



KEY ARTICLES & CLINICAL DEVELOPMENTS OF 2023* IN FAMILY MEDICINE

BY DAN WALDMAN, MD

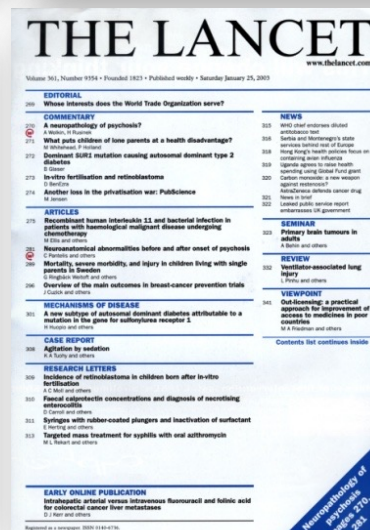
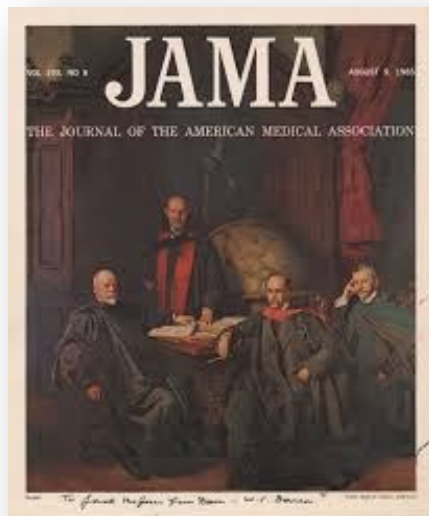
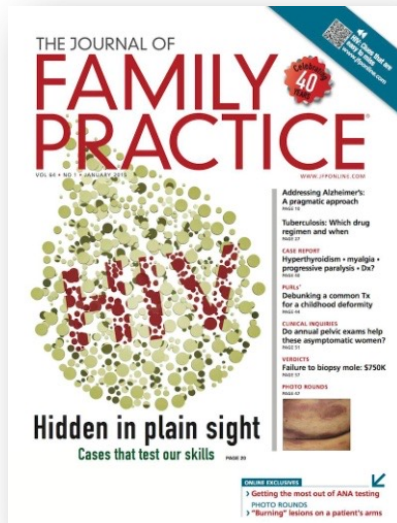
DEPARTMENT OF FAMILY & COMMUNITY MEDICINE

Disclosures: None

Learning Objectives

At the end of this presentation, the attendee will be able to:

1. Cite important and clinically-relevant research articles of the past year in the field of Family Medicine.
2. Describe methods for staying current in clinical medicine.



How Did I Choose Things?

Essential Evidence/Daily POEMS

Journal Watch

Our Faculty

Various “Top” Lists

Prioritized:

- key areas of FM practice
- might directly change clinical practice
- might be leading to paradigm changes

GLPs: More Indications?

Mounjaro® (tirzepatide)

VS

Wegovy® (semaglutide)

VS

Ozempic® (semaglutide)



RYBELSUS®
semaglutide tablets

Background

Several GLP-1 receptor agonists have favorable CV effects in patients with diabetes

2023: Two (industry-sponsored) trials suggested that these drugs also improve outcomes in patients **without** diabetes but with:

- Obesity
- CV disease

GLP Article #1

RCT 18,000 patients

BMI ≥ 27 kg/m² plus

Prior MI, stroke, or peripheral artery disease (**not diabetes**)

Intervention: Weekly injections of semaglutide (titrated to 2.4 mg) vs placebo

Average follow-up ~3 years

Incidence of composite outcome (MI, stroke, or CV related death) lower in the semaglutide group than in the placebo group (6.5% vs. 8.0%)

N Engl J Med 2023 Nov 11; [e-pub]

