Top 10: EBM Updates From The Medical Literature

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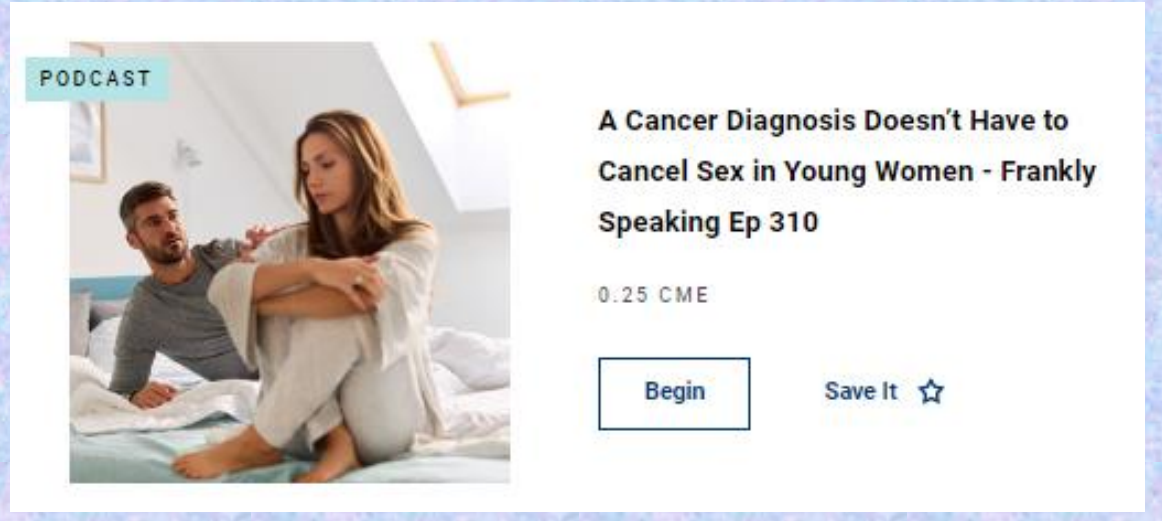
PODCAST: **Frankly Speaking About Family Medicine**

THANK YOU!


primed
Frankly Speaking
About Family Medicine


PODCAST
A Cancer Diagnosis Doesn't Have to Cancel Sex in Young Women - Frankly Speaking Ep 310
0.25 CME
Begin
Save It


PODCAST
Tirzepatide: A New Treatment for Diabetes- Frankly Speaking EP 285
0.25 CME
Begin
Save It

By the end of this session, the learner will:

- 1. Implement recently published data into clinical practice
- 2. Analyze the medical statistics included in these publications
- 3. Identify bias in medical publications that can lead to inaccurate conclusions and maintain a healthy skepticism

- I have Nothing to Disclose

SR: Pilates Improves Delivery Outcomes

SR: 13 studies 719 pregnant women
Pilates Group vs Placebo

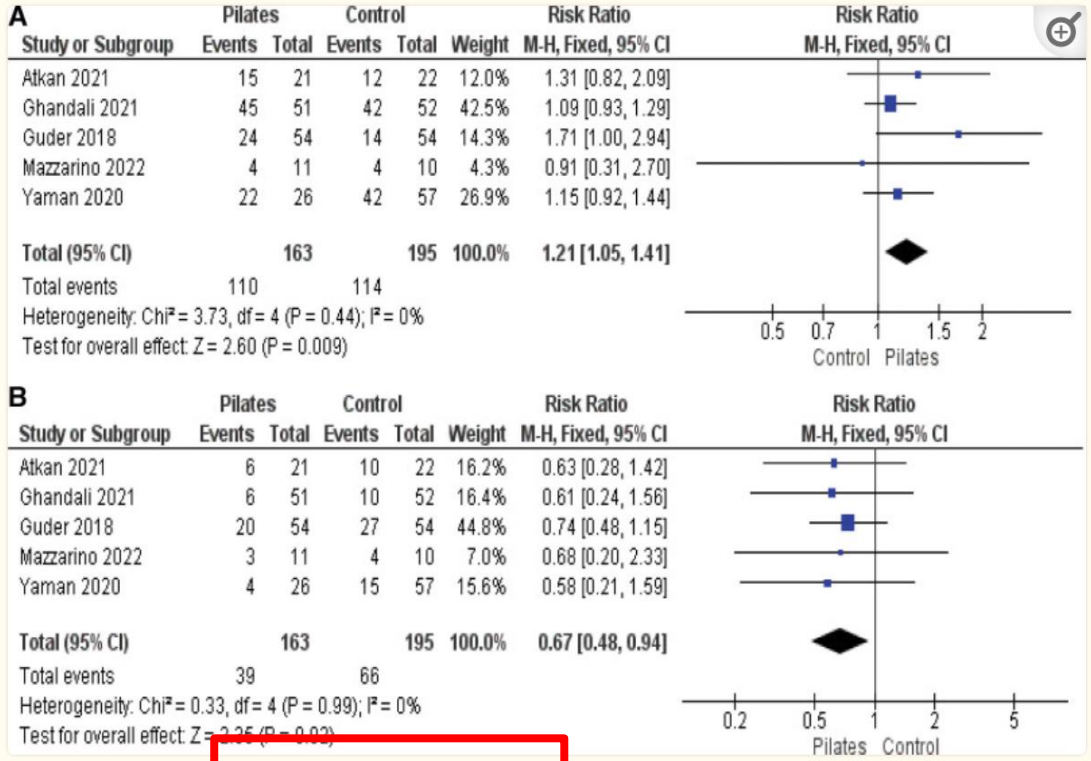
Results:

- **↑ risk deliver vaginally** than control (RR = 1.21, 95% CI [1.05 to 1.41]).
- **Shorten active labor** (min) [(MD = **−84.89**, 95% CI [−130.89−38.90])
- **Lower Cesarean delivery** (RR = 0.67, 95% CI [0.48–0.94]).
- **Less Weight Gain** during pregnancy (−3.48 kg, 95% CI [−6.17 to −0.79], *P* = .01)

Medicine (Baltimore). 2023 May 26;102(21):e33688

Pilates Influence on Birth Outcomes

↑Vaginal Birth

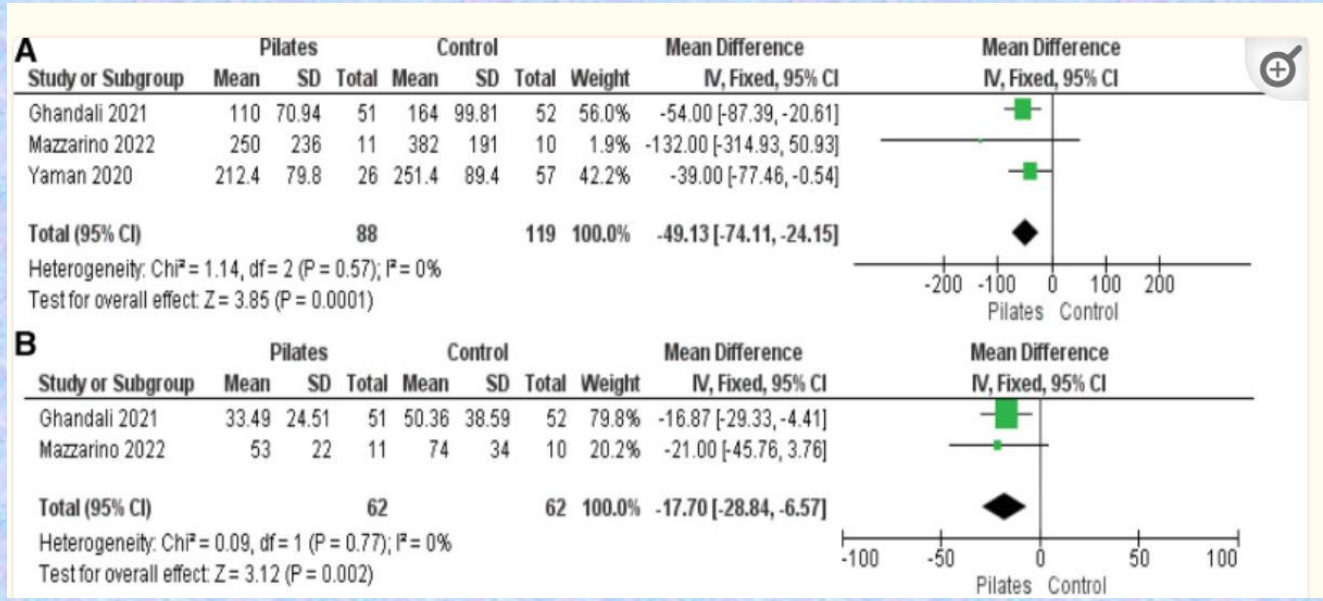


↓C/Section

Figure 3.

(A) Forest plot of type of delivery (Vaginal). (B). Forest plot of type of delivery (Cesarean).

↓Active Labor



↓2nd Stage Labor

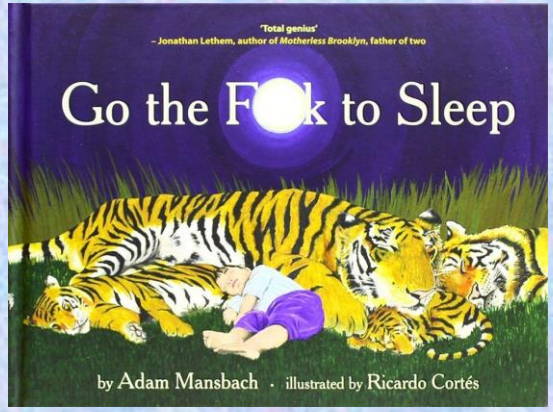
Lamaze Breathing Still Works!

SR: 22 RCT's **Lamaze** breathing plus **nursing interventions:**
(postural, delivery ball, doula, massage and psychological nursing)

- Results:
- **Inc Vaginal delivery** ([RR] = 2.97, 95% [CI] [2.48, 3.56]),
- **Shortened length of labor** (-2.604, 95% CI [-3.120, -2.087]),
- **Alleviated labor pain** (RR = 0.194, 95% CI [0.115, 0.325])
- **Reduced postpartum bleeding** (-2.966, 95% CI [-4.056, -1.877]).

Medicine (Balt). 2021 2021 Jan 29;100(4):e23920.

Baby And Sleep



- Real world study of 2090 parent-infant dyads with sleep issues (3-18 months): Baby Monitor to determine best method to help child sleep through the night
- Unmodified Extinction (27.6%) ***crying it out-*** just leave the infant alone till morning,
- Modified Extinction (42.7%) ***controlled crying*** – leave the infant alone, but periodically intervening with minimal interaction (talking w/o touching)
- Parental Presence (10%) ***camping out*** – staying in the room with the child.
- Outcomes:
- Unmodified and Modified Extinction were rated as significantly **more difficult** vs Parental Presence AND were --**MORE Successful and Quicker** to show improvements AND led to longer Infant sleep vs Parental Presence

J Pediatr. November 11, 2022. https://doi.org/10.1016/j.jpeds.2022.10.038

WTF:
YOU DID
WHAT?

At 8 Months:
Gave him a chicken Leg to Munch on….

Really….
Why Did You
Do That?

Baby Led Weaning

Baby Led Weaning

- BLW: let infant eat based upon what they can feed themselves

- Cross-sectional survey of children 6 - 36 months of age
- BLW method
  - More likely to have their diets expanded after 6 months of age,
  - More likely to be given broader range of food.
  - **More Vomiting, Food Spitting, Gagging & More Frequent Choking**.

Front Pediatr. 2022 Oct 21;10:992244. doi: 10.3389/fped.2022.992244

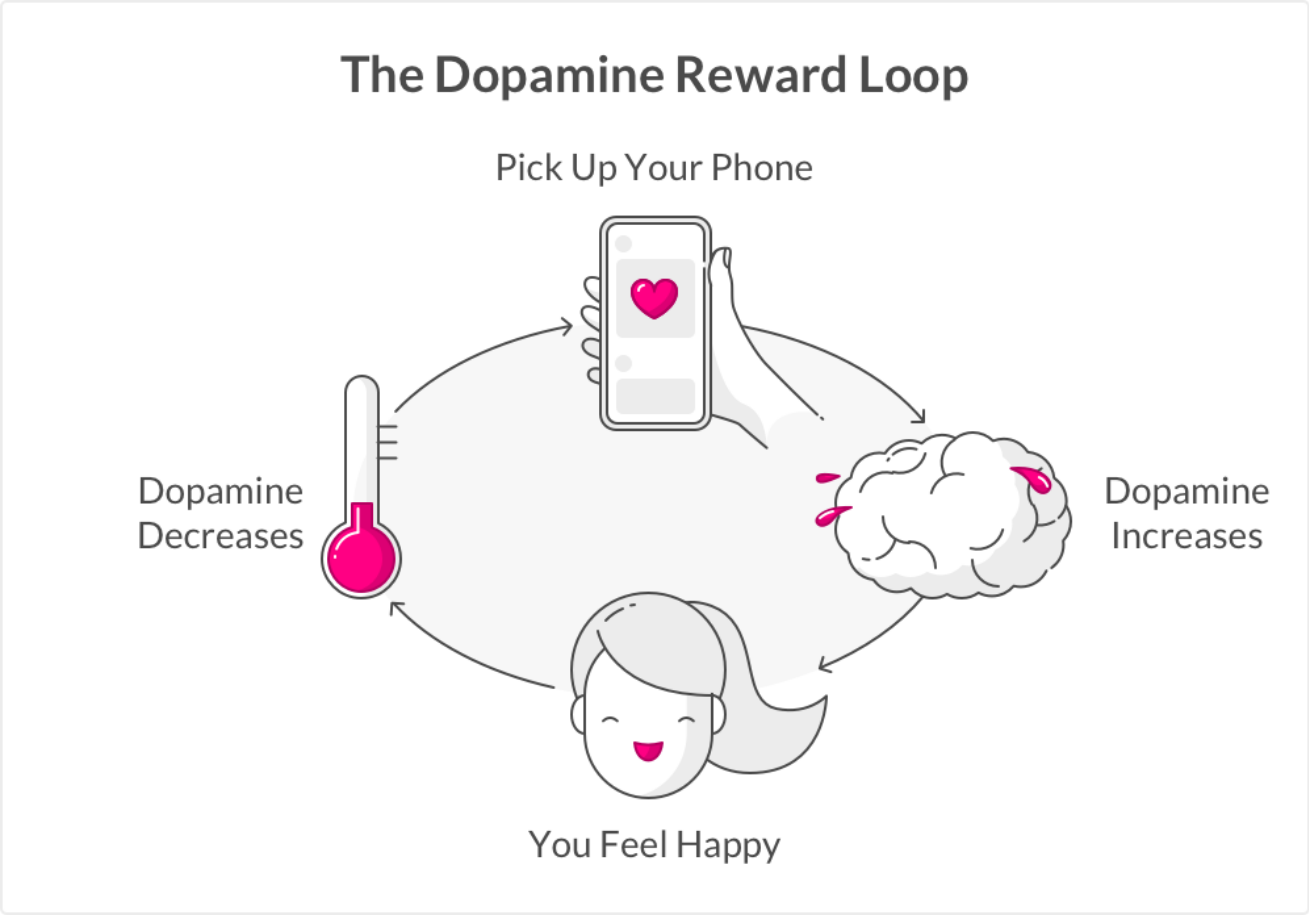
“How I Screwed up…”

58 Y/O male with PMHx: HTN, Hyperlipidemia, Obesity, NAFLD, smokes 1 ½ PPD, alcoholic; consuming 8 beers per night….

1. Why did you say he was a Male?

2. Instead, say Alcohol Use Disorder

Dopamine Use Disorder (DUD)



Screentime is a BIG Problem For Parents: Un. Of Michigan Mott Children's Hospital Survey

- Survey 2000+ Parents: Big problems, Somewhat of a problem, or Not a problem.

- Top "big problems" were:

1. Overuse of devices or screen time (67%),
2. Social media (66%),
3. Internet safety (62%)
4. Depression and suicide (57%)
5. Bullying (53%)

- Low Income Parents: Depression/suicide, bullying, school violence

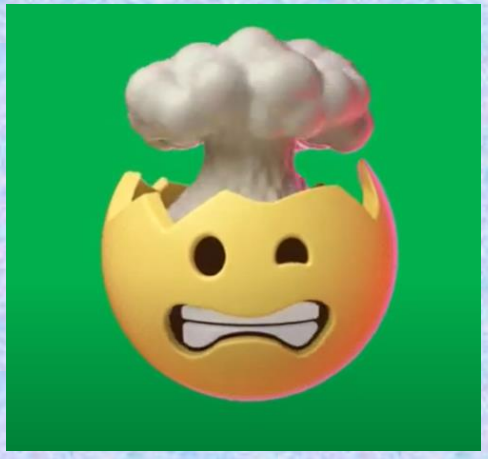
https://mottpoll.org/reports/overuse-devices-and-social-media-top-parent-concerns

Screentime at Age 1 Increases Risk of Developmental Delay

- Cohort study 7097 mother-child pairs **Screen Time at age 1 year** and Developmental Delays at ages 2 and 4 years
- Time on Screens (Hours/Day):
  --48.5% of children < 1 hour
  --29.5% 1 - 2 hours/day
  --17.9% 2 - 4 hours/day
  --4.1% >/= 4 hours/day.
- At 2 Years, high Screen time associated with Developmental Delay in:
- Communication: ([OR], 1.61]: 1 to <2 h/d; 2.04: 2-4 h/d; 4.78: ≥4 vs <1 h/d),
- Fine motor (1.74 [1.09-2.79] for ≥4 vs <1 h/d),
- Problem-solving (1.40 [1.02-1.92] for 2 to <4 h/d; 2.67 [1.72-4.14] for ≥4 vs <1 h/d), and
- Personal and social skills (2.10 [1.39-3.18] for ≥4 vs <1 h/d) domains.
- At 4 years: Communication and Problem-solving

JAMA Pediatr. 2023.doi:10.1001/jamapediatrics.2023.3057

SR: High Screen Use → ↑Obesity & Depression



- SR: 13 studies on association between HIGH screentime on "children and young people (0-18)":

- Strong Evidence: **Obesity/adiposity**, **Depressive** symptoms
- Moderate: Higher energy intake/**Poor Diet, Lower QOL**
- Weak: for behavior problems, anxiety, hyperactivity and inattention, poorer self-esteem, poorer fitness, poorer cognitive development, lower educational attainments & poor sleep
- *Small amounts* of daily screen use not harmful

BMJ Open. 2019 Jan 3;9(1):e023191. doi: 10.1136/bmjopen-2018-023191.

