KEY ARTICLES & CLINICAL DEVELOPMENTS OF 2021* IN FAMILY MEDICINE

BY DAN WALDMAN, MD

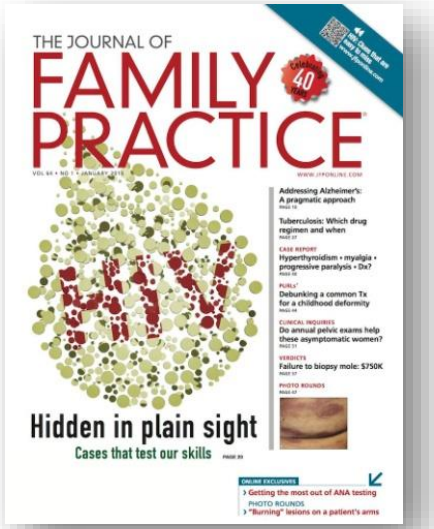
DEPARTMENT OF FAMILY & COMMUNITY MEDICINE

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.

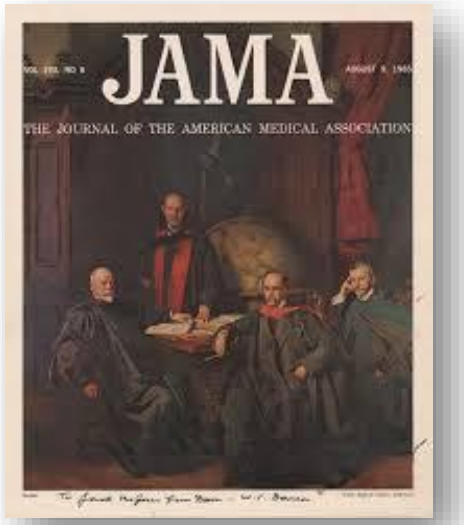

THE JOURNAL OF
FAMILY PRACTICE
Hidden in plain sight
Cases that test our skills


Annals of Internal Medicine


American Family Physician
60TH ANNIVERSARY
Celebrating Six Decades of Publishing


BMJ
OVERDIAGNOSIS
Harming the healthy


ANNALS OF
FAMILY MEDICINE


JAMA
THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION


The NEW ENGLAND
JOURNAL of MEDICINE


THE LANCET


OBSTETRICS &
GYNECOLOGY


The American Journal of
Sports
Medicine

How Did I Choose Things?

Essential Evidence/Daily POEMS

Journal Watch

Our Faculty

Various “Top” Lists

<u>Prioritized:</u>

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

Proton Pump Inhibitors

PPI's work and have their uses. But...

Increased risks: Cdif, atrophic gastritis, B12 malabsorption, Inflammatory Bowel Disease, Interstitial Nephritis, Drug-induced Lupus, effects on bone metabolism *(partial list)*

Associations of unclear significance (potential for confounders):

- Covid 19
- Dementia
- Pneumonia
- Mortality

Can be hard to deprescribe PPI's

~15 million taking PPI's. Large % of PPI prescriptions are "inappropriate" (>50%). Also available OTC.

PPI's and Gastric Cancer

PPIs cause hypergastrinemia -> hyperplasia of the gastric mucosa

Study compared 973,000 new users of PPIs to 198,000 new users of histamine-2–receptor antagonists (H2RAs/"H2 Blockers")

New PPI users: **more likely than new H2 blocker users to develop new gastric cancer** (hazard ratio, 1.45); NNH ~2100 at 5 years, 1200 at 10 years

Association strengthened with higher PPI dose and longer time use

Prior studies also said this but were observational

Gut

Abrahami D, McDonald EG, Schnitzer ME, Barkun AN, Suissa S, Azoulay L. Proton pump inhibitors and risk of gastric cancer:population-based cohort study. Gut 2022;71(1):16-24

Gastroenterology 2022;162:1334–1342

CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review

Laura E. Targownik,[1] Deborah A. Fisher,[2] and Sameer D. Saini[3,4]

Best Practice Advice 1

All patients taking a PPI should have a regular review of the ongoing indications for use and documentation of that indication. This review should be the responsibility of the patient's primary care provider.

Best Practice Advice 2

All patients without a definitive indication for chronic PPI should be considered for trial of de-prescribing.

Best Practice Advice 3

Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.

Best Practice Advice 4

Patients with complicated gastroesophageal reflux disease, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.

Best Practice Advice 5

Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.

Best Practice Advice 6

PPI users should be assessed for upper gastrointestinal bleeding risk using an evidence-based strategy before de-prescribing.

Best Practice Advice 7

Patients at high risk for upper gastrointestinal bleeding should not be considered for PPI de-prescribing.

Best Practice Advice 8

Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper gastrointestinal symptoms due to rebound acid hypersecretion.

Best Practice Advice 9

When de-prescribing PPIs, either dose tapering or abrupt discontinuation can be considered.

Best Practice Advice 10

The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PAAEs. The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