GLP Article #2

RCT 529 patients with HFpEF + BMI ≥ 30 kg/m², and **no diabetes**

Weekly injections of semaglutide (titrated to 2.4 mg) or placebo

At 1 year: improvements seen: in walk distance + symptom questionnaire

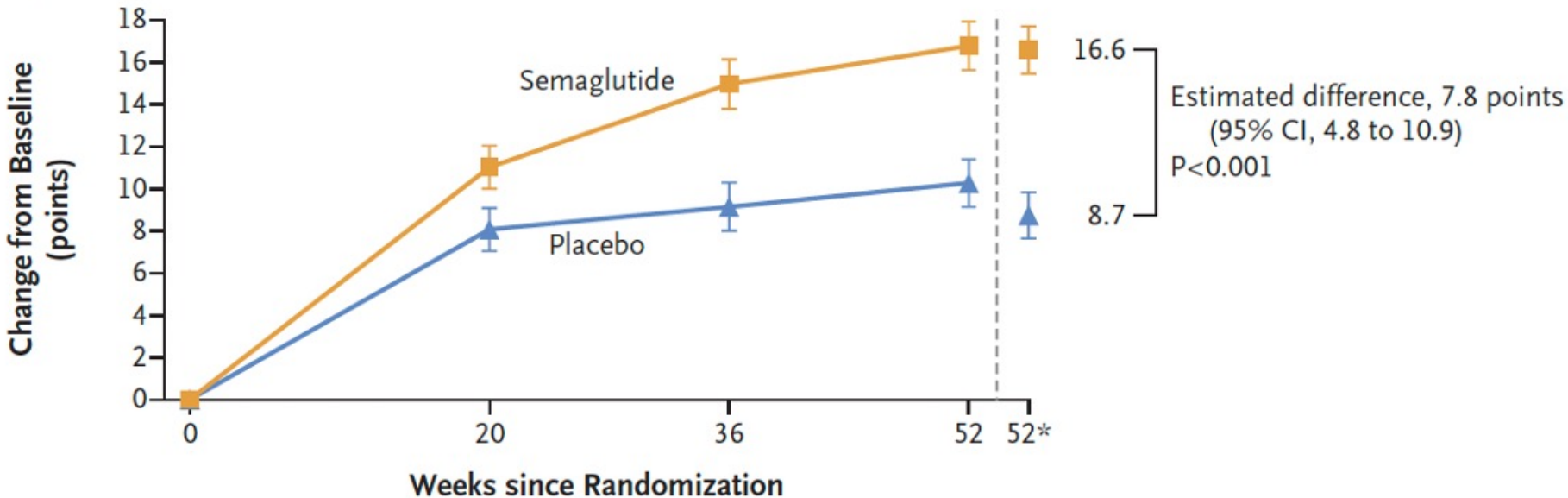
Mean weight loss: 13% vs 3% with placebo

Fewer serious adverse events in the semaglutide group driven by fewer cardiac events (2.7% vs 11.3%; $P < .001$)

NNT = 12 for 1 year

N Engl J Med 2023; 389:1069

A Change in KCCQ-CSS



No. of Participants

Semaglutide	263	249	225	243	263
Placebo	266	242	217	237	266

Figure 1. Changes from Baseline to Week 52 in the Dual Primary End Points.

Analyses are based on the treatment policy estimand, reflect the full analysis population, and are from the in-trial period. Shown are the observed (i.e., as-measured) mean changes from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations) and percentage changes in body weight. I bars indicate the standard error, and the numbers below the graphs are the numbers of participants contributing to the mean. The data at week 52* are the estimated mean changes from baseline to week 52 based on analysis of covariance (ANCOVA) and an imputation approach for missing data.

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	Extremely Limited	Quite a bit Limited	Moderately Limited	Slightly Limited	Not at all Limited	Limited for other reasons or did not do the activity
a. Showering/bathing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Walking 1 block on level ground	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Hurrying or jogging (as if to catch a bus)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	1	2	3	4	5	6

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
1	2	3	4	5

Notes

~10% of semaglutide recipients in both trials discontinued treatment because of GI side effects (vs 2% on placebo)

Costs ~\$17k annually

GLPs and depression/dysphoria?