PARENTS

Put down the screen

- RCT: Limit Parental Screen time on child sleep & recreation.
- Screen Reduction Group: exchanged Parent (smartphones, tablets) for a ***non–smart phone*** (allow calls & texts) & limit screen use to </= **3 hours per week for 2 weeks**.
- Control group families carry on as usual
- Results: **INCREASE** in non-sedentary activity of children

  Intervention was **44.8 Min/day** vs Control **1.0 min/day**

JAMA Pediatr. 2022 Aug 1;176(8):741-749

SR: Digital eye strain > 4 Hours/Day & Blue Screen Filters No Benefit

- SR on Factors **aggravate or alleviate Digital eye strain (DES)** in < 40 years old; 10 studies/2365 participants.
-

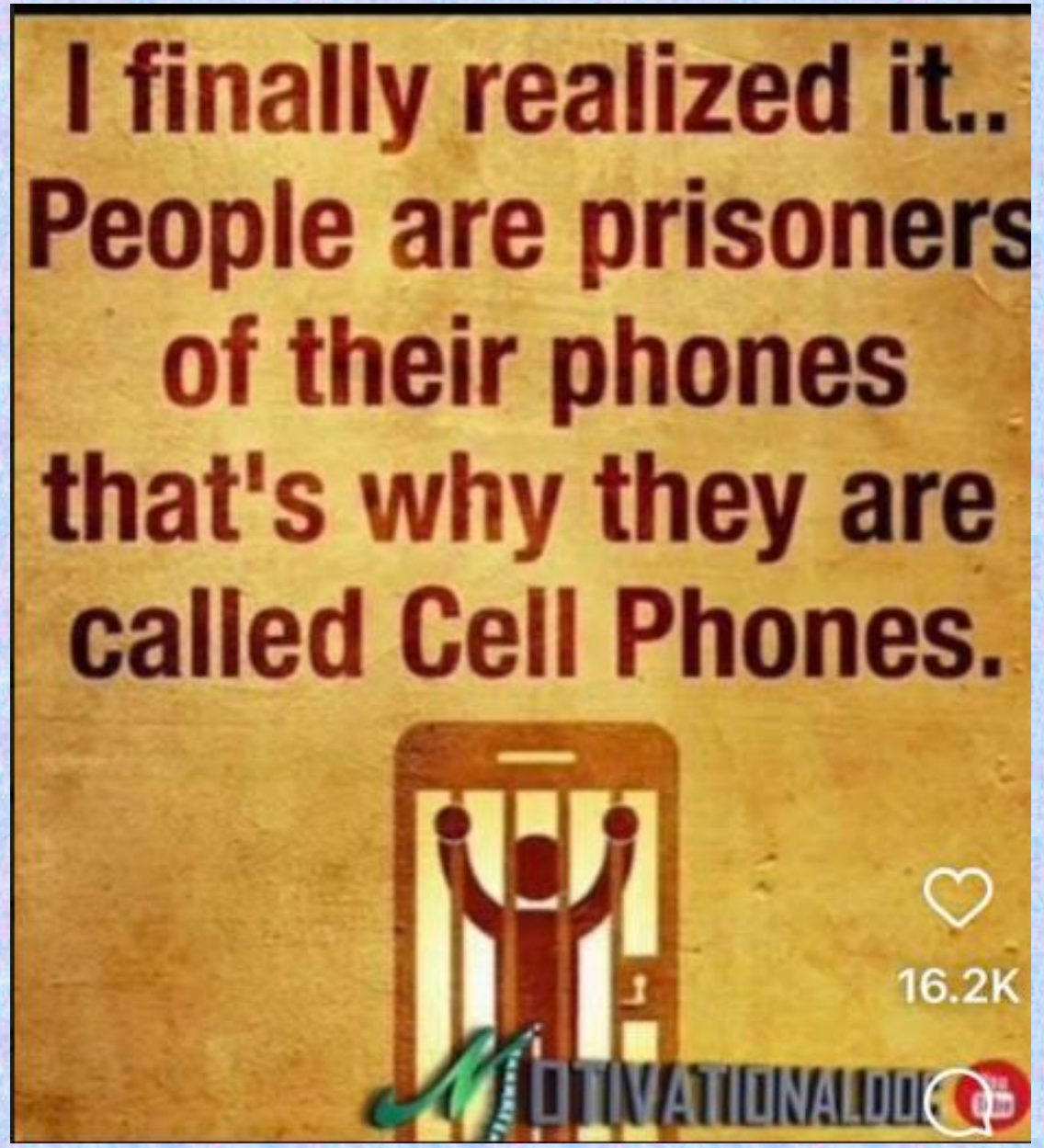
  Conclusion:
- DES Associated w/Screen Use **> 4 h/day** & **Poor ergonomics** (glare, uneven lighting) **Blue-blocking filters** do NOT prevent DES (2 studies, 130 participants)

  Prev Med 2023 May;170:107493. doi: 10.1016/j.ypmed.2023.107493

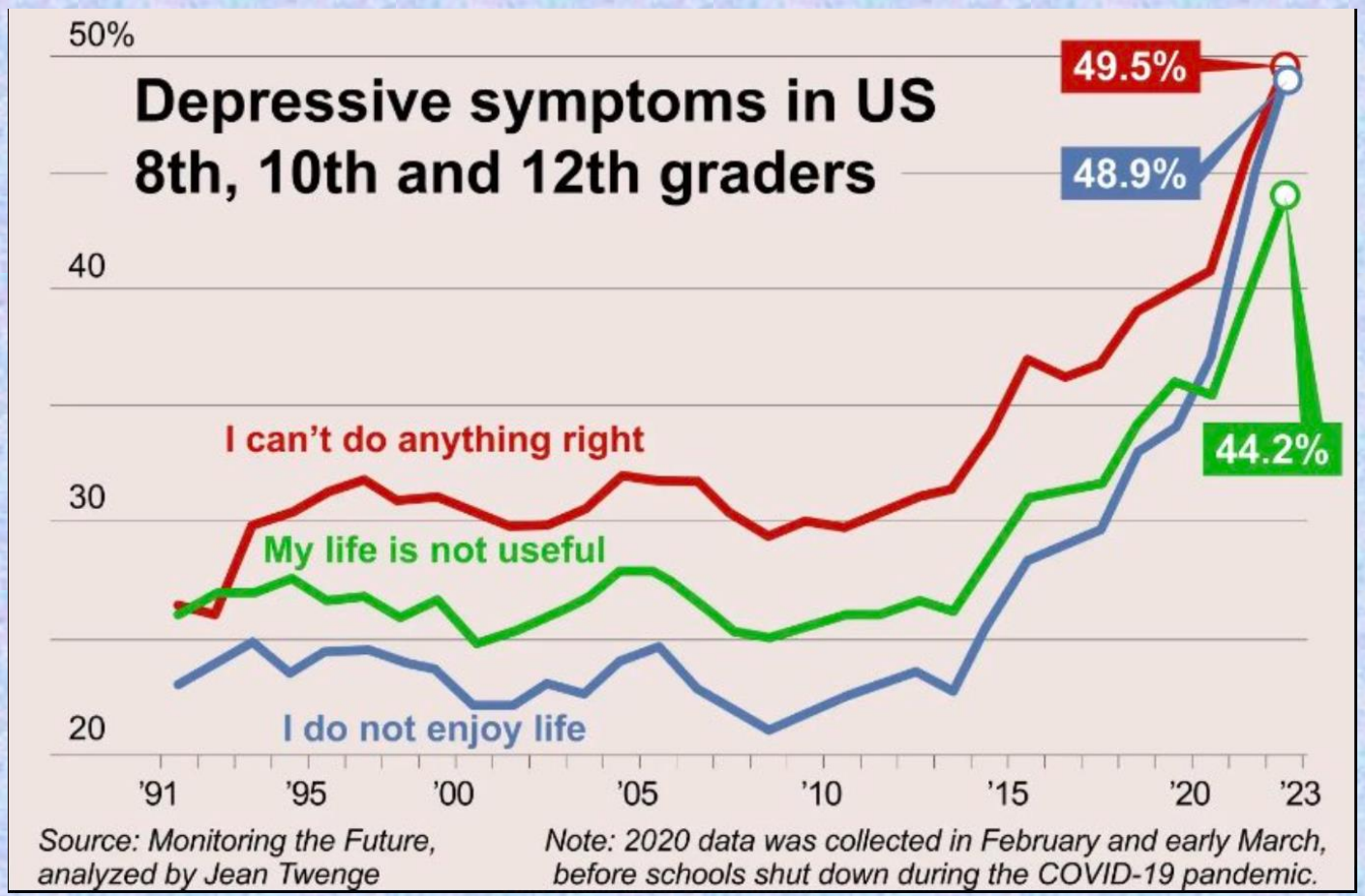
- 2023 CDSR: 17 RCT's: Blue Screens→ No Benefit

  CDSR: 8 CD013244. DOI: 10.1002/14651858.CD013244.pub2. 17 RCT's:

No Blue Screen


I finally realized it..
People are prisoners
of their phones
that's why they are
called Cell Phones.
16.2K

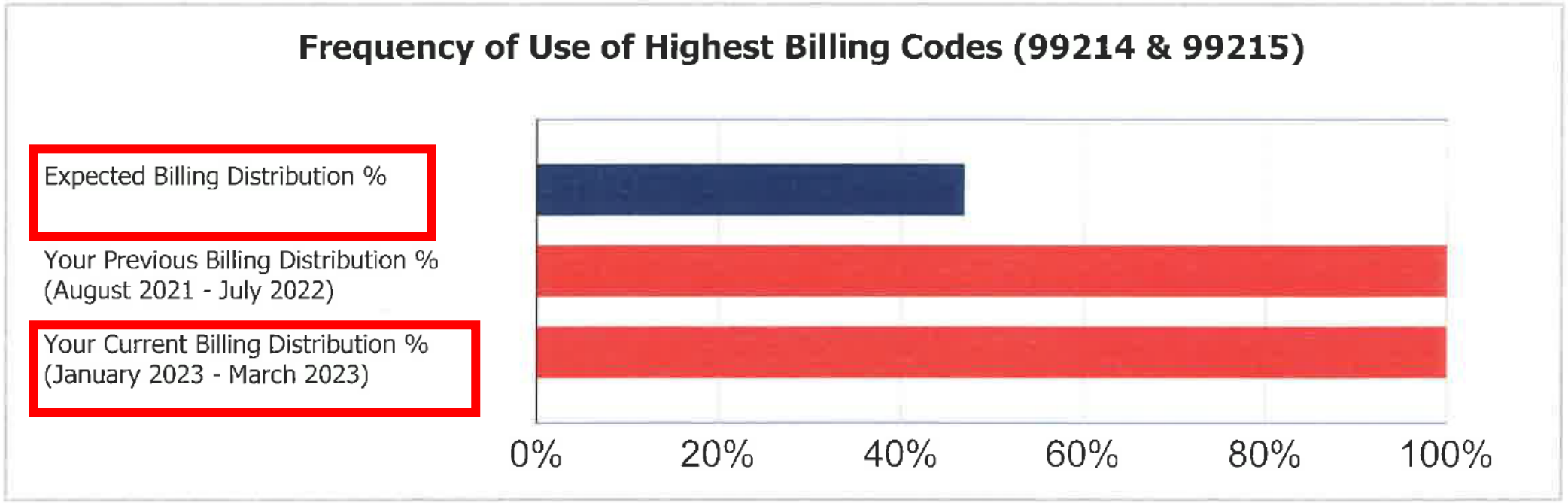
Monitoring The Future Project: Data Before School Closure in 2020



I NEED your Help Billing: 99215

Update on your billing

We recently conducted a subsequent analysis based on paid claims from January 2023 through March 2023. As you will see below and in the more detailed attached report, **your billing of these services <u>continues to be</u> considerably greater than the expected billing distribution of your specialty group.**

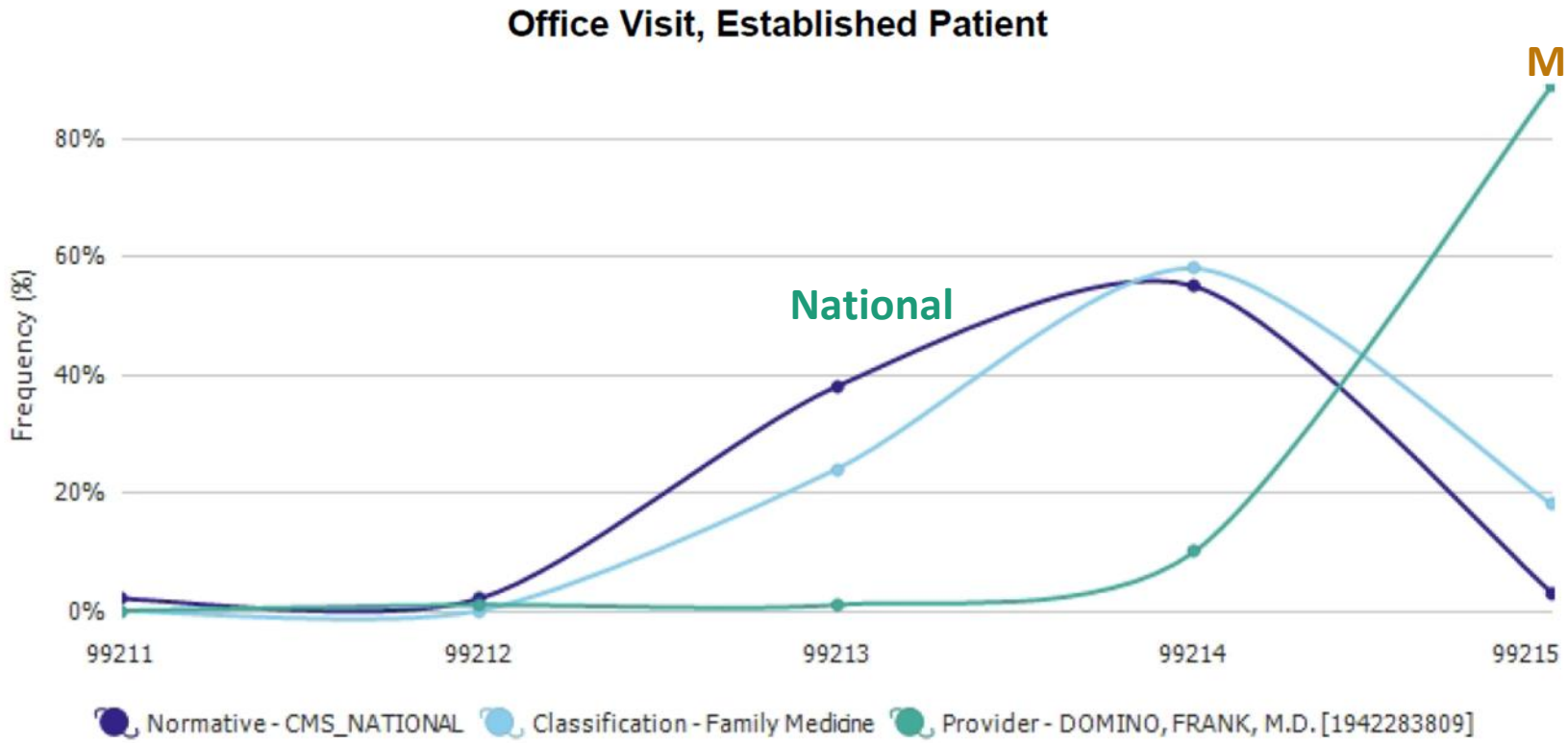


E&M Bell Curve

DOMINO, FRANK, M.D. [1942283809]

CMG Family Medicine Shrewsbury Fam Practice 604 Main St

11/01/2022 - 04/30/2023



58 Y/O: PMHx HTN, Hyperlipidemia, Obesity, NAFLD, TUD & AUD

- A/P

- HTN: Continue Losartan 50 mg/day. Discussed adding aerobic activity over lunch by walking up/downstairs at office
- Hyperlipidemia: On atorvastatin 10 mg; exercise as above
- Obesity/NAFLD: ALT > AST, FIB4 score < 1.3. Offered referral to dietician-refused. Discussed weight loss meds—refused.
- Social: Daughter heading off to college this fall
- TUD/AUD: Pre-contemplative; reviewed their understanding of Risks.

WHAT CODE WOULD YOU BILL?

99213, 99124, 99215

Coding Conundrums: SOLVED!

COMPARISON OF CODES 99214 AND 99215

Key components (2 of 3 required, plus medical necessity)	99214	99215	Difference
History	Detailed: • 4+ HPI elements or status of 3 or more chronic diseases • Review of 2 to 9 systems • 1 PFSH element	Comprehensive: • 4+ HPI elements or status of 3 or more chronic diseases • Review of 10 or more systems • 2 PFSH elements	• Review of additional 8 systems • 1 additional PFSH element
Exam	Detailed: • 12+ exam elements from 2 or more systems	Comprehensive: • 18+ exam elements; 2 exam elements from *each* of 9 systems	• 6 additional exam elements from *each* of 9 systems
Medical decision-making	Moderate complexity: • Prescription medications • Multiple diagnoses or management options	High complexity: • Parenteral controlled substances • Multiple diagnoses or management options	• 1 parenteral controlled substance

HPI = History of present illness; PFSH = Past, family, and social history.