Choosing Wisely Canada "Bye Bye PPI" toolkit

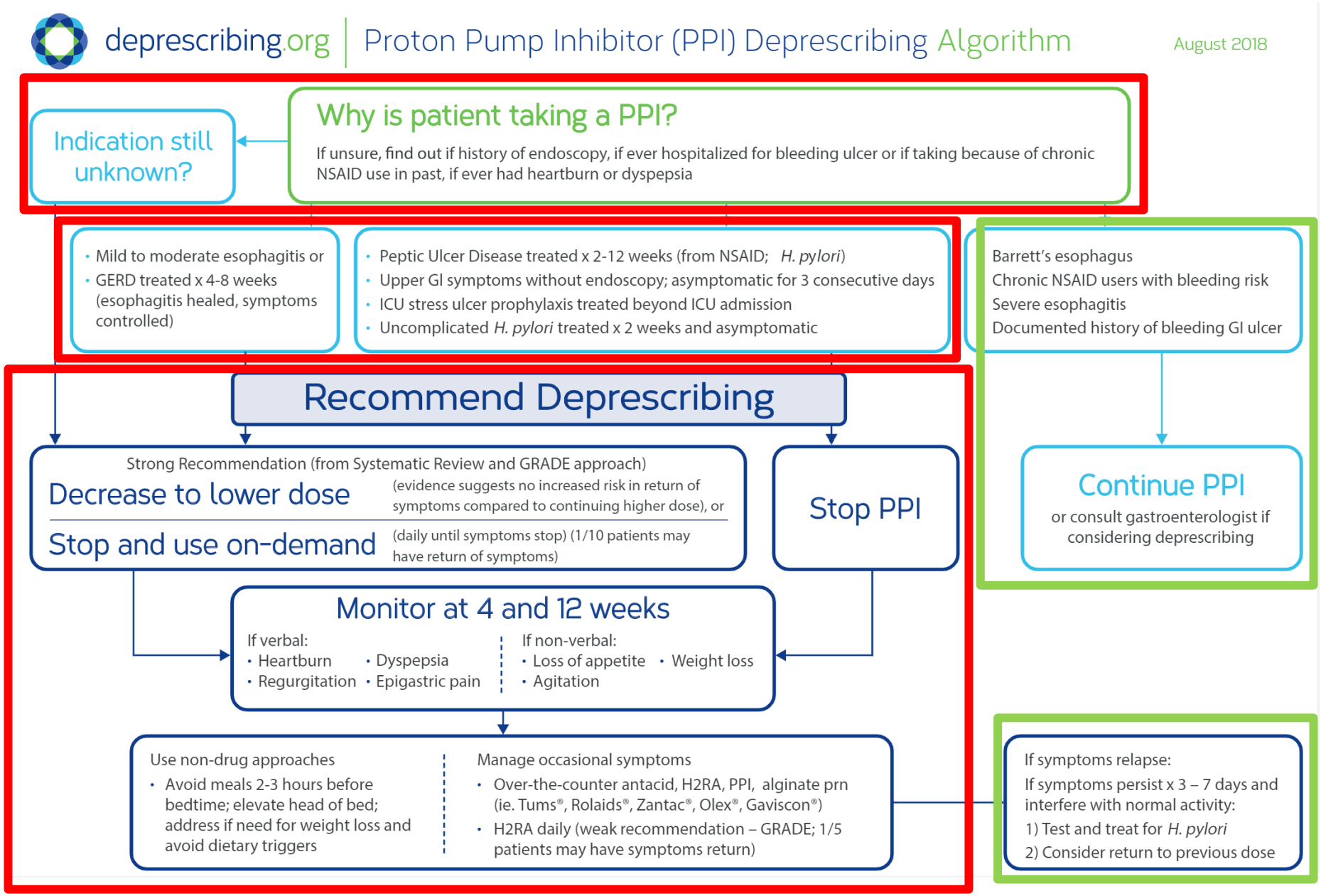


Table 1. Indications for Proton Pump Inhibitor Use

Indications					
Definitely indicated for long-term use (>8 wk)	Conditionally indicated for long-term use	Not indicated for long-term use	Definitely indicated for acute/short-term use (≤8 wk)	Conditionally indicated for acute/short-term use	Not indicated for acute/short-term use
Barrett's esophagus Clinically significant (LA Classification grade C/D) erosive esophagitis Esophageal strictures from GERD (ie, peptic strictures) Zollinger-Ellison syndrome Eosinophilic esophagitis Gastroprotection in users of ASA/nonsteroidal anti-inflammatory drug at high risk for GI bleeding Prevention of progression of idiopathic pulmonary fibrosis	PPI-responsive endoscopy-negative reflux disease, with recurrence on PPI cessation PPI-responsive functional dyspepsia, with recurrence on PPI cessation PPI-responsive upper airway symptoms ascribed to laryngopharyngeal reflux, with recurrence on PPI cessation Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement Secondary prevention of gastric and duodenal peptic ulcers with no concomitant antiplatelet drugs	Symptoms of nonerosive reflux disease with no sustained response to high-dose PPI therapy Functional dyspepsia with no sustained response to PPI therapy Steroid therapy in the absence of ASA/nonsteroidal anti-inflammatory drug therapy Prevention of recurrent upper GI bleeding from causes other than: Peptic ulcer disease, including gastric and duodenal erosions Erosive esophagitis	*Helicobacter pylori* eradication Stress ulcer prophylaxis for ICU patients with risk factors Uninvestigated GERD/dyspepsia Treatment of NSAID-related gastric and duodenal peptic ulcers	Initial or on-demand treatment of endoscopy-negative reflux disease Initial treatment of functional dyspepsia Uninvestigated dyspepsia Ulcer prevention after sclerotherapy or band ligation treatment of esophageal varices Prevention of rebleeding from Mallory-Weiss tears	Empiric treatment of laryngopharyngeal symptomatology Acute undifferentiated abdominal pain Acute nausea and vomiting not believed to be related to GERD/esophagitis Any isolated lower GI symptomatology

ASA, aspirin; ICU, intensive care unit; LA, Los Angeles.

New GERD Guideline

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

AJG The American Journal of GASTROENTEROLOGY

Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease.. Am J Gastroenterol 2022;117(1):27-56.

Outpatient Antibiotics

CLINICAL GUIDELINE

ACP American College of Physicians®
Leading Internal Medicine, Improving Lives

Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians

Rachael A. Lee, MD, MSPH; Robert M. Centor, MD; Linda L. Humphrey, MD, MPH; Janet A. Jokela, MD, MPH; Rebecca Andrews, MS, MD; and Amir Qaseem, MD, PhD, MHA; for the Scientific Medical Policy Committee of the American College of Physicians*

Primary care physicians prescribe antibiotics in ~10% of all outpatient visits

2014: outpts:>250 million Rx for antibiotics in the US, ≥30% were unnecessary, *and* often continued for too long. Particularly for bronchitis and sinusitis

Antimicrobial overuse, especially with broad-spectrum antibiotics, drives resistance and causes adverse events in up to 20% of patients, from allergic reactions to cdif infections

Where there's evidence we should decrease antibiotic duration, and avoid when not clinically indicated