Biologically plausible but no convincing evidence yet (FDA is monitoring)

Expert Opin Drug Saf 2024 Mar 26; [e-pub]

Higher incidence of depression and suicidal ideation noted among patients with diabetes who took semaglutide or liraglutide than among those who took metformin or insulin

Expert Opin Drug Saf 2024 Jan; 23:47]

Lower risk for suicidal ideation among people with diabetes or obesity who were prescribed semaglutide than those prescribed other agents

Nat Med 2024 Jan; 30:168

Ro, healthcare simplified

From the online visit to ongoing care, expect a seamless experience.

Get hard faster
with Ro Sparks

NEW!



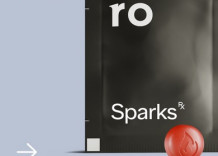
Lose weight
with GLP-1s



Get started
with Ozempic



E.D.



What's in shortage right now?

See which GLP-1s are in shortage according to the FDA and how it compares against community reports.



Ozempic



.68 mg/1 mL

⚡ 945 recent reports

Available according to the FDA but we're receiving shortage reports.



1.34 mg/1 mL

⚡ 416 recent reports

Available according to the FDA but we're receiving shortage reports.



2.68 mg/1 mL

⚡ 410 recent reports

Available according to the FDA but we're receiving shortage reports.



Wegovy



0.25 mg/0.5 mL

⚡ 3803 recent reports

In shortage. Estimated shortage duration TBD



0.5 mg/0.5 mL

⚡ 2207 recent reports

In shortage. Estimated shortage duration TBD



1 mg/0.5 mL

⚡ 1272 recent reports

In shortage. Estimated shortage duration TBD



1.7 mg/0.75 mL

⚡ 827 recent reports

Available according to the FDA but we're receiving shortage reports.



2.4 mg/.75 mL

⚡ 854 recent reports

Available according to the FDA but we're receiving shortage reports.



Statins

LODESTAR trial- Statin initiation in CAD

RCT of 4400 pts in South Korea

Preexisting CAD, 3 years of follow-up

Arm 1: daily high-intensity statins (20-mg rosuvastatin or 40-mg atorvastatin)

Arm 2: “treat to target:” lower doses (10-mg rosuvastatin or 20-mg atorvastatin) initiated and titrated up as needed to achieve LDL of 50-70 mg/dL

JAMA 2023; 329:1078

Also studied: Atorvastatin vs rosuvastatin to compare safety and efficacy

BMJ 2023; 383:e075837

LODESTAR trial- Statin initiation in CAD

First Part

Mean LDL cholesterol values and adverse cardiovascular outcomes similar between the two groups

~1/2 of patients assigned to treat-to-target group achieved LDL cholesterol values <70 mg/dL with moderate-intensity (rather than high-intensity) dosing

JAMA 2023; 329:1078

LODESTAR trial- Statin initiation in CAD

Second Part (atorvastatin vs rosuvastatin)

Mean LDL and CV outcomes similar between the two groups during 3 years of follow-up

Most adverse effects (including myalgias) similar between the two drugs

Patients who took rosuvastatin significantly more likely to:

- Develop diabetes (7.1% vs. 5.5%)
- Undergo cataract surgery (2.5% vs. 1.5%)

BMJ 2023; 383:e075837

LODESTAR trial- Statin initiation in CAD

Take home points

Neither the method of initiation nor the choice of high-intensity statin appeared to affect CV outcomes

Patients concerned about side effects might prefer treat-to-target approaches

Those with limited access to care might prefer initial prescription of high-intensity statins

If using high intensity statins, perhaps choose atorvastatin

BMJ 2023; 383:e075837

Incidence of Statin-Induced Diabetes

Previously: 2008 Jupiter Trial

17,802 participants, median f/u ~2 years

“25% increase in new-onset diabetes for rosuvastatin 20 mg compared with placebo”

Absolute risk: 270 vs 216 new cases of diabetes

N Engl J Med. 2008;359(21):2195-2207

Incidence of Statin-Induced Diabetes

Meta-analysis of 23 RCTs

Incidence of new-onset diabetes slightly (but statistically significantly) higher with low-to-moderate–intensity statins compared with placebo (1.3% vs. 1.2% annually)

Risk for new-onset diabetes more substantial with high-intensity statins compared with placebo (4.8% vs. **3.5% annually**)