Coding Based on Time

New Patients		Established Patients	
99202	15-29 minutes	99211	No time reference
99203	30-44 minutes	99212	10-19 minutes
99204	45-59 minutes	99213	20-29 minutes
99205	60-74 minutes	99214	30-39 minutes
+99417*	75 minutes and beyond for each 15 minutes of time	99215	40-54 minutes
		+99417*	55 minutes and beyond for each 15 minutes of time

*If a new patient/physician interaction occurred on a specific date of service and lasted for a total of 105 minutes, the correct coding would be: CPT 99205, 99417X2 units to equal the 105 minutes.

Document time in the medical record when used for the basis for the code.

Use time for coding whether or not counseling and/or coordination of care dominates the service.

Reimbursed procedures are excluded from total time.

Count the total time on the date of services: 99202-99215.

To count physician or another qualified health care professional's time spent in the supervision of clinical staff who perform the face-to-face services of the encounter, use 99211.

1/2

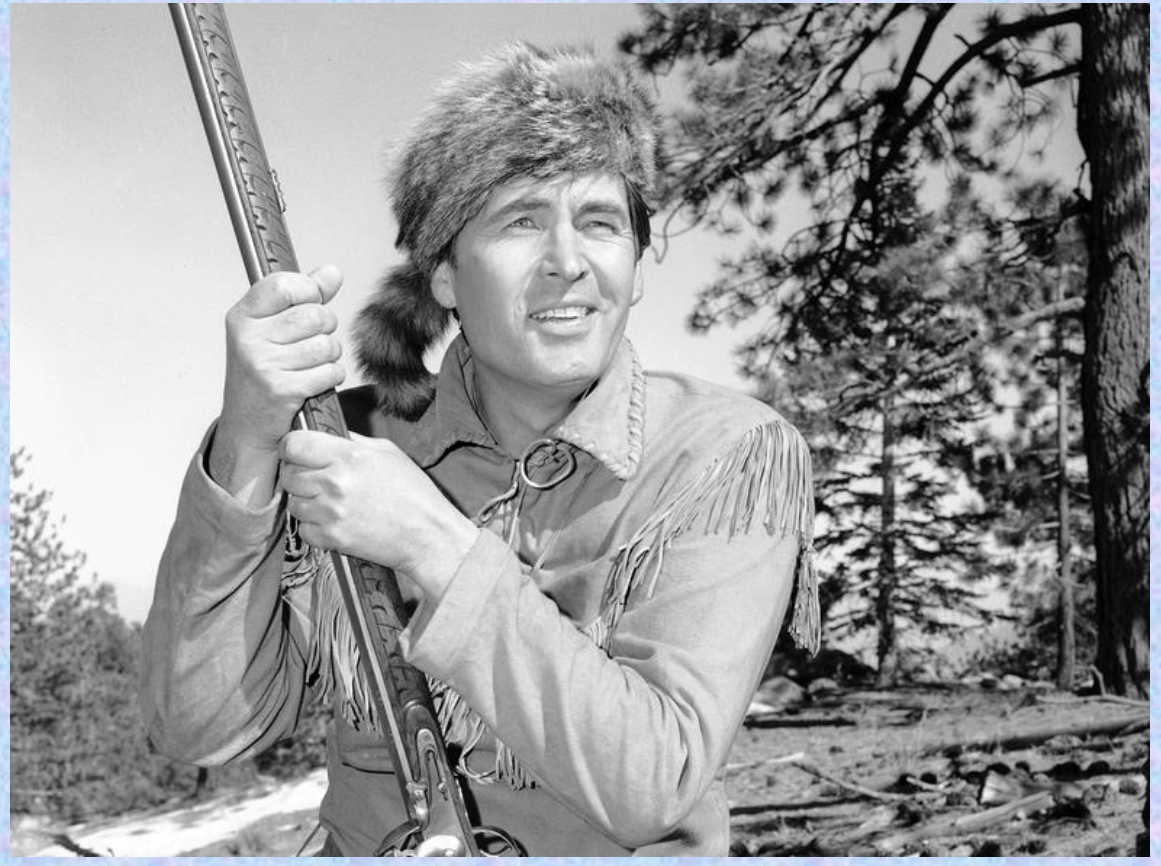
5 Minutes Review Chart before visit
30 Minutes for visit
5-10 Minutes Documentation & Coordination

Epic Challenge: .TOTALTIMEEMBILLING

- I spent a total of *** **(use 45**) minutes on the date of encounter, which included:
- · Preparing to see the patient (e.g., review of test results)
- · Obtaining and/or reviewing separately obtained history
- · Performing a medically appropriate exam and/or evaluation
- · Counseling and educating the patient/family/caregiver
- · Ordering medications, tests, procedures
- · Referring and communicating with other healthcare professionals, when not separately reported
- · Documenting clinical information in the health record
- · Care coordination not separately reported

- **MEDICARE**: 99215: 2.8 RVU/$**200** **13 Pt/D → 36 RVU/Day**
  99214: 1.9 RVU/**$140** **19 Pt/D → 36 RVU/Day**
  99213: 1.3 RVU/$**92** **27 Pt/D → 36 RVU/Day**

Amazing Tracker, but he Did Not Kill a Bear at 3



Consistent Tracking Foods → **10% Weight Loss in 6 Months**

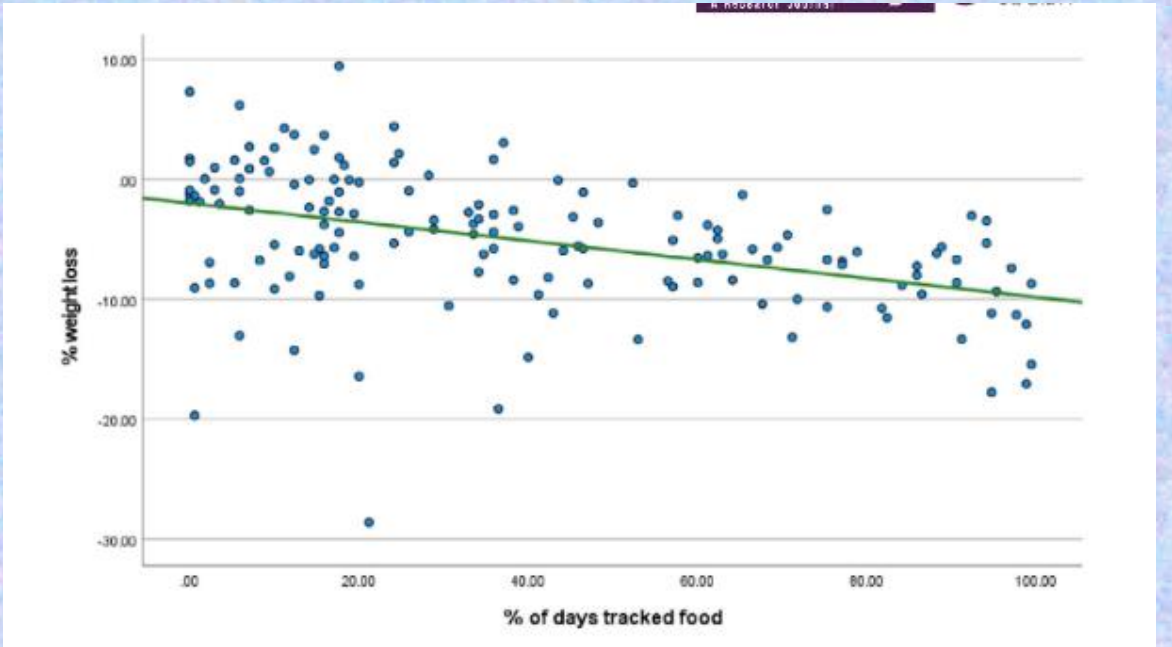
- 153 participants, single-arm trial of a commercial digital weight-management program, WeightWatchers (WW).
- Daily Food Tracking, weekly digital group support & social media group

- Results @ 6 Months:
- Percent Days Food Tracking ($p < 0.001$).

28.5% → 3%

39.4% → 5%

67.1% → 10%



MINDFULNESS IS KEY TO WEIGHT LOSS

Obesity (Silver Spring). 2023 Jun 4. doi: 10.1002/oby.23795

Which Diet will help you live Longer and Better?
Fruits, Vegetables, Nuts, Legumes, Fish, and Dairy

- Prospective Urban Rural Epidemiology (PURE) study of 147 642 people from 21 countries
- Healthy Diet Score: based on 6 foods associated with lower mortality risk:
  Fruits, Vegetables, Nuts, Legumes, Fish, and Dairy (whole-fat); range of scores, 0–6
- 9.3 years, compared ≤1 points vs ≥5 points was associated with a lower risk of:
- **All Cause Mortality** [(HR) 0.70; 95% (CI) 0.63–0.77)],
  CVD (HR 0.82; 0.75–0.91), MI (HR 0.86; 0.75–0.99), and
  Stroke (HR 0.81; 0.71–0.93).
- Vascular Disease, ≥5 → ↓**Mortality** (HR 0.73; 0.66–.81), **CVD** (0.79; 0.72–.87), **MI** (0.85; 0.71–.99)

- **Eat lots of fruits, vegetables, nuts, legumes and moderate amounts of fish and whole-fat dairy**

Eur Heart J. 2023;doi:10.1093/eurheartj/ehad325.

A Mediterranean-Style Diet

A healthy way of eating

What is the Mediterranean diet?

A diet based on fruits, vegetables, beans, fish, lean meats, nuts and olive oil

Daily Servings

Fruits and vegetables
3-4 servings of fruit and at least 3-4 servings of vegetables

Sofrito
2+ servings per week

Sofrito is made of tomatoes, onion, garlic and olive oil, seasoned with aromatic herbs

Whole grains and high fiber vegetables 3-6 servings
(serving = 1/2 cup, 1 slice of whole grain bread, or 3/4 cup of whole grain cereal, lentils, beans, chickpeas and quinoa)

Dairy
3 servings

Olive oil

Weekly Servings

Lentils, Beans and Chickpeas
At least 3 servings

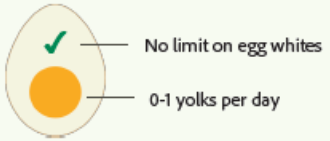
Fish
At least 3 servings

Meat

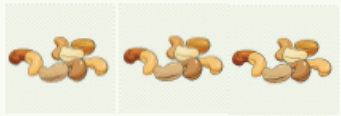
3 servings per week of skinless turkey or chicken

Limit: 1 serving (3 oz.) of lean red meat per week

Eggs



Nuts
At least 3 servings



OR

Nut Butter
2 tablespoons 3 times/week (No added sugar or oils)

Wine (less is better)

Women - 0-1 glasses per day

Men - 0-1 glasses per day

Desserts and Sweets (homemade are best) Limit: 1-2 servings per week

No soda or fruit juice

Len Finn, MD

Why Vegetables, Fruits, etc?

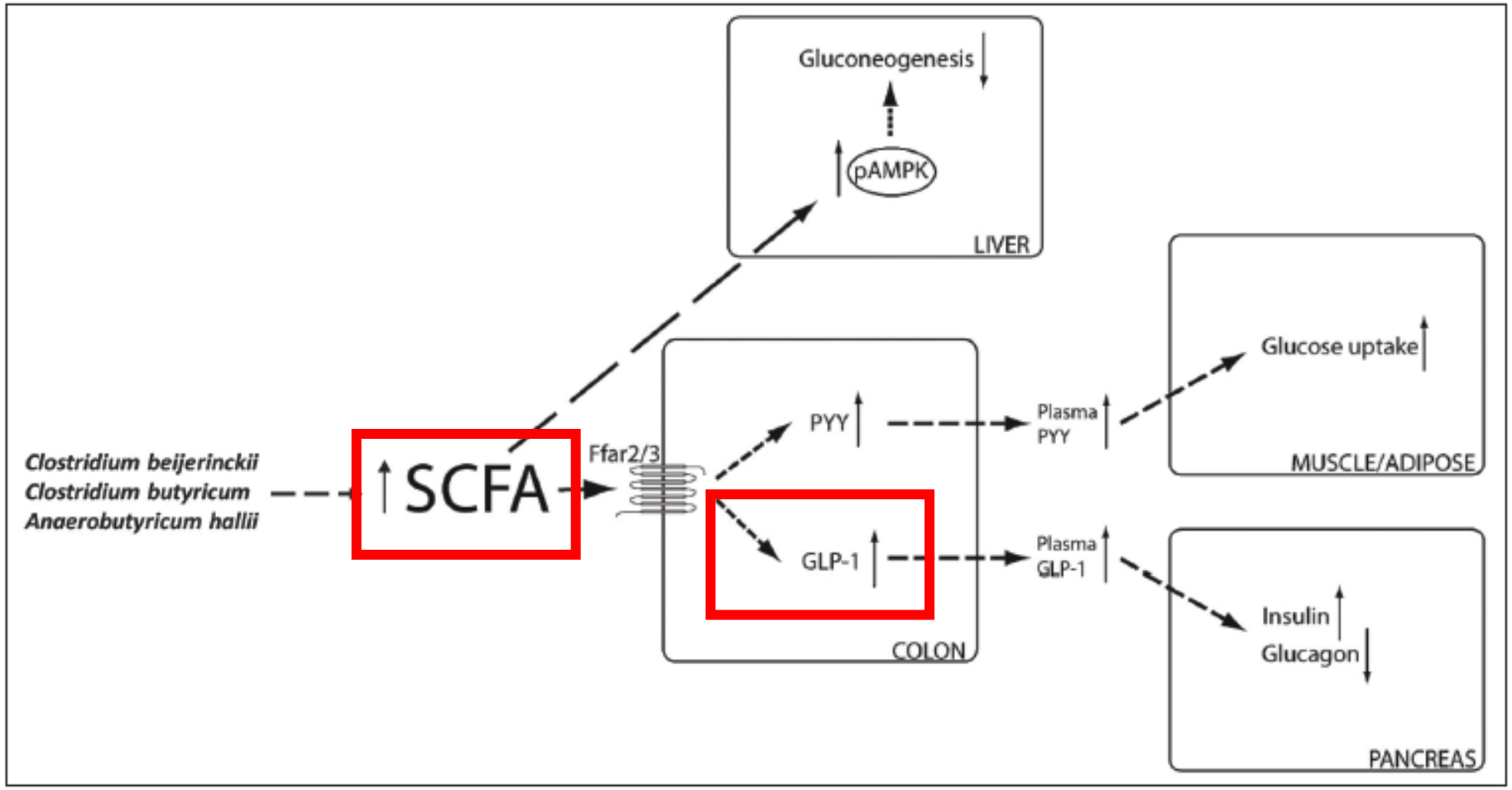
Soluble Fiber

- **Soluble Fiber →**

  ↑ SCFA (Short Chain Fatty Acids) which

- **Stimulates GLP-1 →**
  ↓Gluconeogenesis
  ↓ Appetite
  ↑ Glucose uptake

- **↓ WEIGHT**



SR: Make your Own GLP1 w/Soluble Fiber

- 12 RCT's (n=609) soluble fiber (psyllium) on BMI, Body Weight & Fat, fasting glucose & insulin.
- Average dose ~10 grams per day over 17 weeks.

- Soluble fiber supplementation **reduced**:

-- BMI by 0.84 (95% CI: -1.35, -0.32; P = 0.001),

--Body weight by 2.52 kg (5.5 lbs) (95% CI: -4.25, -0.79 kg; P = 0.004),

--Body fat by 0.41% (95% CI: -0.58%, -0.24%; P < 0.001),

--Fasting glucose by 0.17 mmol/L and Fasting insulin by 15.88 pmol/L

- Rec: Fiber intake: 25-30 grams daily (~ 7-10 servings of fruit and vegetables/d): $$/Planning

- Psyllium: 1 rounded Tsp TID powder or as 500 mg capsules: 6 capsules TID.

Am J Clin Nutr. 2017 Dec;106(6):1514-1528. doi: 10.3945/ajcn.117.163246. Epub 2017 Nov 1.

Weight Loss:
What Medications WORK!

- SR: 168 trials (97 938 T2DM patients):
  Naltrexone/Bupropion, Phentermine/Topirimate, Semaglutide.

- All drugs were associated with greater Weight Loss at 12 months than placebo

1. Semaglutide (mean difference [MD], -9.02 kg [95% CI: -10.42, -7.63]) and
2. Phentermine/topiramate (MD, -8.10 kg [95% CI: -10.14, -6.05]);

- Waist circumference reduction: Semaglutide (-7.84 cm), Phentermine/Topiramate (-6.20 cm); high certainty).
- Lowered CV mortality: Naltrexone/bupropion (odds ratio [OR], 0.62 [95% CI: 0.39, 0.99].

- SAFE: **No evidence** weight loss drugs associated with increased cardiovascular death

Diabetes Obes Metab. 2023 May 31. doi: 10.1111/dom.15138

Start Breast Cancer Screening at 40?

- Cross-sectional study 415,277 breast cancer deaths in US
- Optimal race and ethnicity–specific starting ages to initiate breast cancer screening to address racial disparity
- To have equivalent mortality risk by race/ethnicity, begin screening:
- Black females at 42 years
- White females at 50 years
- American Indian/Alaska Native & Hispanic females at 57 years
- Asian or Pacific Islander females at age 61 years.