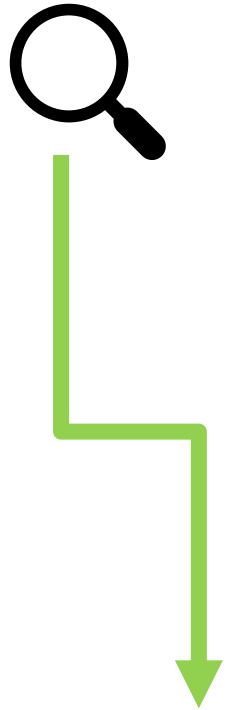
Table. Summary of the ACP Best Practice Advice on Appropriate Use of Short-Course Antibiotics in Common Infections

Condition	Patient Population	Available Guidelines and Evidence*	Best Practice Advice
Acute bronchitis	Adults with COPD	GOLD guideline (18) Meta-analysis of 21 studies comparing ≤5 vs. >5 days (19)	Clinicians should limit antibiotic treatment duration to 5 days when managing patients with COPD exacerbations and acute uncomplicated bronchitis who have clinical signs of a bacterial infection (presence of increased sputum purulence in addition to increased dyspnea, and/or increased sputum volume).
Community-acquired pneumonia	All adults who are not immunocompromised†	IDSA/ATS guideline (20)	Clinicians should prescribe antibiotics for community-acquired pneumonia for a minimum of 5 days. Extension of therapy after 5 days of antibiotics should be guided by validated measures of clinical stability, which include resolution of vital sign abnormalities, ability to eat, and normal mentation.
Urinary tract infection: uncomplicated bacterial cystitis	Nonpregnant adult women†	IDSA/ESCMID guideline (21)	In women with uncomplicated bacterial cystitis, clinicians should prescribe short-course antibiotics with either nitrofurantoin for 5 days, TMP–SMZ for 3 days, or fosfomycin as a single dose.
Urinary tract infection: uncomplicated pyelonephritis	Nonpregnant adults†	IDSA/ESCMID guideline (21) Recent systematic review (22) 3 recent RCTs (23–25)	In men and women with uncomplicated pyelonephritis, clinicians should prescribe short-course therapy either with fluoroquinolones (5 to 7 days) or TMP–SMZ (14 days) based on antibiotic susceptibility.
Nonpurulent cellulitis	All adults	IDSA guideline (26) NICE guideline (27) 1 recent RCT (28)	In patients with nonpurulent cellulitis, clinicians should use a 5- to 6-day course of antibiotics active against streptococci, particularly for patients able to self-monitor and who have close follow-up with primary care.

ATS = American Thoracic Society; COPD = chronic obstructive pulmonary disease; ESCMID = European Society of Clinical Microbiology and Infectious Diseases; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IDSA = Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; RCT = randomized controlled trial; TMP–SMZ = trimethoprim–sulfamethoxazole.

* The Scientific Medical Policy Committee prioritized the highest available level of synthesized evidence: clinical guidelines, followed by systematic reviews, and then individual studies.

† Available evidence in these patient populations is not robust enough to include in this summary table.



1. Clinicians should limit antibiotic treatment duration to 5 days when managing patients with COPD exacerbations and acute uncomplicated bronchitis who have clinical signs of a bacterial infection (presence of increased sputum purulence in addition to increased dyspnea, and/or increased sputum volume).
2. Clinicians should prescribe antibiotics for community-acquired pneumonia for a minimum of 5 days. Extension of therapy after 5 days of antibiotics should be guided by validated measures of clinical stability, which include resolution of vital sign abnormalities, ability to eat, and normal mentation.
3. In women with uncomplicated bacterial cystitis, clinicians should prescribe short-course antibiotics with either nitrofurantoin for 5 days, TMP–SMZ for 3 days, or fosfomycin as a single dose.
4. In men and women with uncomplicated pyelonephritis, clinicians should prescribe short-course therapy either with fluoroquinolones (5 to 7 days) or TMP–SMZ (14 days) based on antibiotic susceptibility.
5. In patients with nonpurulent cellulitis, clinicians should use a 5- to 6-day course of antibiotics active against streptococci, particularly for patients able to self-monitor and who have close follow-up with primary care.

Figure. PEN-FAST Penicillin Allergy Clinical Decision Rule

PEN	*Penicillin allergy reported by patient*	☐ *If yes, proceed with assessment*
F	*Five years or less since reaction*[a]	☐ **2 points**
A	*Anaphylaxis or angioedema*	
	OR	☐ **2 points**
S	*Severe cutaneous adverse reaction*[b]	
T	*Treatment required for reaction*[a]	☐ **1 point**
		☐ **Total points**

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

Two More Antibiotic Studies

Children with CAP seen in ED or hospitalized <2d:

Double-blinded RCT

Patients randomly received (concealed allocation assignment) 1 of 4 treatments:

- amoxicillin (35-50 mg/kg/d) for 3 days
- amoxicillin (35-50 mg/kg/d) for 7 days
- amoxicillin (70-90 mg/kg/d) for 3 days
- amoxicillin (70-90 mg/kg/d) for 7 days

Primary outcome: clinically indicated *antibiotic re-treatment* within 28 days of randomization

Lower-dose was noninferior to higher-dose outpatient oral amoxicillin **and** 3 days was noninferior to 7 days

Bielicki JA, Stohr W, Barratt S, et al, for PERUKI, GAPRUKI, and the CAP-IT Trial Group. Effect of amoxicillin dose and treatment duration on the need for antibiotic re-treatment in children with community-acquired pneumonia. The CAP-IT randomized clinical trial. JAMA 2021;326(17):1713-1724.

A Brief Shared Decision-Making Intervention for Acute Respiratory Infections on Antibiotic Dispensing Rates in Primary Care: A Cluster Randomized Trial

Cluster randomized trial of 27 Australian general practices (13 intervention, 14 control) involving 122 GPs

Intervention group GPs were given brief decision aids for 3 ARIs (acute otitis media, acute sore throat, acute bronchitis) and video-delivered training

Primary outcome: dispensing rate of target antibiotic classes 12 months before and following randomization

The baseline mean dispensing rate of ARI-related antibiotics was 3.5% (intervention GPs) and 3.2% (control GPs). After 12 months, mean rates decreased (to 2.9% intervention; 2.6% control): an 18% relative reduction from baseline but similar in both groups

A Brief Shared Decision-Making Intervention for Acute Respiratory Infections on Antibiotic Dispensing Rates in Primary Care: A Cluster Randomized Trial. Ann Fam Med. Jan-Feb 2022;20(1):35-41.