New-onset diabetes was diagnosed more often in patients with baseline HbA_{1c} in the prediabetes range than in patients with lower HbA_{1c}

The mean HbA1c increased by 0.06% to 0.08%, depending on the intensity of statin therapy

CV benefits of statins are thought to greatly outweigh the risks, for all except perhaps those with borderline indications for statins

Lancet Diabetes Endocrinol 2024 May; 12:306

USPSTF Breast Cancer Screening

Previous Recs

2016: USPSTF

- Every other year mammograms for women **50**–74 (grade B)
- Individualized decision making for those who were 40 to 49 (grade C)

New 2024 Recs

- Every other year mammograms for women **40** to 74 (grade B)
- Recs conclude with *moderate* certainty that such screening has benefit in preventing breast cancer–related mortality.

US Preventive Services Task Force. JAMA 2024 Apr 30
Henderson JT et al. JAMA 2024 Apr 30 Trentham-Dietz A et al. JAMA 2024 Apr 30

Some Background

Screening mammography lowers breast cancer–related mortality*, but incidence of invasive breast cancer is increasing among women in their 40s

Black women: lower incidence but more likely to develop aggressive cancers at younger ages, higher risk for breast cancer–related mortality

New recs apply to women at “average risk” of Br CA

US Preventive Services Task Force. JAMA 2024 Apr 30
Henderson JT et al. JAMA 2024 Apr 30 Trentham-Dietz A et al. JAMA 2024 Apr 30

Average Risk Means

No Personal history of breast cancer

No pts at very high risk of breast cancer due to certain genetic markers

No history of high-dose radiation therapy to their chest at a young age

No high-risk lesion on previous biopsies

US Preventive Services Task Force. JAMA 2024 Apr 30
Henderson JT et al. JAMA 2024 Apr 30 Trentham-Dietz A et
al. JAMA 2024 Apr 30

ACOG Appreciates U.S. Preventive Services Task Force's Updated Guidelines on Breast Cancer Screening

ACOG: start at 40, and choose every 1 or 2 years based on shared decision making (no endpoint)

ACR: risk stratification by 25, start screening in average risk pts at 40, every year, continue after 74 unless severe comorbidities

American Cancer Society: *“Patients should have the opportunity to begin annual breast cancer screening at age 40, with regular screening beginning for all women at age 45... We are disappointed that the updated USPSTF screening recommendations do not include women over the age of 74”*

“Breastcancer.org *has consistently advocated for mammogram screenings every year, starting at age 40, along with regular self-exams and medical exams,”* says Marisa Weiss, MD, founder and chief medical officer of Breastcancer.org. *“I’m pleased to see a shift in the right direction [by the USPSTF], but there’s more to be done.”*

A group of 1000 women at age 40 will have ~40,000 years to live as a cohort

Table 2. Estimated Median Lifetime Benefits and Harms of Biennial Screening Mammography With Digital Breast Tomosynthesis for a Cohort of 1000 Women and a Cohort of 1000 Black Women by Starting Age of 40 vs 50 Years

Screening strategy (interval, start-stop ages in years)	Mammograms	Breast cancer deaths averted	Life-years gained	False-positive results	Overdiagnosis
All women (across 6 models)					
Biennial (40-74)	16 116	8.2	165.2	1376	14
Biennial (50-74)	11 208	6.7	120.8	873	12
Black women (across 4 models)					
Biennial (40-74)	15 801	10.7	228.9	1253	18
Biennial (50-74)	10 905	9.2	176.7	814	16

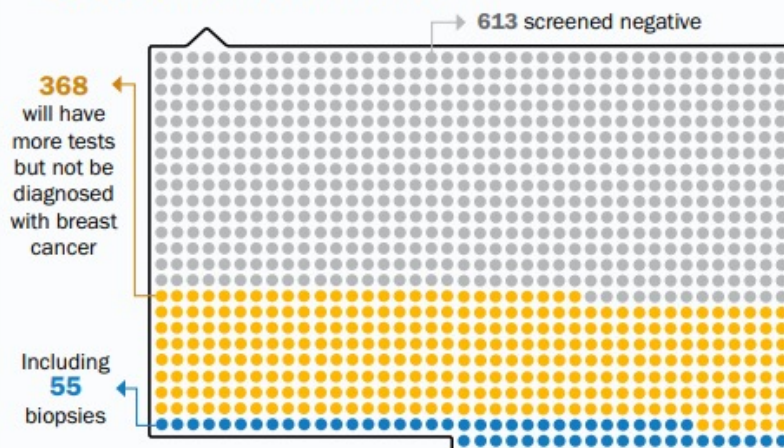
What is Canada Up To?