JAMA Netw Open. 2023 Apr; 6(4): e238893.doi: 10.1001/jamanetworkopen.2023.8893

1. No ALL-CAUSE Mortality Benefit to Mammography

2. Breast Cancer Mortality is Declining worldwide, even in Countries that do not screen

USPSTF/AHRQ
Pub.No. 23-05303-EF-1, May 2023

4. NNS if Start at 40 is > 2,400

Bariatric surgery for women with BMI > 25 → Reduction in Breast Cancer risk

- Cohort of 69,000 women with history of breast cancer; compared bariatric surgery (baseline BMI ≥35 with comorbid conditions or BMI ≥40) and women without a history of bariatric surgery

Results: Risk of Breast Cancer in Non-Surgical Group:

- 1 year: HR 1.40 (95% CI 1.18-1.67)
- 2 years: HR 1.31 (95% CI 1.12-1.53)
- 5 years: HR 1.38 (95% CI 1.21-1.58

- Surgical cohort vs nonsurgical cohort whose BMI <25, risk of breast cancer was **not significantly different**

Conclusions:

- Bariatric Surgery → reduced hazard for patients with BMI ≥25 of breast cancer vs nonsurgical group

JAMA Surg. Published online April 12, 2023. doi:10.1001/jamasurg.2023.0530

Check Evening BP:
Predicts All-Cause Mortality

- 223 Spanish National Health Primary Care sites: Clinic vs Ambulatory BP & Mortality
- At median follow-up of 9·7 years: 12·1% died, 4·0% from CVD
- ↑ 24 HOME SBP associated ↑ all-cause mortality but **NOT clinic blood pressure**
- Night-time BPS most predictive of All-cause death and Cardiovascular death

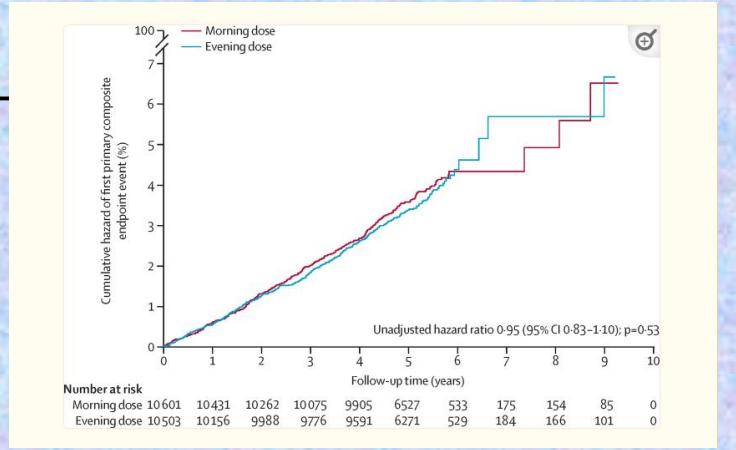
	All-Cause Mortality risk	**CV Mortality risk**
• Masked Hypertension (↑ Home; ↓ Office)	HR 1·24 [1·12–1·37]	1·37 [1·15–1·63]
• Sustained Hypertension (↑ Home; ↑ Office)	HR 1·24 [1·15–1·32])	1·38 [1·22–1·55]
• White Coat Hypertension (↓ Home; ↑ Office)	**HR 1·04 [0·95–1·14] NS**	**1·02 [0·87–1·20] NS**

Lancet. 2023 May 5;S0140-6736(23)00733-X. doi: 10.1016/S0140-6736(23)00733-X

NOW when should I take my BP meds? Whenever…. Hygia vs **TIME**

- Hygia trial bedtime HTN dosing was associated with a **45% decrease** in **all-cause** and cardiovascular death (*Eur Heart J*, 2020; 41(48): 4565–4576):??? Random, Groups Diff @ Baseline

- Treatment in Morning versus Evening (TIME): RCT of 21,000 adults with hypertension; either take all of BP meds in the morning or the evening on the after 5.2 years.
- **Primary composite endpoint:** No Difference on death, hospitalization for non-fatal MI or non-fatal stroke;HR: 0·95 [95% CI 0·83-1·10]; p=0·53).
- **Secondary Endpoint**: No Difference in non-fatal MI, CVA, vascular **mortality**, CHF or death, adverse events (falls, fractures)



Lancet. 2022 Oct 22; 400(10361): 1417–1425. doi: 10.1016/S0140-6736(22)01786-X

Treatments for Anxiety: Meditation Vs. Escitalopram (TAME)

- RCT of 276 adults with anxiety: 8-week treatment Mindfulness-based stress reduction was non-inferior to Escitalopram (10-20 mg) on the Clinical Global Impression of Severity scale (CGI-S).
- At 8 weeks, mean (SD) CGI-S score was reduced by 1.35 for MBSR and 1.43 for escitalopram; mean difference −0.07 (0.16; 95% CI, −0.38 to 0.23; P = .65) **a non-inferior difference**. **BUT:**
- 8% dropped out of the escitalopram group and 0% from the MBSR group due to adverse events.
- Conclusion: For generalized anxiety, mindfulness-based stress reduction meditation was as effective as up to 20 mgs of escitalopram, with fewer dropouts.
  JAMA Psychiatry. 2023;80(1):13-21. doi:10.1001/jamapsychiatry.2022.3679

- A BMJ meta-analysis → the risk for relapse is **tripled** after stopping medication (*BMJ* 2017;358:j3927).

- (https://positivepsychology.com/mindfulness-based-stress-reduction-mbsr/) offers 3 free downloads for them to try before investing any money.
- Jay Winner: Video & Audio library: https://stressremedy.com/audio/
- Apps highly rated for anxiety: MindShift CBT and Insight Timer.

Sparkling Sea Breeze

Fill a 12-ounce glass with ICE

- 1 ½ fluid ounces vodka
- 2 fluid ounces cranberry juice
- 2 fluid ounce grapefruit juice
- Fill Remainder with Seltzer
- 1 lime wedge

But wait… I take a statin…..

YES YOU CAN: Grapefruit & Atorvastatin/Simvastatin

- Grapefruit juice **inhibits** Cytochrome P450 3A4-> ↑Statin level & *potential* adverse events
- 8 Ounces of grapefruit juice **increases** serum Simvastatin & Atorvastatin
  BUT NOT Pravastatin or Rosuvastatin
- Lit Review: Simvastatin or Atorvastatin + grapefruit juice → ↓↓ LDL & No Rhabdo Risk
- ***"The increased rhabdomyolysis risk from grapefruit juice consumption is minimal compared with the greater effect in preventing heart disease"***
- ***"Grapefruit juice should not be contraindicated in people taking statins"***
  Am J Med 2016; Vol 129 (1): 26-29

- Case: 29 Rhabdo./ 313,552 on Simvastatin (I J Card 2015: 174(1): 83-89) **0.0009% RISK**
- Things that cause Rhabdomyolysis: Exercise (X Fit), Marathon/Triathlons, Military Recruit, Dextroamphetamines, OTC weight loss supplements

Are you sure
Grapefruit Juice & Statins Are OK?

- **Observational study of** patients on Atorvastatin: drink 300 ml (10. 5 ounces)/day Grapefruit Juice for 90 days.
- Group A continued current dose of atorvastatin;
  Group B cut dose by 50%.

- **Results:**
- Group A ↑ serum atorvastatin by 19% to 26% from baseline but **no changes in lipid profile and no adverse effects** on LFT's or CPK.
- Group B (HALF dose): ↓atorvastatin levels by 12%-25% from baseline (small but significant **unfavorable** effect in lipids) with no adverse effects on LFT's or CPK.

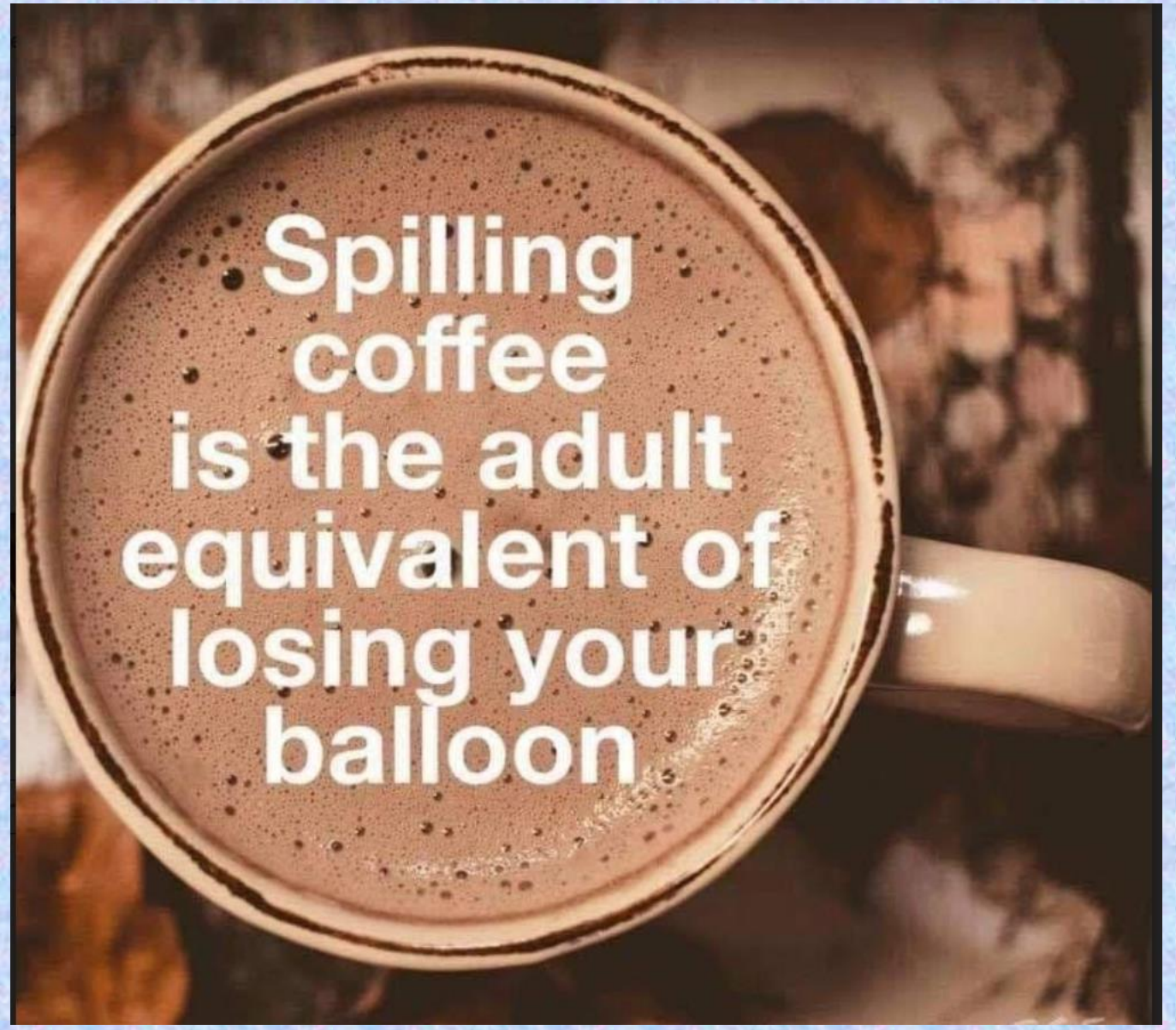
- **Conclusion:** In patients on atorvastatin, **daily** GFJ slightly elevates serum atorvastatin concentrations & causes no adverse liver or muscle effects.

Br J Clin Pharmacol. 2011 Sep;72(3):434-41. doi: 10.1111/j.1365-2125.2011.03996.x

What about Warfarin & Broccoli?

- Warfarin Patients told to NOT eat vitamin-K-rich foods (greens, broccoli, kale, cashews). Dietary vitamin K could alter anticoagulant effect of Vitamin K Antagonists
- SR: relationship between dietary vitamin K and measures of anticoagulation:
- Dietary vitamin K1 began to alter coagulation ONLY with intake >150 µg/day.
- Spinach 1 cup = 144 ug/d
- Kale 1 ½ cups = 150 ug/d
- Broccoli 3/4 cup = 150 ug/d
- Cashews 1 cup = 160 ug/d
- Collard & Turnip Greens ½ cup = > 400 ug
- Evidence does **not** support advice to modify diets when starting VKAs.
- *"Maintain stable dietary habits, avoiding wide changes in vitamin K intake."*

Medicine (Baltimore). 2016 Mar;95(10):e2895


Spilling
coffee
is the adult
equivalent of
losing your
balloon

Coffee: Coffee did NOT Increase Premature Atrial Contractions.

- RCT: 100 adults effects of **caffeinated coffee** on cardiac ectopy, step counts, sleep, glucose
- Daily text messages, over 14 days, randomly instruct participants to consume caffeinated coffee or avoid caffeine.

- **Results:** The consumption of caffeinated coffee was associated with:
  - ~PACs: 58/day vs 53 on avoided days (rate ratio, 1.09; 95% [CI], 0.98 - 1.20; P = 0.10).
  - ↑PVCs: 154 vs 102 daily (rate ratio, 1.51; 95% CI, 1.18 - 1.94);
  - ↑ Steps: 10,646 vs 9665 daily steps (mean Diff, **1058**; 95% CI, 441 - 1675);
  - ↓Sleep: 397 vs 432 minutes of nightly sleep (mean Diff, **36**; 95% CI, 25 - 47); and
  - ~Serum glucose of 95 mg/dL vs 96 mg/dL (mean Diff, -0.41; 95% CI, -5.42 - 4.60).

N Engl J Med 2023; 388:1092-1100DOI: 10.1056/NEJMoa2204737

Know any patients who complain of…

- Fatigue
- Weakness
- Memory Issues
- Cold
- Headaches or dizziness
- Heart palpitations
- Restless Leg Syndrome

Lancet. 2016 Feb;387(10021):907-16. Epub 2015 Aug 24.

How Common is Iron Deficiency in Women by Ethnicity?

- 62,685 adult women with ID (serum ferritin < 15 ug/L)
- ID higher Hispanics (5%) & Blacks (4.3%) than Whites (2%) & Asians (2.1%)
- Prevalence of ID was significantly greater in

  Women ages 25–54 y of all race groups than ages ≥55 y

Race/ethnicity (n)	FeDef, % (n)	Mean age, y (± 1 SD)
Hispanic (8,566)	5.14 (440)	43.91 ± 13.03
Black (17,272)	4.31 (744)	48.69 ± 14.48
White (27,079)	1.99 (539)	51.81 ± 14.22
Asian (7,615)	2.10 (160)	50.04 ± 13.50
Pacific Islander (449)	3.12 (14)	51.82 ± 13.96
Native American (441)	5.22 (23)	47.61 ± 13.97
Other[b] (1,263)	2.93 (37)	49.84 ± 13.50

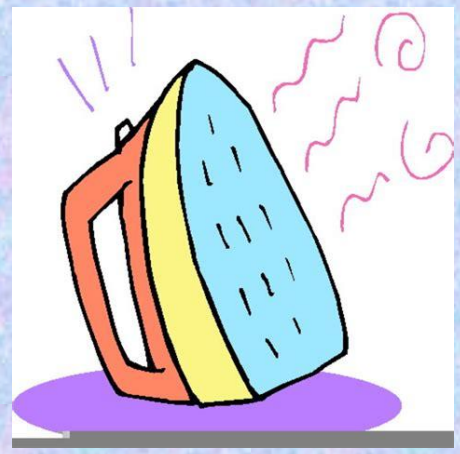
PLoS One 2020; 15(4): e0232125.

Check a Ferritin
Iron Deficiency & Anemia in Young Women

- Using NHANES data nonpregnant females aged 12 to 21 years.
- Hemoglobin cutoffs of >12.5 mg/dL
- Prevalence of Iron Deficiency (ferritin < 15 ng/L) **17%** (95% CI, 15.4%-19.2%)
- Prevalence of Iron-Deficiency Anemia (<12.5 mg/dL) was **11.0%** (95% CI, 9.5%-12.6%)

- In 83% of individuals, **Iron Deficiency was NOT associated with Iron-Deficiency Anemia**

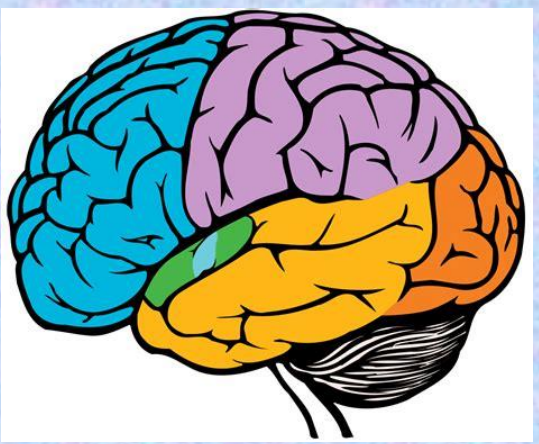
You Cannot Rule Out ID with an H&H



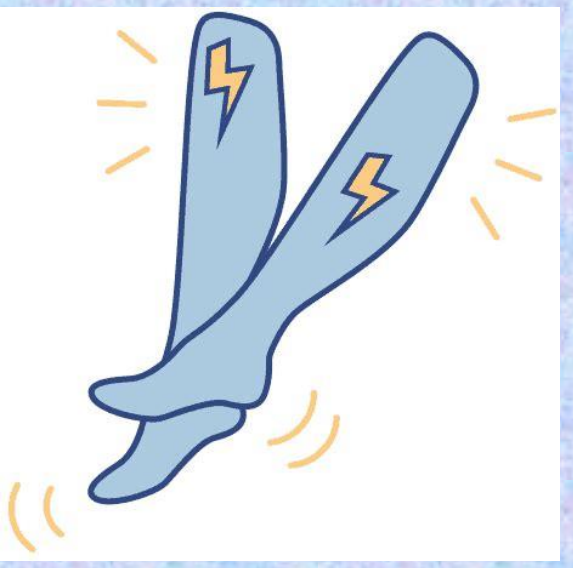
- **Conclusion**: Iron Deficiency is missed by relying upon H & H; **CHECK A FERRITIN!**

JAMA 2023; 329; 24: 2191-2192

Restless Leg and the Brain



- Etiology: SSRI's, Anti-psychotics, Sedating Antihistamines, *Brain Fe Deficiency*
- Case Control: CSF & Serum ferritin levels in 16 patients with idiopathic restless legs syndrome (RLS) and 8 age-matched controls.
- Patients with RLS had **lower CSF ferritin** levels (1. 11 +/- 0.25 ng/mL versus 3.50 +/- 0.55 ng/mL; p = 0.0002) and
- **Higher CSF transferrin saturation** (26.4 +/- 5.1 mg/L versus 6.71 +/- 1.6 mg/L; p = 0.018) vs controls.
- BUT: no difference in **serum** ferritin and transferrin levels.
- Normal Serum ferritin and transferrin levels is NOT indicative of brain levels in patients with idiopathic RLS.