Middle ear infection:
Should my child take antibiotics?

What is this decision aid for?

- This decision aid can help you decide whether to use antibiotics when **your child** has a middle ear infection.
- It is designed to be used with your doctor to help you make a **shared decision** about what is best for you or your child.

What causes middle ear infection?

- It can be caused by a viral or bacterial infection. It is hard for your doctor to tell which it is.
- It is also called 'acute otitis media'. Acute means it is a short-term infection.

How long does the earache last?

Symptoms (such as earache) usually get better in **2–7 days**, without taking antibiotics.

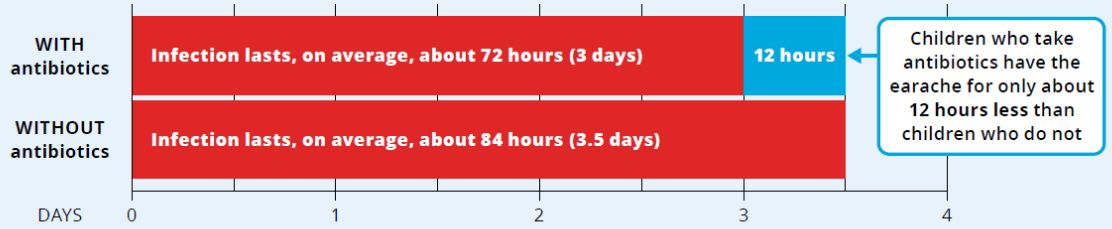
What are the treatment options?

There are two options that you can discuss with your doctor:

1. **Not taking antibiotics** –
   This means letting the infection get better by itself.
2. **Taking antibiotics**.

Symptoms, such as pain and fever, can be treated with over-the-counter medicines. They can be used with either option.

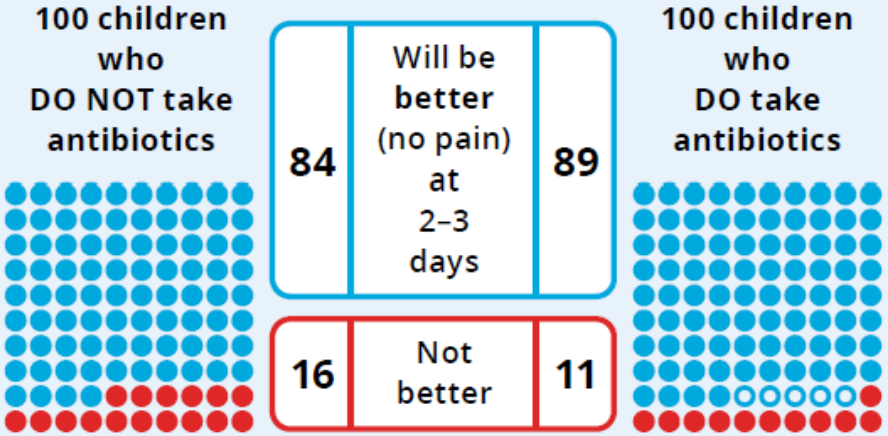
What are the likely benefits and harms of each option?



These figures show what is likely to happen to children with middle ear infection who **do not** take antibiotics and those who **do**. Each circle is one child. We cannot predict who will get better sooner or who will have problems.

Possible benefits

- Gets better by 2–3 days
- Gets better by 2–3 days due to antibiotics
- Not better by 2–3 days

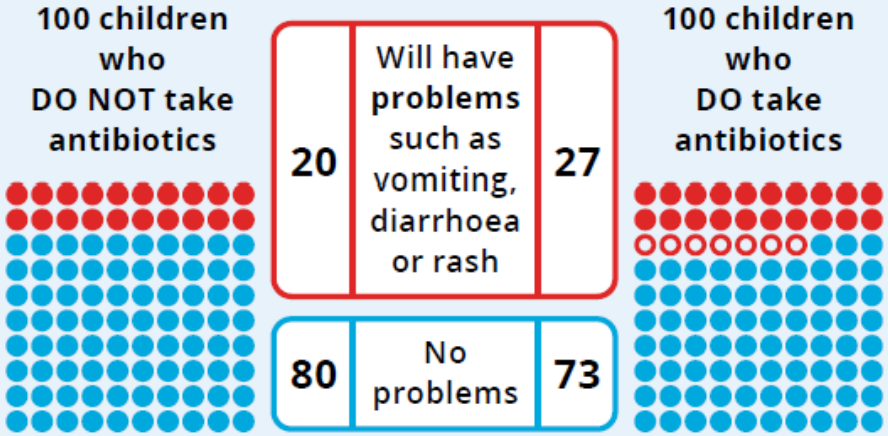


With antibiotics, **5 more children** will be better after 2–3 days.

Without taking antibiotics, most children will be better after about **four days** anyway.

Possible harms

- Has problems
- Has problems due to antibiotics
- No problems



With antibiotics, **7 more children** will have problems such as vomiting, diarrhoea or rash.
Other **antibiotic downsides** are:

- The **cost** of buying them
- **Remembering** to take them
- The risk of **antibiotic resistance** (see below).

When should you see a doctor and get further help?

If your child with a middle ear infection has any of these signs:

- Very drowsy
- Fast or difficult breathing, wheezing, or shortness of breath
- Cold or discoloured hands and/or feet with a warm body
- A high fever (over 38.5°C)
- Pain in the arms and/or legs
- Unusual skin colour (pale or blue) around the lips
- A rash that does not fade when the skin is pressed
- Pain and tenderness of the bone behind the ear
- Blood or discharge from the ear.

Questions to consider when talking with your doctor

- ☐ Does my child need antibiotics?
- ☐ What happens if my child does not take antibiotics?
- ☐ Do I know enough about the benefits and harms of:
  - taking antibiotics?
  - not taking antibiotics?
- ☐ Am I clear about which benefits and harms matter most to me?
- ☐ Do I have enough information and support to decide?

https://www.safetyandquality.gov.au/our-work/partnering-consumers/shared-decision-making/decision-support-tools-consumers

“Increase in knowledge”

Greater increases in knowledge of GPs were seen in the intervention group than control in the number of correct responses to the 22 knowledge questions. Intervention and tools seen as helpful.