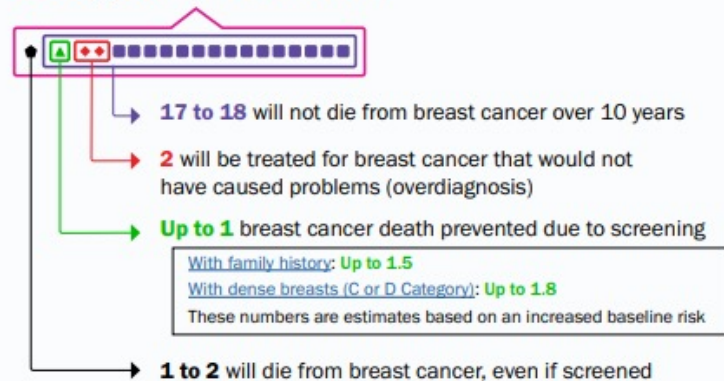
Benefits and Harms of Breast Cancer Screening Over 10 Years

Screening (Mammogram) for 1000 people ages 40-49

981 not diagnosed with breast cancer



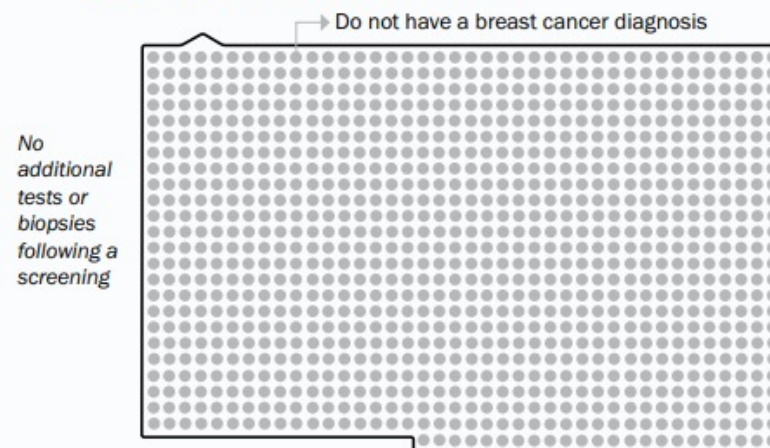
19 diagnosed with breast cancer



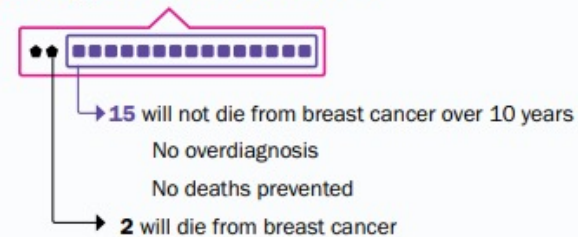
Note: Women in both the screened and unscreened groups may need testing if they experience symptoms. Rounded figures presented are estimates of the available evidence.
For a full breakdown, please review the [full draft recommendations](#).

No screening for 1000 people ages 40-49

983 not diagnosed with breast cancer



17 diagnosed with breast cancer



Benefits and Harms of Breast Cancer Screening Over 10 Years

Screening (Mammogram) for 1000 people ages 40-49

981 not diagnosed with breast cancer

→ **613** screened negative

19 diagnosed with breast cancer



→ **17 to 18** will not die from breast cancer over 10 years

→ **2** will be treated for breast cancer that would not have caused problems (overdiagnosis)

→ **Up to 1** breast cancer death prevented due to screening

With family history: **Up to 1.5**

With dense breasts (C or D Category): **Up to 1.8**

These numbers are estimates based on an increased baseline risk

→ **1 to 2** will die from breast cancer, even if screened

No screening for 1000 people ages 40-49

983 not diagnosed with breast cancer

→ Do not have a breast cancer diagnosis

17 diagnosed with breast cancer



→ **15** will not die from breast cancer over 10 years

No overdiagnosis

No deaths prevented

→ **2** will die from breast cancer

Note: Women in both the screened and unscreened groups may need testing if they experience symptoms. Rounded figures presented are estimates of the available evidence.