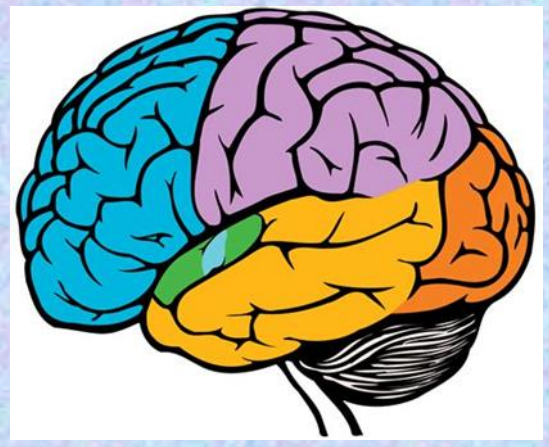
Neurology. 2000 Apr 25;54(8):1698-700. doi: 10.1212/wnl.54.8.1698

Restless Leg Syndrome: Brain Anemia?

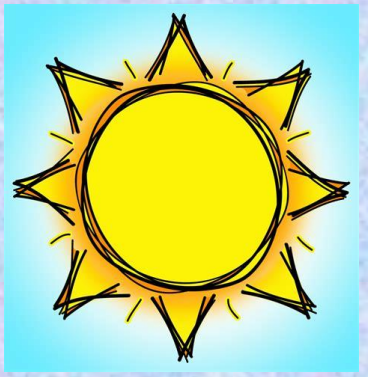
- RCT: RLS: oral iron therapy vs. placebo x 12 weeks.
- After 12 weeks, International Restless Leg Scale IRLS scores decreased with FeSOF4 (10.3+/-7.40) vs placebo (1.14+/-5.64), (p=0.01).
- Ferritin levels increased more in the treatment arm (25.1+/-20.3ng/ml) than in placebo (7.5+/-13.7ng/ml), (p=0.04).

- <u>For Restless Leg Syndrome: Add Oral/IV Iron</u>

Sleep Med. 2009 Oct;10(9):973-5. doi: 10.1016/j.sleep.2008.



Vit. D Deficiency & COVID Vaccine



Take 3-4,000 IU of Vitamin D3 Daily

- Evaluate impact of 25(OH)D levels on 2 doses of Pfizer-BioNTech-vaccine on Ab Persistence. VDD 25OH VD < 20 ng/mL
- At 9 months, Vitamin D Deficiency & Older-age were negative risk factors for antibody persistence ($p = 0.026$, $p = 0.004$; respectively).

- Vitamin D Deficiency reduced immunity to COVID after Immunization

Endocrine (2023). https://doi.org/10.1007/s12020-023-03481-w

Network MA: T2DM Meds & Outcomes

- Network Meta Analysis 816 trials 471 038 patients T2DM Rx on Clinical Outcomes

- All Cause Mortality: GLP-1 receptor agonists (0.88, 0.82 to 0.93) & SGLT-2i (odds ratio 0.88, 95% CI: 0.83 to 0.94)
- CV Death, MI, CHF, ESKD: GLP-1 receptor agonists and SGLT-2 inhibitors
- Non-fatal Stroke: GLP-1 receptor agonists reduce non-fatal stroke;
- QOL: GLP-1 agonists & *probably* SGLT-2 inhibitors and Tirzepatide.
- Weight Loss: Tirzepatide, Semaglitide (SQ, then oral) most effective

- But Wait… What about **Metformin**?
  UKPDS Metformin vs Insulin/Sulfonylurea: Metformin died less (no hypoglycemia)

BMJ 2023;381:e074068.

Interventions	All cause death (OR, 95%CI)	Cardiovascular death (OR, 95%CI)	Non-fatal myocardial infarction (OR, 95%CI)	Non-fatal stroke (OR, 95%CI)	Admission to hospital for heart failure (OR, 95%CI)	End stage kidney disease* (OR, 95%CI)	Health related quality of life score (OR, 95%CI)	Severe hypoglycaemia (OR, 95%CI)	Drug specific adverse events (OR, 95%CI)
SGLT-2 inhibitors	0.88 (0.83 to 0.94)	0.86 (0.80 to 0.94)	0.90 (0.82 to 0.98)	0.99 (0.88 to 1.11)	0.66 (0.60 to 0.73)	0.61 (0.55 to 0.67)	0.30 (0.10 to 0.49)	0.90 (0.79 to 1.02)	Genital infection 3.30 (2.88 to 3.78) Amputation 1.27 (1.01 to 1.61) Ketoacidosis 2.07 (1.44 to 2.98)
GLP-1 receptor agonists	0.88 (0.82 to 0.93)	0.87 (0.81 to 0.94)	0.91 (0.85 to 0.98)	0.85 (0.77 to 0.94)	0.91 (0.83 to 0.99)	0.83 (0.75 to 0.92)	0.17 (0.07 to 0.27)	0.98 (0.90 to 1.06)	Severe gastrointestinal events 1.97 (1.39 to 2.80)
Non-steroidal MRAs	0.89 (0.79 to 1.00)	0.88 (0.75 to 1.02)	0.91 (0.74 to 1.12)	1.00 (0.82 to 1.22)	0.78 (0.66 to 0.92)	0.83 (0.75 to 0.92)	-	0.64 (0.43 to 0.96)	Hyperkalaemia leading to hospital admission 5.92 (3.02 to 11.62)
Tirzepatide	0.83 (0.48 to 1.44)	1.00 (0.35 to 2.85)	0.69 (0.08 to 6.10)	-	0.63 (0.16 to 2.39)	0.68 (0.09 to 4.84)	0.39 (0.13 to 0.65)	1.13 (0.42 to 3.02)	Severe gastrointestinal events 4.59 (1.89 to 11.14)
Metformin	0.84 (0.67 to 1.04)	0.95 (0.48 to 1.88)	0.86 (0.68 to 1.09)	0.97 (0.71 to 1.33)	1.45 (0.28 to 7.36)	1.61 (0.36 to 7.24)	0.04 (-0.25 to 0.33)	1.73 (0.89 to 3.37)	Severe gastrointestinal events 2.22 (0.64 to 7.71)
α-glucosidase inhibitors	0.89 (0.30 to 2.61)	0.99 (0.21 to 4.70)	0.33 (0.06 to 1.92)	9.44 (0.76 to 116.58)	3.25 (0.13 to 82.49)	-	0.03 (-0.34 to 0.39)	1.30 (0.31 to 5.43)	Severe gastrointestinal events 3.40 (0.30 to 38.15)
Thiazolid-inediones	0.95 (0.83 to 1.09)	0.93 (0.77 to 1.12)	0.97 (0.81 to 1.15)	0.85 (0.70 to 1.03)	1.54 (1.27 to 1.88)	0.69 (0.37 to 1.28)	0.20 (-0.13 to 0.52)	1.42 (0.97 to 2.10)	-
DPP-4 inhibitors	1.01 (0.95 to 1.08)	1.00 (0.92 to 1.09)	1.01 (0.92 to 1.11)	0.91 (0.80 to 1.03)	1.05 (0.95 to 1.16)	1.04 (0.93 to 1.16)	0.03 (-0.12 to 0.17)	1.11 (1.00 to 1.23)	-
Sulfonylureas	1.10 (0.97 to 1.26)	1.01 (0.83 to 1.23)	1.00 (0.83 to 1.22)	1.05 (0.84 to 1.32)	0.99 (0.79 to 1.23)	0.68 (0.37 to 1.24)	0.23 (-0.19 to 0.64)	5.22 (3.88 to 7.01)	-
Meglitinides	1.58 (0.51 to 4.92)	0.64 (0.11 to 3.69)	0.28 (0.05 to 1.60)	1.71 (0.26 to 11.40)	-	-	0.17 (-0.29 to 0.63)	3.21 (0.96 to 10.75)	-
Basal insulin	1.10 (0.81 to 1.49)	1.28 (0.83 to 1.99)	0.98 (0.47 to 2.06)	0.76 (0.33 to 1.77)	0.94 (0.62 to 1.43)	1.20 (0.62 to 2.30)	0.00 (-0.25 to 0.24)	2.38 (1.82 to 3.12)	-
Basal bolus insulin	0.79 (0.19 to 3.32)	2.23 (0.23 to 21.92)	0.33 (0.03 to 3.27)	0.58 (0.10 to 3.35)	-	-	-	4.94 (1.06 to 22.96)	-
Bolus insulin	0.48 (0.15 to 1.59)	1.05 (0.11 to 10.26)	1.18 (0.40 to 3.50)	0.86 (0.16 to 4.48)	0.64 (0.07 to 6.22)	2.55 (0.10 to 62.86)	-0.11 (-0.29 to 0.07)	2.46 (1.31 to 4.63)	-
Standard treatments	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

High to moderate certainty evidence	Low to very low certainty evidence
Among the most effective	Possibly among the most effective
Among the intermediate effective	Possibly among the intermediate effective
Not convincingly different from standard treatment	Possibly not convincingly different from standard treatment
Among the intermediate harmful	Possibly among the intermediate harmful
Among the most harmful	Possibly among the most harmful

Benefits and Harms (Odds Ratio)

Interventions	All cause death	Cardiovascular death	Non-fatal myocardial infarction	Non-fatal stroke	Admission to hospital for heart failure	End stage kidney disease	Severe hypoglycaemia	Drug specific adverse events
Baseline risks	170 per 1000 patients	112 per 1000 patients	120 per 1000 patients	120 per 1000 patients	105 per 1000 patients	92 per 1000 patients	30 per 1000 patients	-
SGLT-2 inhibitors	17 fewer (25 fewer to 9 fewer)	14 fewer (20 fewer to 6 fewer)	11 fewer (19 fewer to 2 fewer)	1 fewer (13 fewer to 11 more)	33 fewer (39 fewer to 26 fewer)	34 fewer (39 fewer to 28 fewer)	3 fewer (6 fewer to 1 more)	Genital infection 133 more (112 more to 156 more) Amputation 3 more (0 to 6 more) Ketoacidosis 2 more (1 more to 4 more)
GLP-1 receptor agonists	17 fewer (26 fewer to 10 fewer)	13 fewer (19 fewer to 6 fewer)	10 fewer (16 fewer to 2 fewer)	16 fewer (25 fewer to 6 fewer)	9 fewer (16 fewer to 1 fewer)	14 fewer (21 fewer to 7 fewer)	1 fewer (3 fewer to 2 more)	Severe gastrointestinal events 40 more (16 more to 72 more)
Non-steroidal MRAs	16 fewer (31 fewer to 0)	12 fewer (26 fewer to 2 more)	10 fewer (28 fewer to 12 more)	0 (19 fewer to 23 more)	21 fewer (33 fewer to 8 fewer)	14 fewer (21 fewer to 7 fewer)	11 fewer (17 fewer to 1 fewer)	Hyperkalaemia leading to admission to hospital 10 more (4 more to 21 more)
Tirzepatide	25 fewer (80 fewer to 58 more)	0 (70 fewer to 152 more)	34 fewer (109 fewer to 334 more)	-	36 fewer (87 fewer to 114 more)	28 fewer (83 fewer to 237 more)	4 more (17 fewer to 55 more)	Severe gastrointestinal events 133 more (37 more to 299 more)
Metformin	23 fewer (49 fewer to 6 more)	5 fewer (55 fewer to 80 more)	15 fewer (35 fewer to 9 more)	3 fewer (32 fewer to 34 more)	40 more (73 fewer to 358 more)	48 more (57 fewer to 331 more)	21 more (3 fewer to 64 more)	Severe gastrointestinal events 50 more (16 fewer to 221 more)
α-glucosidase inhibitors	16 fewer (112 fewer to 178 more)	1 fewer (86 fewer to 260 more)	77 fewer (112 fewer to 87 more)	443 more (26 fewer to 821 more)	171 more (90 fewer to 801 more)	-	9 more (21 fewer to 114 more)	Severe gastrointestinal events 93 more (31 fewer to 598 more)
Thiazolid-inediones	7 fewer (25 fewer to 13 more)	7 fewer (23 fewer to 12 more)	3 fewer (21 fewer to 16 more)	16 fewer (33 fewer to 3 more)	48 more (25 more to 76 more)	27 fewer (56 fewer to 23 more)	12 more (1 fewer to 31 more)	-
DPP-4 inhibitors	1 more (7 fewer to 11 more)	0 (8 fewer to 9 more)	1 more (9 fewer to 11 more)	10 fewer (22 fewer to 3 more)	5 more (5 fewer to 15 more)	3 more (6 fewer to 13 more)	3 more (0 to 7 more)	-
Sulfonylureas	14 more (4 fewer to 35 more)	1 more (17 fewer to 22 more)	0 (18 fewer to 23 more)	5 more (17 fewer to 33 more)	1 fewer (20 fewer to 21 more)	28 fewer (56 fewer to 20 more)	109 more (77 more to 148 more)	-
Meglitinides	74 more (75 fewer to 332 more)	37 fewer (98 fewer to 206 more)	83 fewer (113 fewer to 59 more)	69 more (86 fewer to 489 more)	-	-	60 more (1 fewer to 220 more)	-
Basal insulin	14 more (28 fewer to 64 more)	27 more (17 fewer to 89 more)	2 fewer (60 fewer to 99 more)	26 fewer (77 fewer to 74 more)	6 fewer (37 fewer to 39 more)	16 more (33 fewer to 97 more)	39 more (23 more to 58 more)	-
Basal bolus insulin	31 fewer (133 fewer to 235 more)	108 more (84 fewer to 622 more)	77 fewer (116 fewer to 188 more)	47 fewer (107 fewer to 194 more)	-	-	103 more (2 more to 385 more)	-
Bolus insulin	80 fewer (140 fewer to 76 more)	5 more (98 fewer to 452 more)	19 more (68 fewer to 203 more)	15 fewer (99 fewer to 259 more)	35 fewer (97 fewer to 317 more)	113 more (82 fewer to 772 more)	41 more (9 more to 95 more)	-
Standard treatments	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

High to moderate certainty evidence	Low to very low certainty evidence
Among the most effective	Possibly among the most effective
Among the intermediate effective	Possibly among the intermediate effective
Not convincingly different from standard treatment	Possibly not convincingly different from standard treatment
Among the intermediate harmful	Possibly among the intermediate harmful
Among the most harmful	Possibly among the most harmful

Fig 4

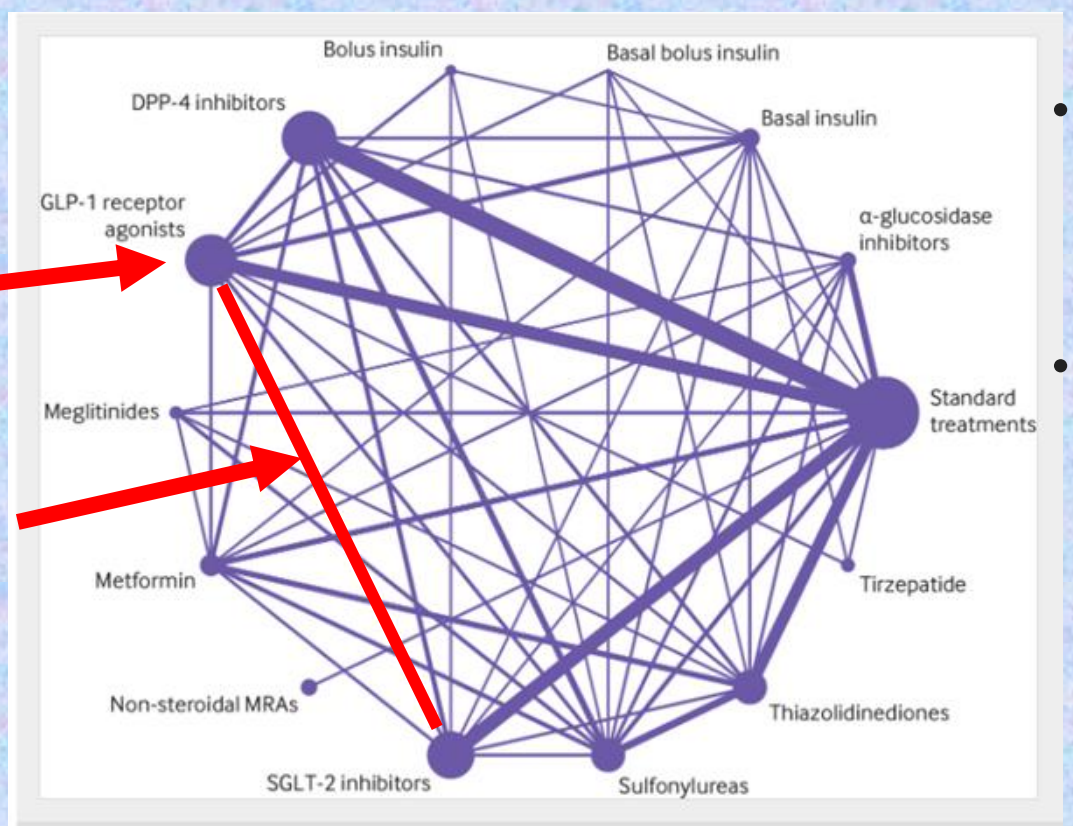
Anticipated absolute effects for patients with type 2 diabetes and chronic kidney disease, by drug treatment. Figure shows absolute benefits and harms of the drugs for patients with type 2 diabetes and chronic kidney disease. Estimates represent risk