Table 1. Rate of Antibiotic Dispensing for Intervention and Control Groups

Group	Mean baseline rate, % (95% CI)	Mean follow-up rate, % (95% CI)	Rate ratio (95% CI)	*P* Value
Primary outcome: rate of antibiotic dispensing for target antibiotic classes				
Intervention	3.5 (2.9-4.3)	2.9 (2.4-3.5)	1.01 (0.89-1.15)	.84
Control	3.2 (2.7-3.8)	2.6 (2.2-3.1)		
Secondary outcome: rate of antibiotic dispensing of all antibiotics for each GP				
Intervention	6.2 (5.5-7.1)	5.3 (4.6-6.0)	1.02 (0.93-1.13)	.64
Control	5.9 (5.2-6.6)	5.1 (4.4-5.8)		

GP = general practitioner.

Aspirin

Aspirin for Primary Prevention Story

Early trials of aspirin use in primary prevention:

- reduction in myocardial infarction risk *(Physicians' Health Study)*
- subsequent studies, (including *Women's Health Study*): no reduction in major cardiovascular disease with primary prevention aspirin use
- reduction in stroke risk in the Women's Health Study

Early trials: small increases in major bleeding risk

Several guidelines (and guidance docs, including 2016 USPSTF) recommended use of primary prevention aspirin for **patients aged 50-59** years at elevated CV risk without history of bleeding (Grade B)

2016 USPSTF rec included individual decision making for patients aged 60-69 years at elevated CV and no bleeding (Grade C) and made no recommendation for patients aged <50 or >69 years (lack of evidence)

USPSTF Report on Aspirin for Primary Prevention. JAMA Cardiol 2022;Apr 26:[Epub ahead of print].

Aspirin for Primary Prevention Story

Over the past 30 years: large CV preventative efforts: use of statins and antihypertensive medications along with reductions in tobacco use

2018: three key trials of primary prevention with aspirin:

- ASPREE: (Pts ≥65 years), use of low-dose daily aspirin associated with increased risk for mortality and *cancer mortality*. There were similar rates of major bleeding
- ASCEND: (Patients with diabetes), reduced the risk of CV events but offset by increased major bleeding risk
- ARRIVE trial: (Middle-aged and older adults at intermediate risk for CVD cardiovascular disease without diabetes), nonsignificant reduction in CV events but increased GI bleeding

By 2018: rates of antihypertensive and statin medications high, tobacco use lower. ***Maybe less opportunity for primary prevention aspirin to demonstrate benefit?***

USPSTF Report on Aspirin for Primary Prevention. JAMA Cardiol 2022;Apr 26:[Epub ahead of print].

Three new aspirin trials in three different populations:

ARRIVE

Moderate Risk
(ASCVD > 20%)

↔ MACE
↑ bleeding

ASCEND

Diabetes

↓ MACE
↑↑ bleeding

ASPREE

Age > 70

↔ MACE
↑ bleeding
↑ mortality

The Curbsiders Episode #128: Aspirin: Overhyped and Overused

THE CURBSIDERS INTERNAL MEDICINE

Effect of Aspirin on Cancer

RCT: 19,114 older adults living in Australia and the United States. ASPREE data.

Randomized the participants (allocation was concealed) received a daily dose of enteric-coated aspirin (100 mg; n = 9525) or placebo (n = 9589)

Study was terminated after just 3 years because of unexpected increase in all-cause mortality in the aspirin-treated group. **This paper provides more details**

JNCI
Journal of the National Cancer Institute

McNeil JJ, Gibbs P, Orchard SG, et al, for the ASPREE Investigator Group. Effect of aspirin on cancer incidence and mortality in older adults. J Natl Cancer Inst 2021;113(3):258-265.

Effect of Aspirin on Cancer

Distribution of prior cancer at baseline (19%) and known cancer risk factors between the two groups were comparable

Rate of incident cancers: similar for aspirin and placebo-treated persons (23.9 vs 23.0 per 1000 person-years). However, cancer mortality higher among those treated with aspirin (6.4 vs 4.8 per 1000 person-years; number needed to treat to harm [NNTH] = 629)

Higher mortality partially explained by higher rates of **metastatic cancers** (6.1 vs 5.1 per 1000 person-years; NNTH = 1006)

Rate of **stage 4 cancers** also higher in those treated with aspirin (6.5 vs 5.3 per 1000-person years; NNTH = 839)

JNCI
Journal of the National Cancer Institute

McNeil JJ, Gibbs P, Orchard SG, et al, for the ASPREE Investigator Group. Effect of aspirin on cancer incidence and mortality in older adults. J Natl Cancer Inst 2021;113(3):258-265.

Final Recommendation Statement

Aspirin Use to Prevent Cardiovascular Disease: Preventive Medication

April 26, 2022

U.S. Preventive Services TASK FORCE

Recommendation Summary

Population	Recommendation	Grade
Adults aged 40 to 59 years with a 10% or greater 10-year cardiovascular disease (CVD) risk	The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit.	C
Adults 60 years or older	The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older.	D

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Stopping Antidepressants

Discontinuing Antidepressants

RCT: 478 patients (75% women) with depression in remission who were taking sertraline, fluoxetine, citalopram, or mirtazapine and who felt ready to discontinue their antidepressant

Had to be taking for >9 months. Majority reported at least three prior episodes of depression and had been taking antidepressants continuously for at least 3 years.

Patients were randomized to continue their current antidepressant or to taper over 2 months

Discontinuing Antidepressants

At 1 year: relapse occurred in 39% of the maintenance group and in 56% of the discontinuation group. So relapse could be attributed to discontinuing antidepressants in only about **1 in 6 patients** discontinuing (17%)

By the end of the trial, most patients who relapsed in the discontinuation group had resumed antidepressant medications.