For a full breakdown, please review the [full draft recommendations](#).

Additional thoughts

Women ≥ 75 : “evidence insufficient” to rec anything (risk of “overdiagnosis” increases with age)

Ann Intern Med 2023;176(9):1172-1180

Women with dense breasts: inadequate evidence to make a rec on supplemental screening with US or MRI after negative mammography

Equity issues: expand beyond screening

US Preventive Services Task Force. JAMA 2024 Apr 30
Henderson JT et al. JAMA 2024 Apr 30
Trentham-Dietz A et al. JAMA 2024 Apr 30

New Approaches to Depression Treatment

New Approaches to Depression Treatment

Probiotics

Ketamine

Esketamine (enantiomer of racemic ketamine)

Psilocybin

New Approaches to Depression Treatment

Probiotics

Small study: 49 pts with **moderate to severe depression**

Short: 8 weeks

Probiotic manufacturer (Bio-Kult) provided funding

Antidepressant plus either

- Commercially available multistrain probiotic
- Placebo

Improvement with the probiotic borderline statistical significance vs placebo

Probiotic recipients: more likely to report “much” or “very much” improvement at 8 weeks (54% vs. 32%)

Some probiotic users had mild/transient GI side effects



JAMA Psychiatry 2023; 80:842

New Approaches to Depression Treatment

Ketamine

365 patients with **treatment-resistant depression**

3-week courses of 2x-weekly IV ketamine vs 3x-weekly electroconvulsive therapy (ECT)

At 3 weeks: more ketamine recipients than ECT recipients had positive responses (55% vs. 41%)

At 6 months, a substantial proportion of patients in both groups had relapsed (56% of ECT responders and 35% of ketamine responders)

Worth it? (potential addiction potential, cost/insurance coverage issues)

N Engl J Med 2023; 388:2315



u/mindbloom Promoted

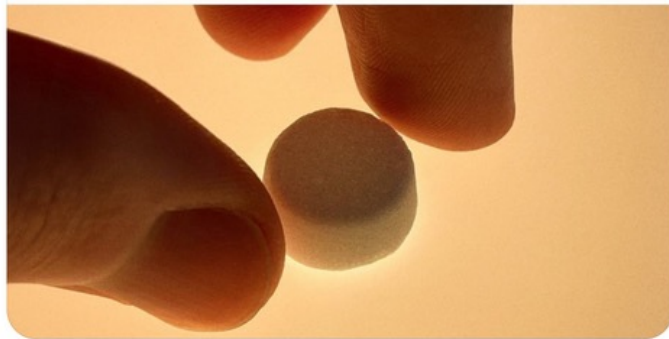


Is traditional therapy not working? Mindbloom offers a new approach with ketamine therapy. See if it's right for you - \$99 to get started with a consult.

Read [Important Safety Information](#) and learn more about our [Clinical Outcomes](#).

Women'sHealth

"Before I started using **ketamine**, I felt like I had run up against a wall in therapy."



New Approaches to Depression Treatment

Esketamine

676 patients with **treatment-resistant major depression**

Oral antidepressant plus:

Esketamine nasal spray (2x weekly) vs daily oral quetiapine

Remission rates greater with esketamine than quetiapine at 2 months (27% vs. 18%) and 8 months (49% vs. 33%)

Serious adverse events ~5% in both groups

Side effect–related dropouts more common with quetiapine (11% vs. 4%)

N Engl J Med 2023; 389:1298

New Approaches to Depression Treatment

Psilocybin

104 pts, 11 sites

Major Depressive Disorder

Single dose 25mg

Placebo was niacin

At 6 weeks, psilocybin recipients were more likely than placebo recipients to have sustained response (42% vs. 11%) and remission (25% vs 9%)



JAMA 2023; 330:843

New Approaches to Depression Treatment

Psilocybin

6-8 hours of prep sessions with doctoral-level facilitators

7-10 hour treatment session

Music provided through headphones in a comfortable room

4 hours of post-dose “integration sessions”

JAMA 2023; 330:843

Themes?