Absolute Benefits and Harms/ 1000 Patients

Network (Meta) Analysis:
New Relationships: Algorithms, SM & AI's Output

NODES

EDGES



Network Visualization

- NMA: Compare multiple treatments simultaneously by combining direct and indirect evidence within a network of RCT's → comparative effectiveness.
- Finds associations where there were none before;
  AI: How Social Networks predict:
  --What Ads you See
  --Who is recommended you "friend"
  --What OTHER info appears on your SM

Keep Metformin & Add Montelukast in T2DM? (Not yet EBM)

- Montelukast: Leukotriene Antagonist
- RCT of 100 adults T2DM: Metformin 1 gm BID or Met. + Montelukast 10 mg/day
- Diet: 1,000–1,200 kc/d female;1,500–1,800 kc/d male & Exercise 150 min/Wk

REDUCTIONS At 12 weeks:	Metformin	Metformin + Montelukast
Weight(kg)/BMI	↓ 4.1kg/1.65%	↓ **7.7kg/2.75%**
Body Fat(kg)/% BF	↓ 3.51kg/1.99%	↓ **10kg/8.58%**
Waist (cm)	↓ **2. 88 cm**	↓ **6.8 cm**
A1c	↓0.78	↓ **1.42**

Front Pharmacol. 2023; 14: 1153653

Fall Rates Going UP

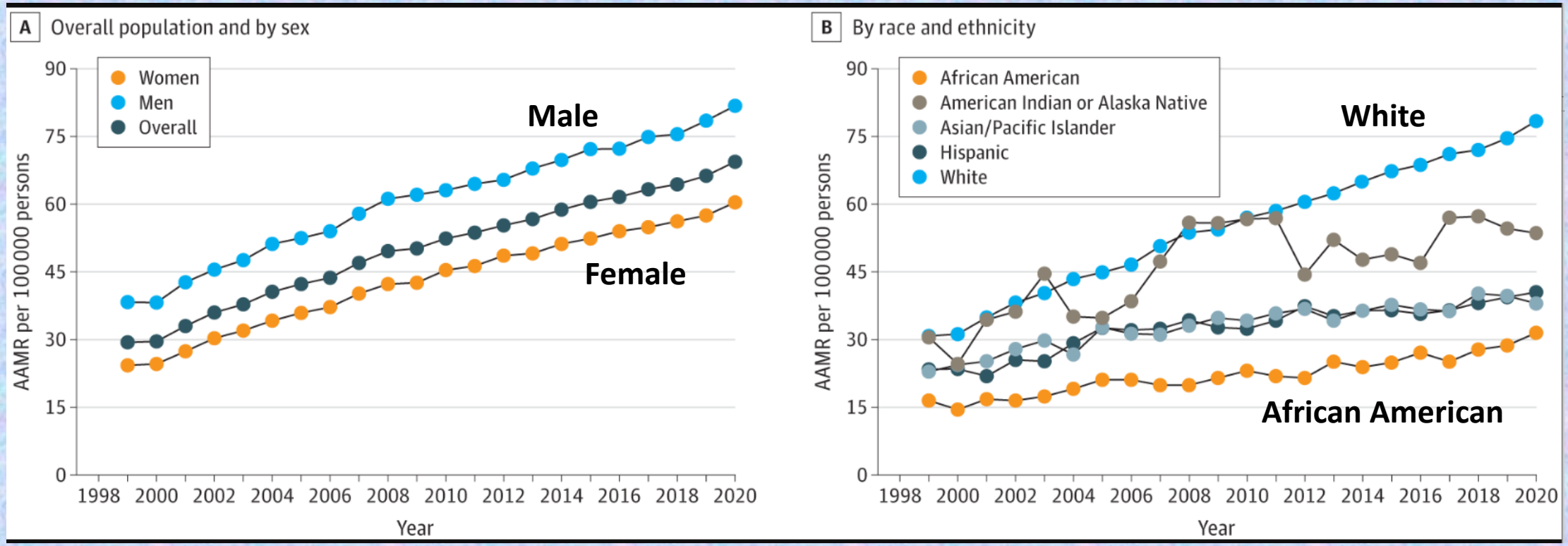
- 2020,> 36,500 Americans over age 65 died fall-related injury.
  1999: ~10,100 deaths.
- White older adults had the **highest death rate** from falls
- Death rates also rose Black, Hispanic, Asian & Native American seniors.

- CDC: ~ 25% of older Americans fall each year. ~3 million end up in ED,
  > 800,000 have to be hospitalized (head injury or hip fracture).
- Resulting in **$50 billion per year in medical costs**

- Ask "When was the last time you fell?" or "How often do you fall?"
- Exam: Timed Get up and Go: Stand (TUG), walk 10' & return; < 13.5 seconds

JAMA. 2023;329(18):1605-1607. doi:10.1001/jama.2023.3054

Age-Adjusted Mortality Rates for Falls Among Adults Aged 65 Years or Older, 1999-2020



OUCH…. MOM!

Mothers Kissing Boo Boos

- RCT of 943 maternal–toddler pairs to evaluate if maternal kissing of minor injuries of childhood (*boo-boos*) vs sham kissing vs control improves Toddler Discomfort Index (TDI)
- <u>Results:</u>
- @ 1 & 5-minute: TDI scores did not differ between the maternal and sham kiss groups.
- Both groups had higher DISCOMFORT scores at 5 minutes vs the no intervention group.
- <u>Conclusions</u>
- Maternal kissing of boo-boos confers no CHILD benefit in children with minor traumatic injuries compared to doing nothing.
- *"The practice of maternal kissing of boo-boos is not supported by the evidence and we recommend a moratorium on the practice"*

J Eval Clin Pract . 2015 Dec;21(6):1244-6. doi: 10.1111/jep.12508

What Do You Do to Keep SANE?

- Listening to music
- Solving puzzles
- Singing or dancing
- Drawing, painting or sculpting
- Crafting
- Creative writing

A	R	I	S	E
R	O	U	T	E
R	U	L	E	S
R	E	B	U	S

APA Survey: Good Mental Health

- Healthy Minds Monthly Poll: surveyed 2,202 adults on how they relieve stress and anxiety
- 46% of Americans **use creative activities to relieve stress or anxiety**,
- Those who rate their mental health as **very good** or **excellent** are more likely to engage in creative activity more often than those who rate their mental health as fair or poor.
- 77% said listening to **music**;
- 39% said solving puzzles;
- 25% said singing or dancing;
- 24% said drawing, painting or sculpting;
- 19% said crafting;
- 16% said creative writing.

Psychiatry.org - New APA Poll: Americans Who Engage in Creative Activities at Least Weekly Report Better Mental Healt

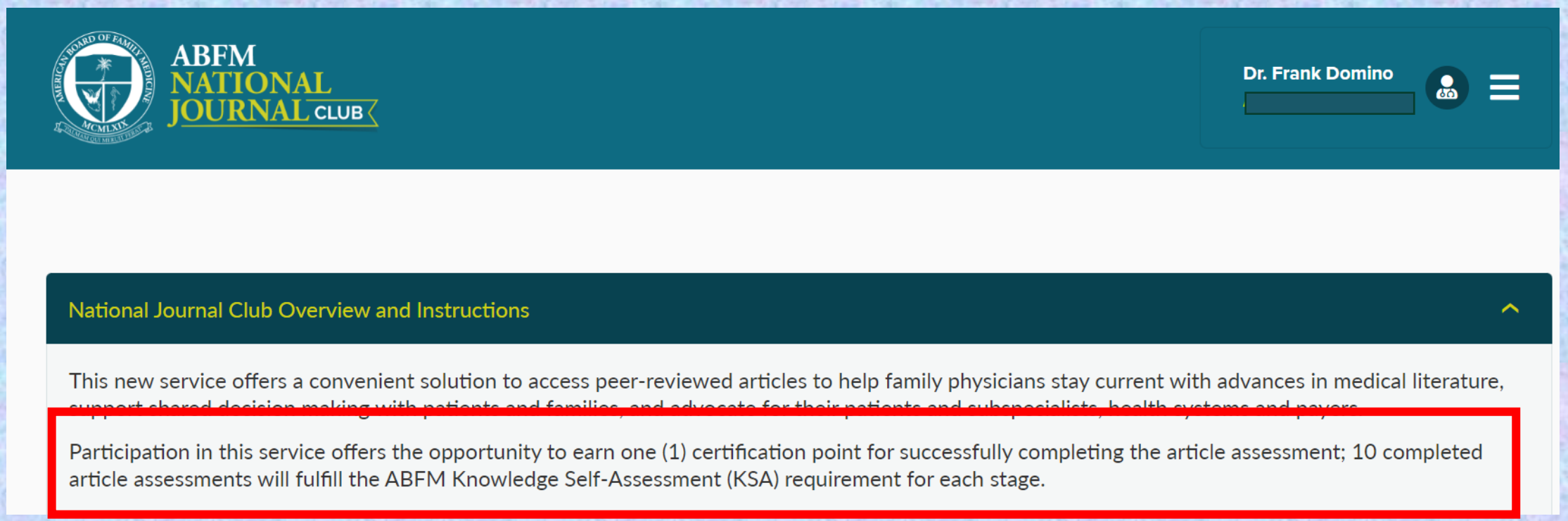
Take Care of Yourself and be CREATIVE

My watercolors

Summary

- Pilates for Prenatal Care
- Sleep Issues: Cry it OUT
- Screen Use: ↑ Risk of Develop Delay, Obesity, Depression
- Bill 99214/5 on Time
- Weight Loss: Track it, Soluble Fiber, Use Rx
- Breast Cancer: Screening, Bariatric Surgery
- BP Meds when Convenient
- Meditation for Anxiety
- Grapefruit Juice, Broccoli & Coffee are NOT harmful
- Iron Deficiency: √ Ferritin
- GLP1 & SGLT2i for all
- Falls are UP, but no Kissing
- Be CREATIVE to Keep Sane

Instead of a KSA: ABFM Journal Club
3-4 Per Grand Rounds → 10-12/Year



Top 10: EBM Updates From The Medical Literature

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PODCAST: **Frankly Speaking About Family Medicine**

new

NAFLD And Fibrosis

- distribution of the biomarker scores Fibrosis-4 (FIB4), nonalcoholic fatty liver disease (NAFLD) fibrosis score (NFS), and aspartate aminotransferase to platelet ratio index (APRI), and the associations between risk categories and all-cause mortality.

- Materials and methods: This was a retrospective cohort study of 12 589 patients, with follow-up from January 2012 until November 2021. The cut-off points used to identify low risk were: FIB4 <1.3 if aged <65 years or <2.0 if aged ≥65 years; NFS < -1.455 if aged <65 years or <0.12 if aged ≥ 65 years; APRI <1 (independent of age). High-risk cut-off points were FIB4 >2.67, NFS >0.676 and APRI ≥1 (all independent of age). Multivariable Cox regression analysis was performed to assess the association between liver fibrosis scores and all-cause mortality.

- Results: The mean ± standard deviation age was 65.2 ± 12.1 years, 54.5% were men and the median (interquartile range) diabetes duration was 5.8 (2.8-9.3) years. The prevalence of high-risk categories was 6.1% for FIB4, 23.5% for NFS and 1.6% for APRI. During a median follow-up of 9.8 years, 3925 patients (31.1%) died, resulting in a crude mortality rate of 40.4 per 1000 person-years. The overall adjusted all-cause mortality hazard ratios (95% confidence intervals [CIs]) in the high- compared with low-fibrosis-risk groups were 3.69 (1.95-2.75) for FIB4, 2.32 (2.88-4.70) for NFS, and 3.92 (2.88-5.34) for APRI. Stratified adjusted all-cause mortality hazard ratios for individuals under 65 years and people over 65 years of age at cohort entry were 3.89 (95% CI 2.99-5.05) and 1.44 (95% CI 1.28-1.61) for FIB4, 2.50 (95% CI 1.89-3.18) and 1.35 (95% CI 1.24-1.48) for NFS and 3.74 (95% CI 2.73-5.14) and 1.64 (95% CI 1.24-2.17) for APRI.

- Conclusions: All three fibrosis risk scores were positively associated with all-cause mortality in people with type 2 diabetes, with higher relative risks in younger than older people. Effective interventions are required to minimize excess mortality in people at high risk of liver fibrosis.

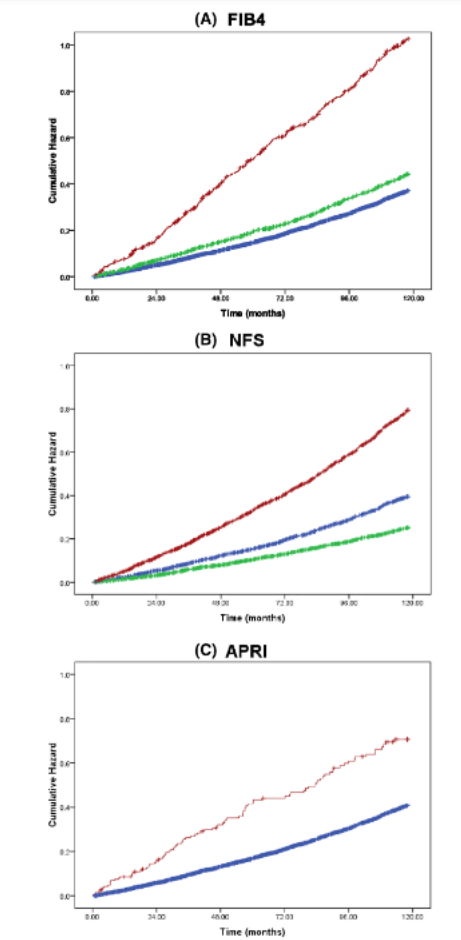


FIGURE 3 Kaplan-Meier estimation curves of cumulative all-cause mortality during follow-up in subjects classified by **A**, Fibrosis 4 (FIB4) score and **B**, nonalcoholic fatty liver disease fibrosis score (NFS) into high (red), intermediate (green) and low (blue) categories, and by **C**, aspartate aminotransferase to platelet ratio index (APRI) score into high (red) and low (blue) categories

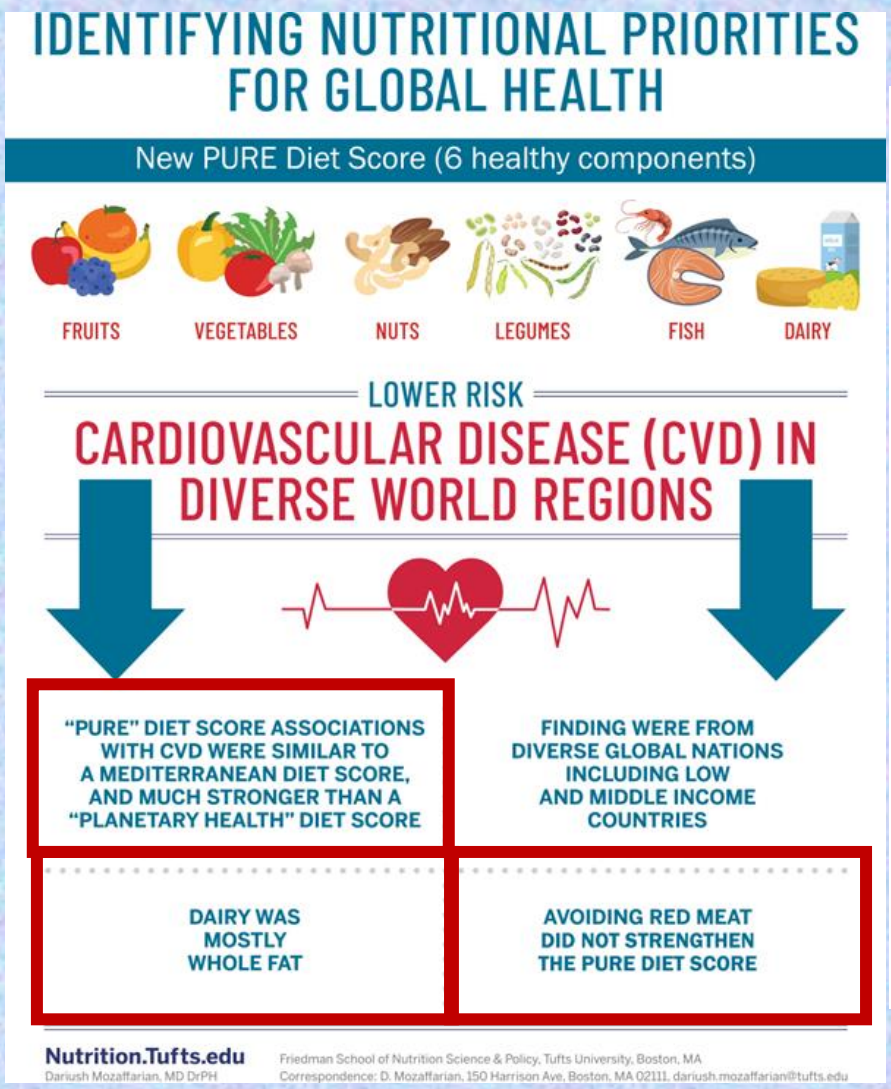
SR: No Statins for Primary Prevention > 80