No suicides or suicide attempts were reported

The largest differences between groups in secondary outcomes like PHQ–9 scores occurred **soon after discontinuation**, so some worsening symptoms in the discontinuation group likely be attributable/impacted by withdrawal (vs relapse)

Discontinuing Antidepressants

After stopping antidepressants, about ½ will have a relapse of depression by 1 year

This is a high %, but many pts on antidepressants also have relapses

Some are going through med withdrawal, so pay attention early on

Counseling about all this is important

Referral for psychotherapy can help prevent relapses in patients who discontinue medications

Question for the future: what are the predictors of relapse? Should we be encouraging things like CBT even more, specifically as a way to try to make discontinuation more successful?

The NEW ENGLAND JOURNAL of MEDICINE

Sodium, Potassium and CV Disease

Salt Substitute Study 1

RCT from rural China, 21k people (600 rural villages) with histories of stroke or inadequately controlled hypertension, older than 60. Mean age 65

Randomized to replace regular salt with a salt substitute (75% sodium chloride, 25% potassium chloride) or to continue using regular salt (100% sodium chloride)

To further enhance sodium restriction, intervention participants were instructed to use the salt substitute more sparingly than they had used regular salt

The NEW ENGLAND JOURNAL of MEDICINE

Neal B, Wu Y, Feng X, et al. Effect of salt substitution on cardiovascular events and death. N Engl J Med 2021;385(12):1067-1077

Salt Substitute Study 1

At 5 years, rates of stroke, major adverse CV events, and mortality were each significantly lower in the salt-substitute group — by roughly 2 or 3 events per 100 participants

Blood pressure was reduced in the salt substitute group by a mean of 3 mm Hg/1 mm Hg

According to 24-hour urine electrolyte measurements, the intervention lowered sodium intake by only about 10% but increased potassium intake by about 50%

No difference in hyperkalemia

The NEW ENGLAND JOURNAL of MEDICINE

Neal B, Wu Y, Feng X, et al. Effect of salt substitution on cardiovascular events and death. N Engl J Med 2021;385(12):1067-1077

Salt Substitute Study 2

Pooled data from 6 cohort studies, 10,709 total participants

People with no history of CV or renal disease submitted multiple 24-hour urine collections for sodium and potassium levels, reflecting dietary intake

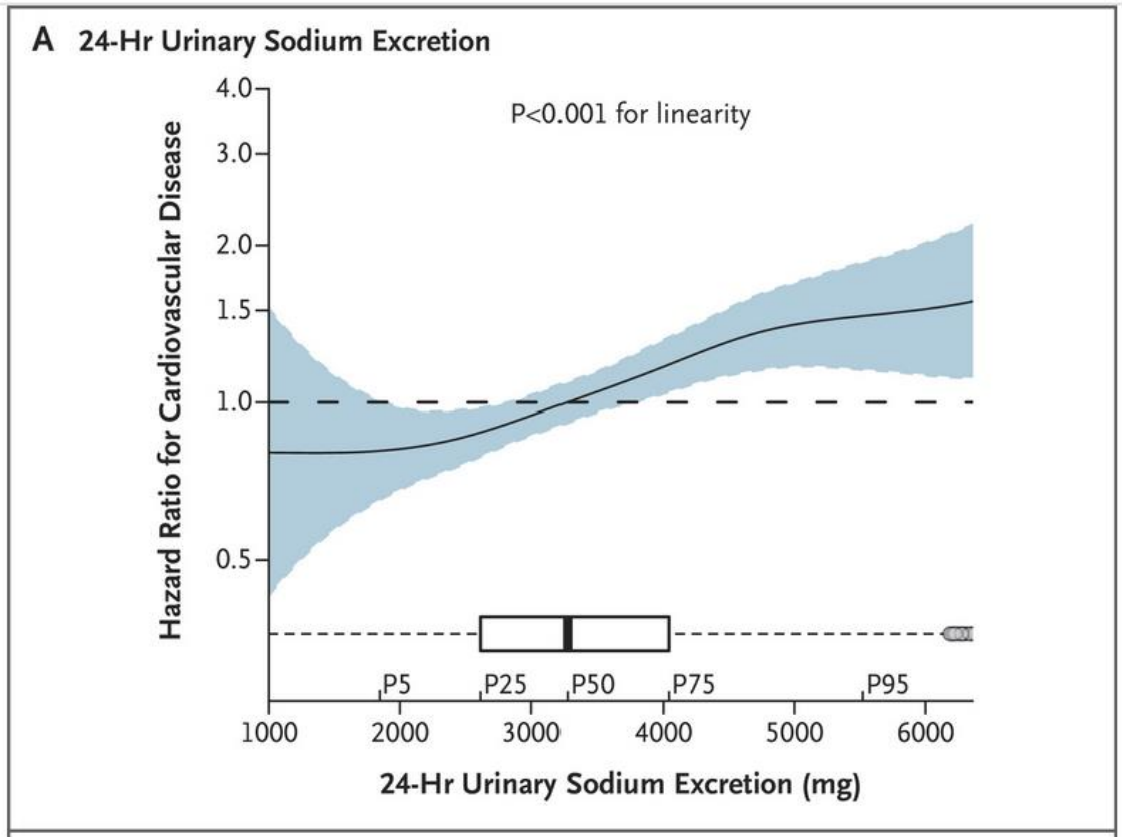
At average follow-up of 9 years, those with sodium excretion of ~2 g daily had 2-3 fewer CV events per 100 people, compared with those whose sodium excretion was ~5 g daily.