Treating depression remains challenging for some patients

At best, remission or response rates for the investigated treatments were ~50%

Often not a lot better than existing treatments

Psychotherapy often not addressed (also happening?)

PCPs not in a great position to initiate most of these

....but you may get asked about them, and pts may be trying them

Low Risk PE's and Hospitalization

Low Risk PE: Still Too Many Are Hospitalized

Initial studies in 2011

CHEST guidelines 2016 and 2021: outpt mgmt. for low risk PE – *if meds available and care can be arranged*

Serial cross-sectional analyses of data from >1.6 million ED visits (2012–2020)

ED Discharge rates have remained relatively constant

Of the $\geq 50\%$ of pts who are low risk via risk calculators/hemodynamic stability only 1/3 discharged from ED

Ann Intern Med 2024 Jan 30; [e-pub]

Simplified PESI (Pulmonary Embolism Severity Index)

Predicts 30-day outcome of patients with PE, with fewer criteria than the original PESI.

When to Use ▼	Pearls/Pitfalls ▼	Why Use ▼
Age, years	<div>≤80 0</div>	<div>>80 +1</div>
History of cancer	<div>No 0</div>	<div>Yes +1</div>
History of chronic cardiopulmonary disease	<div>No 0</div>	<div>Yes +1</div>
Heart rate, bpm	<div><110 0</div>	<div>≥110 +1</div>
Systolic BP, mmHg	<div>≥100 0</div>	<div><100 +1</div>
O ₂ saturation	<div>≥90% 0</div>	<div><90% +1</div>

Cellulitis: When Should We Get Worried?

Cellulitis: full resolution takes time

Responses to treatment among 247 adults

Mean age, 52; 67% men

Confirmed lower-extremity cellulitis

7-10 days of a β -lactam drug, with or without clindamycin



Open Forum Infect Dis 2023 Oct; 10:ofad488

Cellulitis: full resolution takes time

Between baseline and day 5, surface area of affected skin decreased by 34%

By day 10, the affected area had shrunk by ~55%

Swelling lessened by almost 50% by day 10

Many patients still had substantial swelling, *affected leg remained warmer than the unaffected one for most patients*

More than half of patients continued to report discomfort in the affected leg at day 10

Pain scores >5 (out of 10) reported by 14%

CRP levels fell dramatically during treatment, reaching near-normal levels in all patients by day 10

But....Some are Misdiagnosed

Meta-analysis, 7 studies

Unblinded

858 inpatients with initial dx of cellulitis

Secondary eval by dermatologist or ID physician

39% received alternative diagnoses by specialists

J Hosp Med 2023 Mar

TABLE 2 Alternative diagnoses made by consultants.

Alternative diagnoses total patients = 327 ^a					
Noninfectious	221	68%	Infectious	111	34%
Stasis dermatitis/ venous stasis	60	18%	Abscess	32	10%
Trauma	21	6%	Septic bursitis	17	5%
Eczematous dermatitis	17	5%	Osteomyelitis	16	5%
Gout/pseudogout	12	4%	Infected ulcer	14	4%
Unspecified dermatitis	10	3%	Erythema migrans	8	2%
Allergic reaction/ dermatitis	10	3%	Septic arthritis	6	2%
Lymphangitis	7	2%	Viral rash	3	1%
Deep vein thrombosis	4	1%	Tenosynovitis	3	1%
Edema	4	1%	Other ^c	12	4%
Erythema nodosum	4	1%			
Chronic wound	3	1%			
Other ^b	69	21%			

^aTotal adds up to greater than 100% as some patients had more than one alternative diagnosis due to rounding.