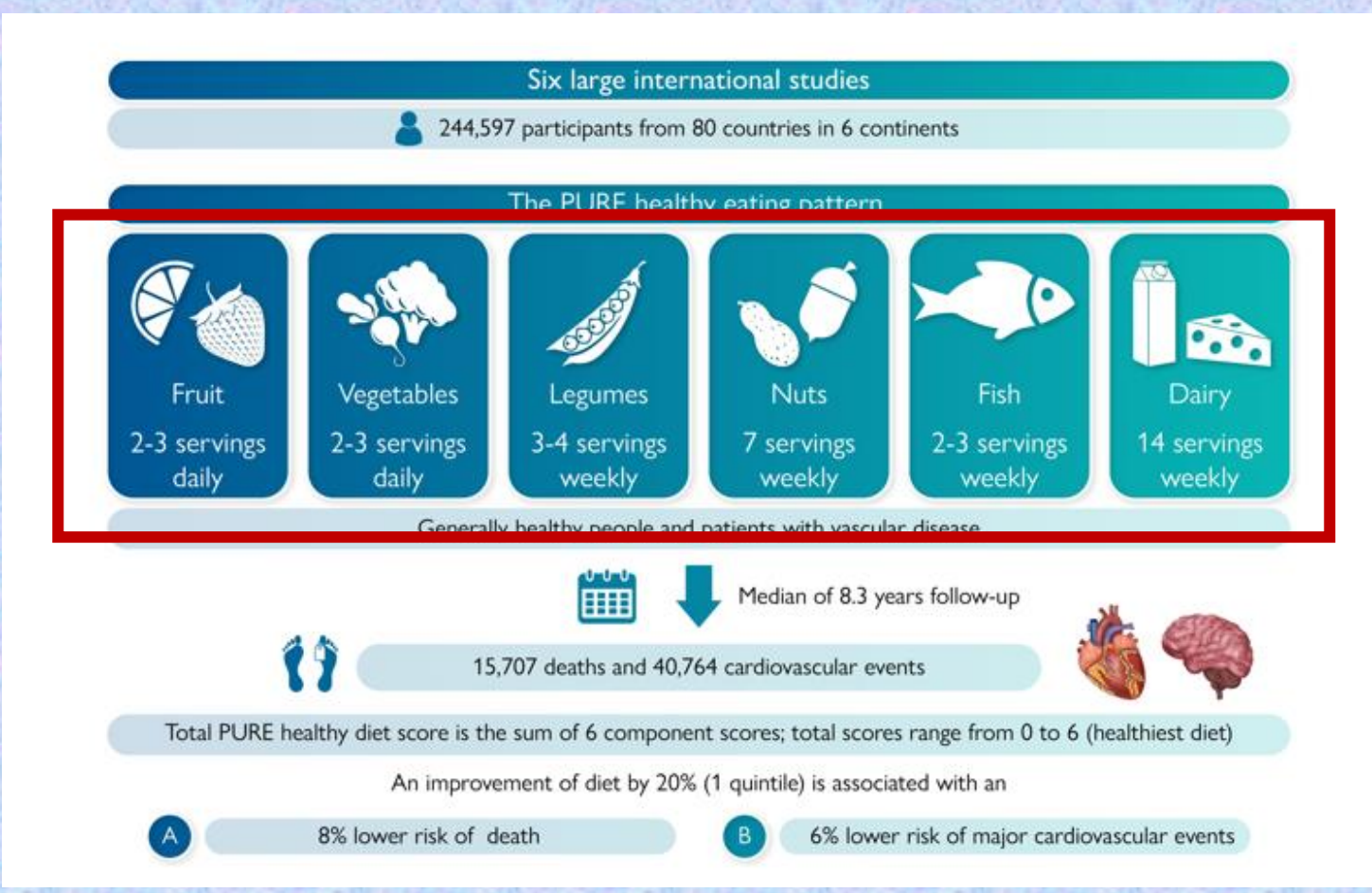
- 3 SR Tried to answer:

1. Relationship between hypercholesterolemia and mortality/major CV events in >80 years
2. Efficacy of statins for primary prevention of CV events > 80 years, and
3. Safety and tolerance of statins in this population.

- **Results**
- 1. NO association between total cholesterol and LDL with an increased rate of major CV events in > 80 Years (*and 3 studies AN ↑ risk of major CV events with lower levels of cholesterol)*.
- 2. Statins Use did NOT → a ↓in major CV events.
- 3. Side effects (muscular, hepatic, & GI) were more frequent than in the younger population.
- **For Primary Prevention, consider statins only in case-by-case basis.**

Am J Cardiol . 2023 Jan 15;187:62-73. doi: 10.1016/j.amjcard.2022.10.015





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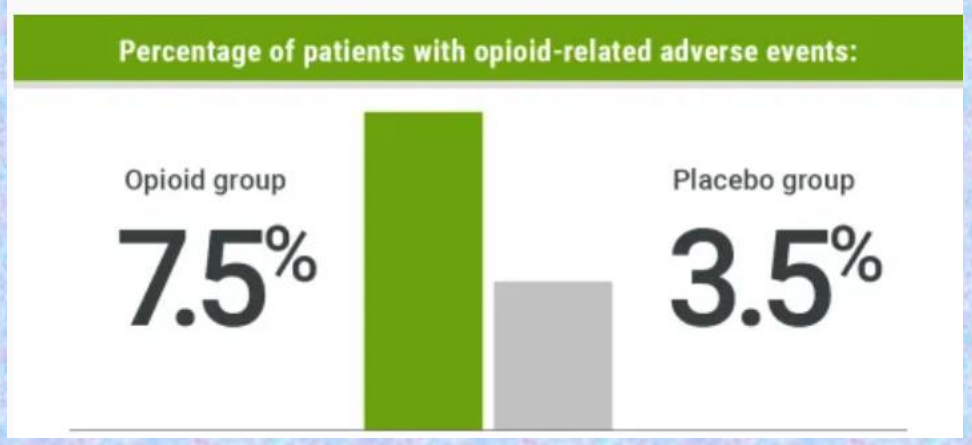
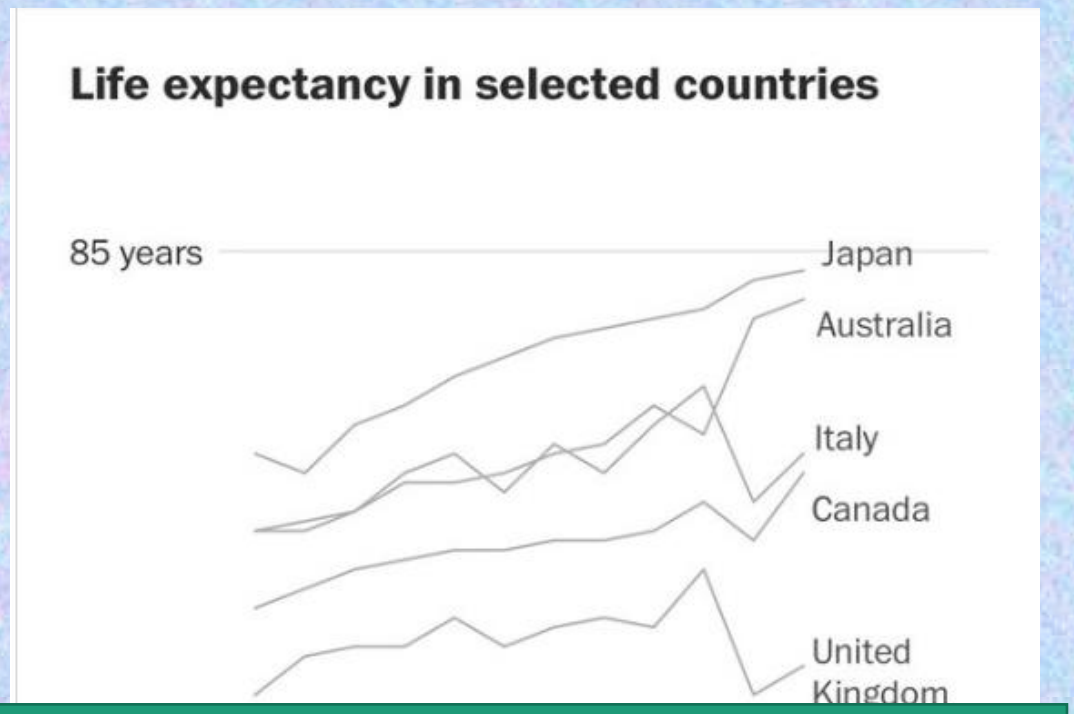
Telling stories: Your Favorite Dessert

They Still Do Not Work: Opioids of MS Pain

- Triple-blinded, placebo-controlled RCT adults presenting to one of 157 primary care or emergency department sites in Sydney, NSW, Australia, with 12 weeks or less of low back or neck pain (or both) of at least moderate pain severity.
- Guideline-recommended care plus oxycodone–naloxone, up to 20 mg oxycodone per day orally) or placebo, for up to 6 weeks.
- 151 participants in the opioid group and 159 in the placebo group were included in the primary analysis.
- Mean pain score at 6 weeks was 2·78 (SE 0·20) in the opioid group versus 2·25 (0·19) in the placebo group (adjusted mean difference 0·53, 95% CI –0·00 to 1·07, p=0·051).
- 61 (35%) of 174 participants in the opioid group reported at least one adverse event versus 51 (30%) of 172 in the placebo group (p=0·30), but more people in the opioid group reported opioid-related adverse events (eg, 13 [7·5%] of 174 participants in the opioid group reported constipation vs six [3·5%] of 173 in the placebo group).
- Lancet: 6.28. 23DOI:https://doi.org/10.1016/S0140-6736(23)00404-X



From EVP Shawn Martin



Pre Op “Clearance”

- Twelve eligible studies including 832 patients were identified. Pooled results indicated
- several positive associations for HIIT when compared with standard care either on CRF ($\dot{V}O_2$ peak,
- 6MWT, anaerobic threshold, or peak power output) or postoperative outcomes (complications, LOS,
- quality of life), although there was significant heterogeneity in study results. In 8 studies including
- 627 patients, there was moderate-quality evidence of significant improvement in $\dot{V}O_2$ peak
- (cumulative mean difference, 2.59 mL/kg/min; 95% CI, 1.52-3.65 mL/kg/min; P < .001).
- In 8 studies including 770 patients, there was moderate-quality evidence of a significant reduction in
- complications (odds ratio, 0.44; 95% CI, 0.32-0.60; P < .001). There was no evidence that HIIT
- differed from standard care in hospital LOS (cumulative mean difference, −3.06 days; 95% CI, −6.41
- to 0.29 days; P = .07).

JAMA Network Open. 2023;6(6):e2320527. doi:10.1001/jamanetworkopen.2023.20527 (

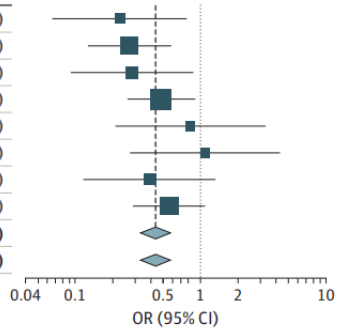
Cut Complication Rate almost in half; no decrease in LOS

Figure 3. Forest Plots of the Outcomes of High-Intensity Interval Training (HIIT) Compared With Standard Care on Clinical Outcomes and Postoperative Quality of Life

A Patients with complications

Study	HIIT, No. Events	HIIT, No. Total	Comparison, No. Events	Comparison, No. Total	OR (95% CI)	Weight, % Common	Weight, % Random
Banerjee et al,[35] 2018	5	27	14	28	0.23 (0.07-0.77)	6.6	6.6
Barberan-Garcia et al,[3] 2018	19	62	39	63	0.27 (0.13-0.57)	17.8	17.8
Berkel et al,[36] 2022	12	28	21	29	0.29 (0.09-0.86)	8.0	8.0
Molenaar et al,[40] 2023	21	123	38	128	0.49 (0.27-0.89)	26.8	26.8
Dunne et al,[17] 2016	8	19	7	15	0.83 (0.21-3.25)	5.3	5.3
van Rooijen et al,[42] 2019	5	20	7	30	1.10 (0.29-4.10)	5.6	5.6
Woodfield et al,[6] 2022	10	22	17	25	0.39 (0.12-1.29)	6.9	6.9
Licker et al,[37] 2017	27	74	39	77	0.56 (0.29-1.07)	23.1	23.1
Common effect model	**375**		**395**		**0.44 (0.32-0.60)**	**100.0**	**NA**
Random effects model					**0.44 (0.32-0.60)**	**NA**	**100.0**

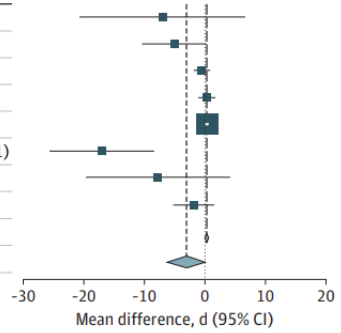
Heterogeneity: $I^2 = 0\%$; $\tau^2 < 0.0001$, $P = .46$



B Hospital length of stay

Study	HIIT Mean (SD), d	Comparison Mean (SD), d	Mean difference, d (95% CI)	Weight, % Common	Weight, % Random
Banerjee et al,[35] 2018	27 (25.00-21.00)	28 (32.00-30.00)	-7.00 (-20.65 to 6.65)	0.0	4.5
Barberan-Garcia et al,[3] 2018	2 (8.00-8.00)	63 (13.00-20.00)	-5.00 (-10.32 to 0.32)	0.3	12.4
Dunn et al,[17] 2016	19 (5.00-1.60)	15 (5.50-2.00)	-0.50 (-1.74 to 0.74)	5.0	17.7
Licker et al,[37] 2017	74 (10.00-3.02)	77 (9.70-4.50)	0.30 (-0.92 to 1.52)	5.2	17.7
Molenaar et al,[40] 2023	123 (3.67-1.50)	128 (3.33-0.74)	0.33 (0.04 to 0.63)	88.6	18.1
Morkane et al,[41] 2020	7 (13.00-5.50)	9 (30.00-11.40)	-17.00 (-25.49 to -8.51)	0.1	8.4
van Rooijen et al,[42] 2019	20 (8.00-10.37)	30 (15.70-30.40)	-7.70 (-19.49 to 4.09)	0.1	5.6
Woodfield et al,[6] 2022	22 (5.50-4.50)	25 (7.36-6.53)	-1.86 (-5.04 to 1.32)	0.8	15.6
Common effect model	**354**	**375**	**0.23 (-0.05 to 0.51)**	**100.0**	**NA**
Random effects model			**-3.06 (-6.41 to 0.29)**	**NA**	**100.0**

Heterogeneity: $I^2 = 73\%$; $\tau^2 = 16.1116$, $P < .001$



Mineralocorticoid receptor antagonists (MRAs) & A. Fib.

- MRA's improve clinical outcomes in HFREF.
- SR/MA of 10 RCT's of (11,000+) patients on MRAs & new onset AF.
- MRAs reduce the risk of overall AF (RR 0.77, 95% CI 0.65 to 0.91, p = 0.003, I2 = 40%).
- Both new-onset AF (RR 0.84, 95% CI 0.61 to 1.16, p = 0.28, I2 = 43%) Recurrent AF (RR 0.73, 95% CI 0.59 to 0.90, p = 0.004, I2 = 26%)

Am J Cardiol 2023;199:85–91

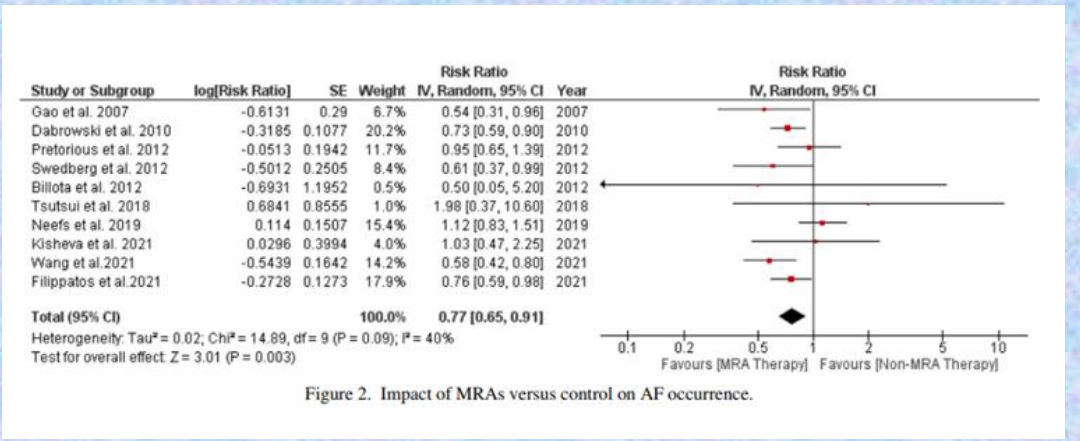


Figure 2. Impact of MRAs versus control on AF occurrence.

Black women have significantly higher risk for breast cancer mortality and would likely benefit from mammography screening starting at age 40. For other women, the data is less clear

- Screening recommendations for breast cancer in women of average risk have been the subject of much controversy over the years. Mammography decreases breast cancer-specific mortality for women aged 50-79, and most guidelines recommend mammography screening for women aged 50-74 every 1-2 years. That part is pretty clear. But for women aged 40-49 there is much uncertainty about the benefits and harms. Sadly, robust data has been lacking. As a result, recommendations from various guideline groups differ significantly, some recommending starting as early as age 40, others at age 50, and some in between. All include some degree of shared decision making. In 2016, the United States Preventive Services Task Force (USPSTF) recommended against routine screening for women aged 40-49, but recommended screening every 2 years if requested by an informed patient. However, a new **draft proposal** by this group recommends all women start screening at age 40.

- Recent data suggests that the risk of breast cancer is not the same across various racial and ethnic groups. **An article** in JAMA Network Open examined breast cancer rates among 5 groupings of women: White women, Black women, American Indian/Alaskan Native women, Hispanic women, and Asian/Pacific Islander women. While breast cancer mortality is decreasing in general, for 40-49 year olds annual mortality was 27/100,000 for Black women, 15 for White women, and around 11 for the 3 remaining groups mentioned above. Specifically, a 42-year-old Black woman has the same chance of dying from breast cancer over the next 10 years as a 51-year-old White woman, a 57-year-old American Indian/Alaska Native or Hispanic woman, or a 61-year-old Asian or Pacific Islander woman. Waiting until age 50 to start mammography screening in Black women may be part of the reason Black women have higher breast cancer mortality despite higher rates of screening. This indicates that Black women may benefit from initiating screening at age 40.

