vascular surgery...**

Practice Summary

Things to Do:

- 7. Request endovascular / lytic therapy for large territory and basilar artery acute strokes**

Practice Summary

Things to Consider:

1. Adding acetazolamide to loop diuretics to augment diuresis – not just for alkalosis any more
2. Referring 'new' Afib and low risk for EP ablation
3. Silly walking to inc exercise; pickle juice for cirrhotic cramps...

Practice Summary

Things Not to Do:

1. Use IV iron dextran or feromoxytol over other IV iron formulations

THANK YOU!

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