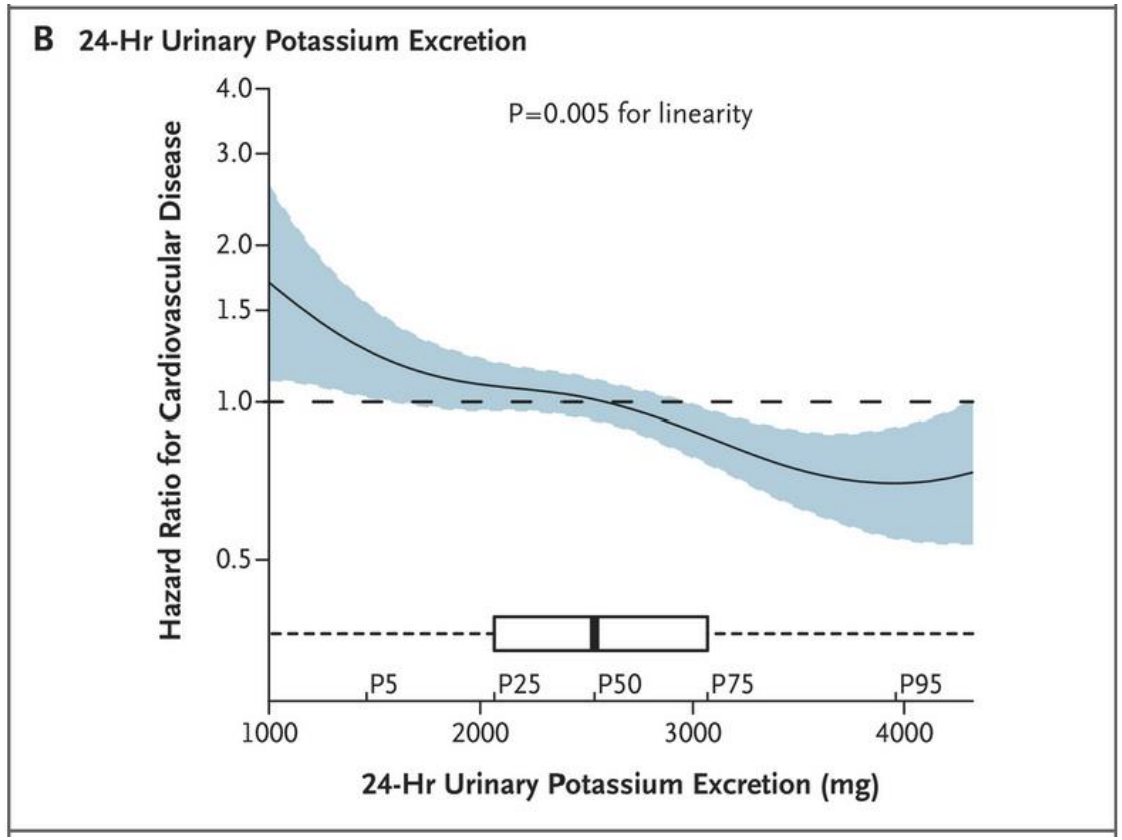
Also: people with high potassium excretion had 1 fewer CV event per 100 people, compared with those whose potassium excretion was low

Applied to people with or without diagnosed hypertension

The NEW ENGLAND JOURNAL of MEDICINE

24-Hour Urinary Sodium and Potassium Excretion and Cardiovascular Risk. N Engl J Med. 2022 Jan 20;386(3):252-263.


A 24-Hr Urinary Sodium Excretion
P<0.001 for linearity
Hazard Ratio for Cardiovascular Disease
4.0
3.0
2.0
1.5
1.0
0.5
P5
P25
P50
P75
P95
1000
2000
3000
4000
5000
6000
24-Hr Urinary Sodium Excretion (mg)


B 24-Hr Urinary Potassium Excretion
P=0.005 for linearity
Hazard Ratio for Cardiovascular Disease
4.0
3.0
2.0
1.5
1.0
0.5
P5
P25
P50
P75
P95
1000
2000
3000
4000
24-Hr Urinary Potassium Excretion (mg)

Salt Substitute Study 3

Meta-analysis of 85 studies

Conclusion: ~linear, dose-response relation between estimated sodium intake and SBP and DBP, seen during entire range of exposure (1-36 months)

More pronounced effect in pts with higher BP levels during all months (1 to 36) months of observation

At the extremes of intake (6 g vs. 1 g of sodium intake), the systolic BP difference was ~12 mm Hg; for diastolic BP, the difference was ~5 mm Hg

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

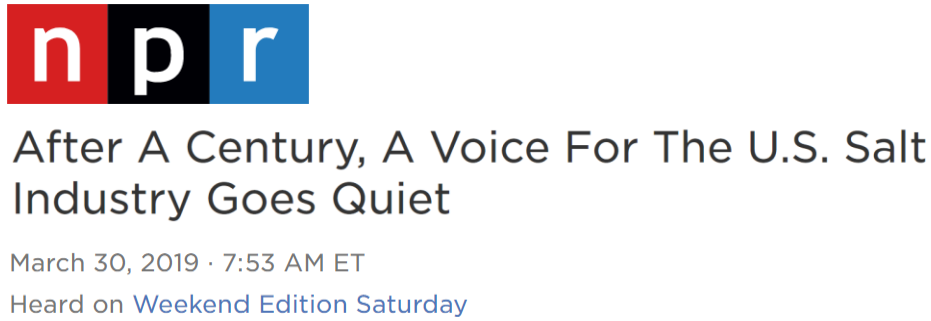
Blood Pressure Effects of Sodium Reduction. Circulation. 2021;143:1542–1567

Conclusions of the Na/K studies

We now have patient-oriented outcomes

Lifestyle change is hard, but we should increase our efforts to promote low sodium, high-potassium diets for many patients, especially those with hypertension

Caveat: that excessive potassium intake should be avoided in patients at risk for hyperkalemia



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Blood Pressure Effects of Sodium Reduction. Circulation. 2021;143:1542–1567

Weight Loss Meds

Medications for Weight loss

Meta-analysis

Weight, but not health outcomes. Did look at some surrogate outcomes like BP

included 143 unique trials with 49,810 participants, 75% of whom were women

Median length of the trials was 24 weeks

Methodologic concerns: authors identified a high risk of bias due to protocol deviations, some missing outcome data, concerns about how adverse events were assessed

THE LANCET

Shi Q, Wang Y, Hao Q, et al. Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomised controlled trials. Lancet 2022;399(10321):259-269