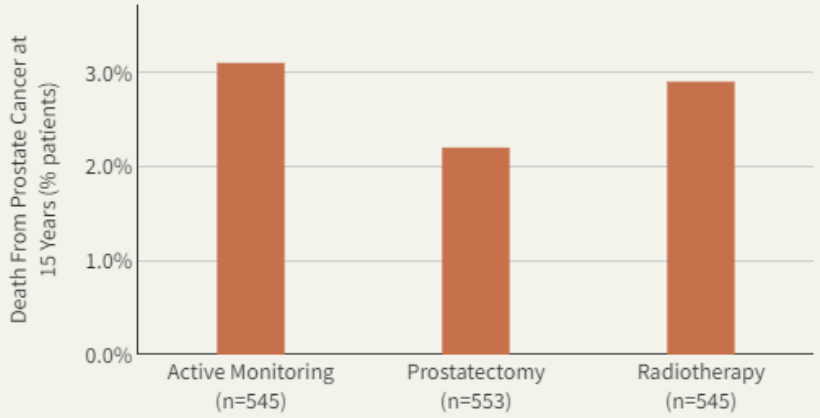
- Soon after the JAMA article was published, the USPSTF released the draft of the update to their breast cancer screening guidelines (this was not likely informed by the JAMA article). If the draft does not undergo significant changes, they will be issuing a B recommendation for biennial screening of all 40-74 year-old women. The B recommendation means either a high certainty of moderate net benefit or moderate certainty of moderate-to-substantial net benefit. One of the things often ignored in debates over screening for cancer are the harms associated with screening. False positive test results and overdiagnosis are two obvious downsides to increased screening. (Overdiagnosis refers to cancers which are diagnosed but would not have become clinically evident in the absence of screening.) Some estimates for the rate of overdiagnosis from mammographic screening are as high as 15%! Clearly, this is an area for ongoing shared decision making. While it may make sense to start screening at age 40 for women at increased risk and it appears Black women should be considered at increased risk, whether this applies to all women remains to be seen

Prostate Cancer Treatment & Mortality

- 1999 and 2009 in the United Kingdom, 82,429 men between 50 and 69 years of age received a prostate-specific antigen (PSA) test. Localized prostate cancer was diagnosed in 2664 men. Of these men, 1643 were enrolled in a trial to evaluate the effectiveness of treatments, with 545 randomly assigned to receive active monitoring, 553 to undergo prostatectomy, and 545 to undergo radiotherapy.
- At a median follow-up of 15 years (range, 11 to 21), we compared the results in this population with respect to death from prostate cancer (the primary outcome) and death from any cause, metastases, disease progression, and initiation of long-term androgen-deprivation therapy (secondary outcomes).
- Follow-up was complete for 1610 patients (98%). A risk-stratification analysis showed that more than one third of the men had intermediate or high-risk disease at diagnosis. Death from prostate cancer occurred in 45 men (2.7%): 17 (3.1%) in the active-monitoring group, 12 (2.2%) in the prostatectomy group, and 16 (2.9%) in the radiotherapy group (P=0.53 for the overall comparison). Death from any cause occurred in 356 men (21.7%), with similar numbers in all three groups. Metastases developed in 51 men (9.4%) in the active-monitoring group, in 26 (4.7%) in the prostatectomy group, and in 27 (5.0%) in the radiotherapy group. Long-term androgen-deprivation therapy was initiated in 69 men (12.7%), 40 (7.2%), and 42 (7.7%), respectively; clinical progression occurred in 141 men (25.9%), 58 (10.5%), and 60 (11.0%), respectively. In the active-monitoring group, 133 men (24.4%) were alive without any prostate cancer treatment at the end of follow-up. No differential effects on cancer-specific mortality were noted in relation to the baseline PSA level, tumor stage or grade, or risk-stratification score. No treatment complications were reported after the 10-year analysis.
- After 15 years of follow-up, prostate cancer–specific mortality was low regardless of the treatment assigned. Thus, the choice of therapy involves weighing trade-offs between benefits and harms associated with treatments for localized prostate cancer.

N Engl J Med 2023; 388:1547-1558 DOI: 10.1056/NEJMoa2214122

Hamdy, et al. - New Engl J Med (2023)



Population: Men With Localized Prostate Cancer

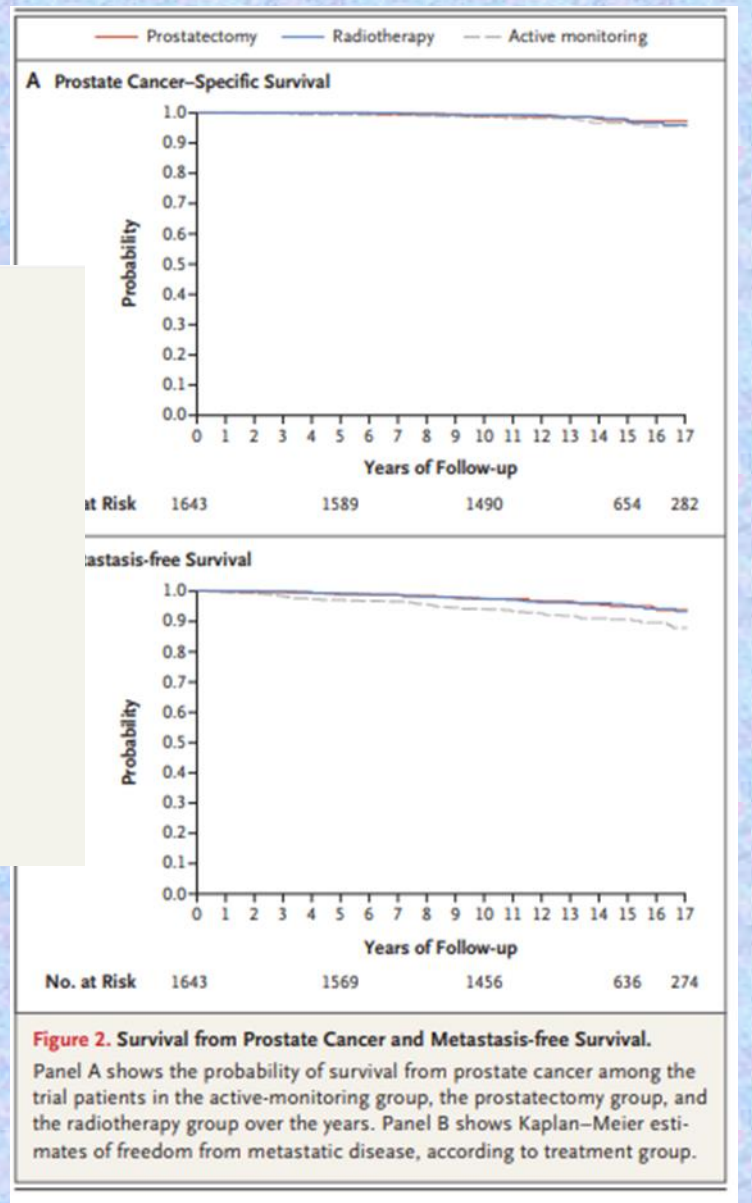


Figure 2. Survival from Prostate Cancer and Metastasis-free Survival.
Panel A shows the probability of survival from prostate cancer among the trial patients in the active-monitoring group, the prostatectomy group, and the radiotherapy group over the years. Panel B shows Kaplan–Meier estimates of freedom from metastatic disease, according to treatment group.

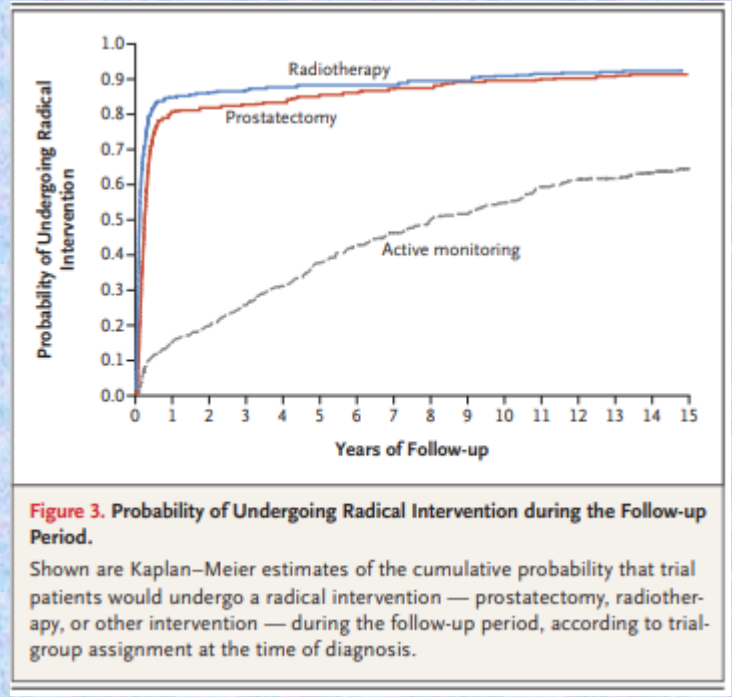


Figure 3. Probability of Undergoing Radical Intervention during the Follow-up Period.
Shown are Kaplan–Meier estimates of the cumulative probability that trial patients would undergo a radical intervention — prostatectomy, radiotherapy, or other intervention — during the follow-up period, according to trial-group assignment at the time of diagnosis.

REAL Journal Article Titles

THE JOURNAL OF PHYSICAL CHEMISTRY B

Feature Article

Cite This: J. Phys. Chem. B 2019, 123, 8341−8350

pubs.acs.org/JPCB

Proteins: "Boil 'Em, Mash 'Em, Stick 'Em in a Stew"

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ABSTRACT: Cells of the vast majority of organisms are subject to temperature, pressure, pH, ionic strength, and other stresses. We discuss these effects in the light of protein folding and protein interactions *in vitro*, in complex environments, in cells, and *in vivo*. Protein phase diagrams provide a way of organizing different structural ensembles that occur under stress and how one can move among ensembles. Experiments that perturb biomolecules *in vitro* or in cells by stressing them have revealed much about the underlying forces that are competing to control protein stability, folding, and function. Two phenomena that emerge and serve to broadly classify effects of the cellular environment are crowding (mainly due to repulsive forces) and sticking (mainly due to attractive forces). The interior of cells is closely balanced between these emergent effects, and stress can tip the balance one way or the other. The free energy scale involved is small but significant on the scale of the "on/off switches" that control signaling in cells or of protein−protein association with a favorable function such as increased enzyme processivity. Quantitative tools from biophysical chemistry will play an important role in elucidating the world of crowding and sticking under stress.

Open Access Article

Smells Like Teen Spirit—A Model to Generate Laundry-Associated Malodour In Vitro

by Marc-Kevin Zinn [1], Marco Singer [2] and Dirk Bockmühl [1,*]

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Microorganisms **2021**, *9*(5), 974; **https://doi.org/10.3390/microorganisms9050974**

Received: 29 March 2021 / Revised: 27 April 2021 / Accepted: 27 April 2021 / Published: 30 April 2021

(This article belongs to the Special Issue **Structure and Function of the Microbiota in Domestic Environments**)

One Ring to Rule Them All: a simple solution to multi-view 3D-Reconstruction of shapes with unknown BRDF via a small Recurrent ResNet

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Use the Force, Luke!
Learning to Predict Physical Forces by Simulating Effects

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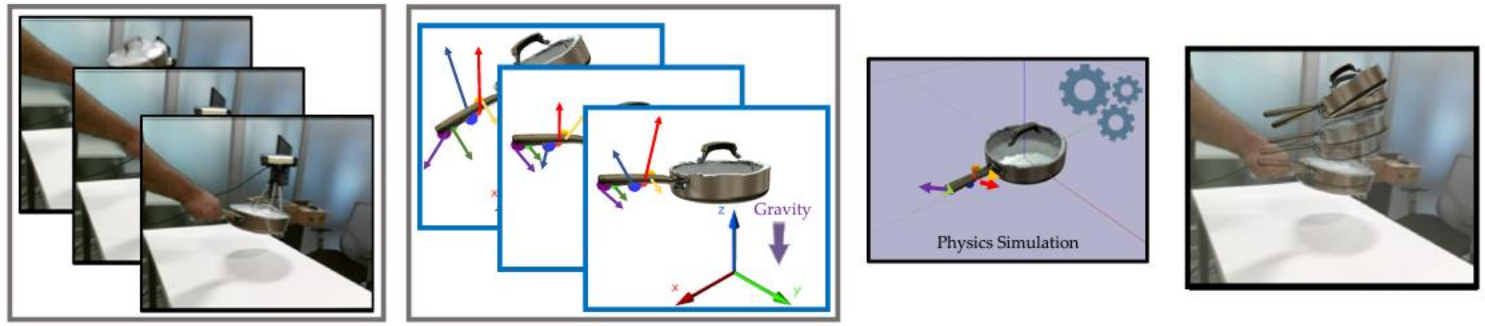
https://ehsanik.github.io/forcecvpr2020



Input Videos | Output Contact points + Forces | Applying Forces | Simulated Result

And Now for Something Completely Different: Visual Novelty in an Online Network of Designers

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Leading Article | Open Access | Published: 14 July 2016

May the Force Be With You: The Light and Dark Sides of the Microbiota–Gut–Brain Axis in Neuropsychiatry

Eoin Sherwin, Kiran V. Sandhu, Timothy G. Dinan & John F. Cryan

CNS Drugs **30**, 1019–1041 (2016) | Cite this article

The Journal of Experimental Biology 208, 3103-3107
Published by The Company of Biologists 2005
doi:10.1242/jeb.01735

Shaken, not stirred: a serendipitous study of ants and earthquakes

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Accepted 6 June 2005

THE JOURNAL OF AABB

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TRANSFUSION

TRANSFUSION MEDICINE ILLUSTRATED

Horton sees a speck: automated testing undone by a fragment

Penny C. Szklarski, Garrett S. Booth

First published: 12 March 2018 | https://doi.org/10.1111/trf.14408 | Citations: 1

Naltrexone reduces Binge Drinking in High Risk Population

RCT_naltrexone in sexual and gender minority men (SGM) who binge drink and have mild to moderate alcohol use disorder.

The study compared oral naltrexone (50 mg) or placebo; all participants received weekly counseling for 12 weeks.

Using intention to treat analysis, they found naltrexone:

--reduced reported number of binge-drinking days (incidence rate ratio [IRR]=0.74, 95% CI=0.56, 0.98; number needed to treat [NNT]=2),

--weeks with any binge drinking (IRR=0.83, 95% CI=0.72, 0.96; NNT=7.4),

--number of drinks per month (IRR=0.69, 95% CI=0.52, 0.91; NNT=5.7 for 10 drinks), and

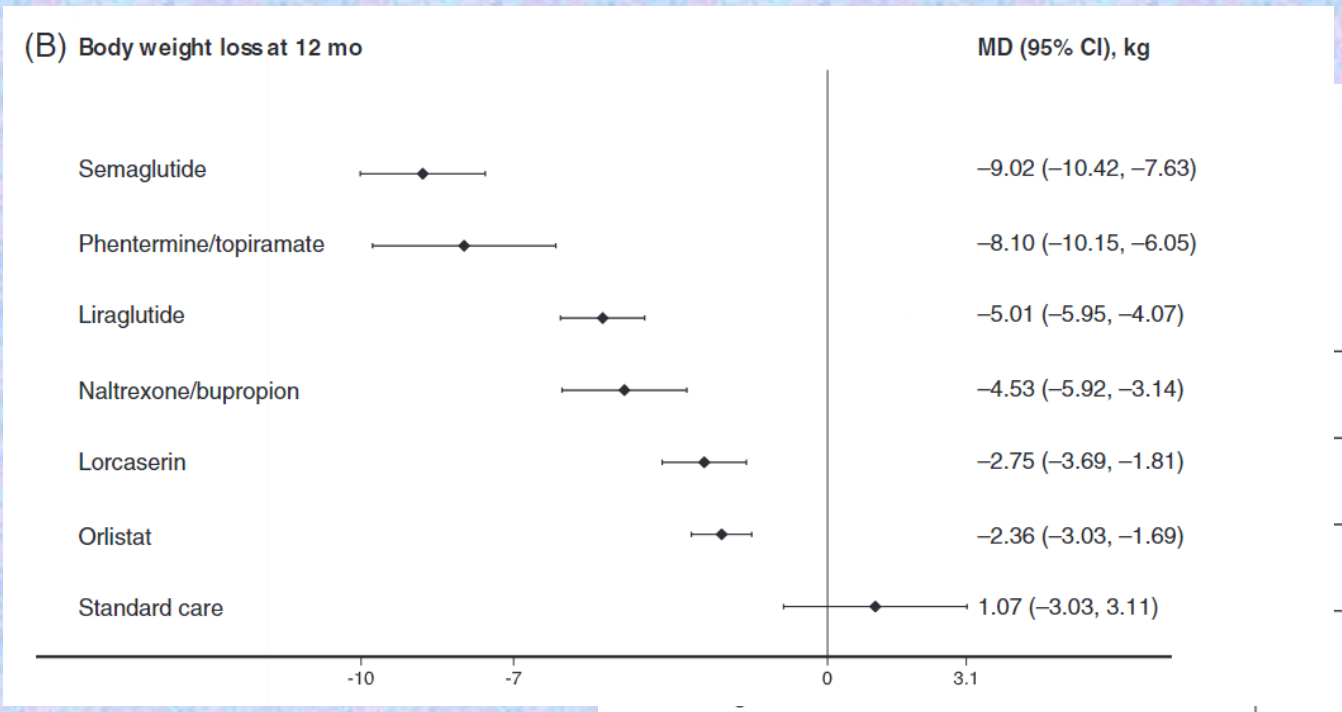
--alcohol craving scores (coefficient=−9.25, 95% CI=−17.20, −1.31).

Conclusions:

In a population at high risk for binge drinking, taking 50 mg of naltrexone per day lowered the risk of binge drinking and cravings. Critical to successful changing of behavior is BOTH the neurochemical ability to choose and the awareness of those behaviors and the rationale of its benefit.

Am J Psychiatry: 26 Oct 2022https://doi.org/10.1176/appi.ajp.20220335

WEIGHT LOSS



CV MORTALITY