^bInfrequent noninfectious diagnoses included limb ischemia, calciphylaxis, autoimmune chondritis, psoriasis, cryoglobulinemia, chronic paronychia, vestibulitis, flexor tenosynovitis, phytophotodermatitis, Charcot joint, osteoarthritis, balanoposthitis, dry gangrene, lipodermatosclerosis, necrobiosis lipoidica diabetorum, pyoderma gangrenosum, vasculitis, peristomal irritation, myositis, and "other."

^cInfrequent infectious diagnoses included molluscum contagiosum, varicella zoster, dacrocystitis, folliculitis, furunculosis, impetigo, infected hematoma, odontogenic, septic thrombophlebitis, wet gangrene, and otitis externa.

Quicker Summaries

Quicker Summaries

Steroids probably help the sicker patients with CAP (meta-analysis)

Chest 2023;163(3):484-497

American Urological Association Guideline: PSA screening Age 50-69, q2-4 years.

- Re-screening intervals should be longer for men with PSA levels below age-specific medians (e.g., <1.0 ng/mL at age 60), due to low lifetime risk for developing aggressive prostate cancer
- Thresholds of PSA elevation warranting further evaluation should vary with age (e.g., 3.5 ng/mL for men in their 50s, and 4.5 ng/mL for those in their 60s)
- Men with newly elevated PSA levels: repeat testing a few months later before referral

J Urol 2023; 210:46

(2018 USPSTF PSA screening is a “C” for 55-69)

Quicker Summaries

Intensive motivational interviewing to decrease BMI *increases* BMI in children (vs “usual care”)

Pediatrics 2024;153(2):e2023062462

Outpatient oseltamivir evidence isn't strong. Updated meta-analysis of 15 RCTs: Patients who received oseltamivir as outpatients:

- not less likely to be hospitalized (relative risk [RR] 0.79; 95% CI 0.48 - 1.29)
- didn't reduced hospitalizations in older patients (RR 1.01; 0.21 - 4.90) or in high-risk patients (RR 0.65; 0.33 - 1.28).
- increases in nausea (NNTH = 9) and vomiting (NNTH = 6)
- Previous study main positive finding: 21 hrs symptom reduction

JAMA Intern Med 2024;184(1):18-27

Quicker Summaries

New Chronic Coronary Artery Disease recs

Key changes include:

Shortening the duration of dual antiplatelets and beta blockers

Not recommending fish oil or omega-3 fatty acids

Not using e-cigarettes as first-line agents for smoking cessation

Incorporating SGLT-2 inhibitors and GLP-1 agonists for some patients with chronic coronary disease.

Routine surveillance using stress tests, coronary CT, or angiography not recommended in the absence of a change in symptoms or function

Circulation 2023;148(9):e19-e119

And finally...

Virtual Visits With and Subsequent ED Visits

Virtual Visits and Subsequent ED Visit

Canadian Study

5 million Ontario residents who had virtual visits 2021-2022

~20% of virtual visits were with providers other than PCP

Did not include virtual visits with another physician within the same group

JAMA Netw Open. 2023;6(12):e2349452

Virtual Visits and Subsequent ED Visit

Outcome looked at: ED visit after virtual visit with PCP or other (non practice group) provider

Subsequent emergency department use was lower following a virtual visit with a patient's own family physician compared with a visit with another physician

JAMA Netw Open 2023 Dec

Likelihood of ED visit: 66% higher for patients who saw non PCP physicians (outside their practice)

1 additional ED visit for every 77 virtual visits

This difference was accentuated ~5x when virtual visits were with direct-to-consumer telemedicine clinics

This study provides evidence to support policy changes that prioritize virtual visits **within an existing therapeutic relationship**

JAMA Netw Open. 2023;6(12):e2349452

How to Stay Current?

Staying Current

Read everything....? (*good luck!*)

Journal clubs with your colleagues

****Services: Essential Evidence, Journal Watch, etc**

Podcasts (POEM of the week, Frankly speaking, Curbsiders)

Teach, Precept

ABFM CKSA's: 25 q's per quarter (they also have an app)

Do a talk like this!

Thanks!