	Benefit outcomes					Harm outcomes	
	Percentage bodyweight change from baseline, MD (95%)	Participants with bodyweight reduction ≥5%, OR (95% CI)	Participants with bodyweight reduction ≥10%, OR (95% CI)	Quality-of-life score, SMD (95% CI)	Depression symptom score, SMD (95% CI)	Discontinuation due to any adverse event, OR (95% CI)	Total gastrointestinal adverse events, IRR (95% CI)
Phentermine–topiramate	**−7·97 (−9·28 to −6·66)**	**8·02 (5·24 to 12·27)**	**9·74 (5·95 to 15·94)**	**0·42 (0·19 to 0·65)**	−0·17 (−0·59 to 0·26)	**2·40 (1·69 to 3·42)**	**1·62 (1·13 to 2·31)**
GLP-1 receptor agonists	**−5·76 (−6·30 to −5·21)**	**6·33 (5·00 to 8·00)**	**7·83 (5·89 to 10·40)**	**0·29 (0·15 to 0·43)**	−0·08 (−0·36 to 0·20)	**2·17 (1·71 to 2·77)**	**2·79 (2·42 to 3·23)**
Naltrexone–bupropion	−4·11 (−5·19 to −3·02)	**5·04 (3·50 to 7·27)**	**5·19 (3·33 to 8·08)**	**0·36 (0·18 to 0·54)**	0·19 (−0·06 to 0·45)	**2·69 (2·11 to 3·43)**	**3·86 (2·93 to 5·08)**
Orlistat	−3·16 (−3·53 to −2·78)	**2·73 (2·32 to 3·22)**	**2·43 (1·94 to 3·04)**	0·15 (−0·24 to 0·53)	−0·04 (−0·75 to 0·66)	**1·72 (1·44 to 2·05)**	**2·03 (1·80 to 2·29)**
Metformin	**−2·50 (−3·25 to −1·74)**	**2·10 (1·13 to 3·91)**	2·11 (0·85 to 5·24)	..	..	1·19 (0·62 to 2·28)	**2·05 (1·53 to 2·74)**
SGLT2 inhibitors	−2·07 (−3·01 to −1·13)	**2·88 (1·69 to 4·90)**	0·96 (0·26 to 3·58)	..	..	1·42 (0·82 to 2·46)	0·95 (0·58 to 1·54)
Pramlintide	−2·19 (−4·36 to −0·03)	2·24 (0·97 to 5·14)	3·21 (0·99 to 10·45)	..	..	2·43 (0·46 to 12·79)	1·92 (0·51 to 7·14)
Levocarnitine	−1·88 (−3·80 to 0·04)	..	..	..	..	1·11 (0·60 to 2·08)	1·45 (0·66 to 3·19)
Drug effect for GLP-1 receptor agonists							
Semaglutide	**−11·41 (−12·54 to −10·27)**	**9·82 (7·09 to 13·61)**	**13·32 (9·94 to 17·83)**	**0·27 (0·08 to 0·46)**	..	**1·99 (1·35 to 2·92)**	**2·79 (2·14 to 3·64)**
Liraglutide	−4·68 (−5·30 to −4·06)	**4·91 (3·78 to 6·38)**	**4·80 (3·60 to 6·41)**	**0·32 (0·08 to 0·56)**	−0·08 (−0·36 to 0·20)	**2·45 (1·80 to 3·33)**	**3·10 (2·59 to 3·71)**
Exenatide	−3·72 (−4·82 to −2·62)	**2·86 (1·27 to 6·47)**	**3·12 (1·17 to 8·32)**	..	..	1·50 (0·66 to 3·44)	**1·72 (1·19 to 2·50)**

Figure 3: **Summary of relative effects of weight-lowering drugs on benefit and harm outcomes**

What now?

No long term outcomes...yet?

Low NNTs

High potential cost

GLP1 may be the best option of these?

Many of us have existing biases against weight loss meds. Good thing? Bad thing?

THE LANCET

Shi Q, Wang Y, Hao Q, et al. Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomised controlled trials. Lancet 2022;399(10321):259-269

Quicker Summaries

Quick Summaries

Large increases seen in the risk of CV events in the year following COVID-19 infection that required hospitalization. Hazard ratio for most kinds of CV events: between 1.5 and 2.5. Large population effects!

Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. Nat Med 2022;28:583-590.

2027 (English) Adults at least 60, followed 8 years:

- Among the participants with prediabetes based on *HbA1C*, 12.9% developed diabetes, 11.6% died, and 37.6% became normoglycemic
- Of those with prediabetes based on *fasting glucose levels*, 15.6% developed diabetes, 13.8% died, and 58.2% became normoglycemic

Veronese N, Noale M, Sinclair A, et al. Risk of progression to diabetes and mortality in older people with prediabetes: The English longitudinal study on ageing. Age Ageing 2022;51(2):afab222.

Quick Summaries

Dual antiplatelet therapy, either with clopidogrel or ticagrelor, is more effective than aspirin monotherapy in preventing recurrent stroke but not death in adults with a recent minor stroke or transient ischemic attack

Lun R, Dhaliwal S, Zitikyte G, Roy DC, Hutton B, Dowlatshahi D. Comparison of ticagrelor vs clopidogrel in addition to aspirin in patients with minor ischemic stroke and transient ischemic attack: a network meta-analysis. JAMA Neurol 2022;79(2):141-148.

Combination therapy using an SSRI, SNRI or TCA with an antagonist of presynaptic alpha 2-autoreceptors (mirtazapine or trazodone) more effective than monotherapy for first-line treatment of *acute severe depression* and for those patients who are initially nonresponders to monotherapy

Henssler J, Alexander D, Schwarzer G, Bschor T, Baethge C. Combining antidepressants vs antidepressant monotherapy for treatment of patients with acute depression. A systematic review and meta-analysis. JAMA Psychiatry 2022;79(4):300-312.

Quick Summaries

Negative Platelet-Rich Plasma studies for: achilles tendinopathy, ankle OA, knee OA

JAMA Jul 13; 326:137
JAMA Oct 26; 326:1595
JAMA Nov 23; 326:2021

Oral is the new IV? For infective endocarditis, bacteremia, osteomyelitis. Meta-analysis of RCTs. Oral antibiotics are at least as effective, safer, and lead to shorter hospitalizations than IV-only therapy; no contrary data were identified. Maybe guidelines to adjust soon?

Wald-Dickler N, Holtom PD, Phillips MC, et al. Oral Is the new IV. Challenging decades of blood and bone infection dogma: a systematic review. Am J Med 2022;135(3):369-379.e1.

Quick Summaries

USPSTF: more evidence from multiple RCTs that aspirin use in pregnant persons at increased risk of preeclampsia was significantly associated with lower risks of preeclampsia, perinatal mortality, preterm birth, and IUGR. No significant association of aspirin use with postpartum hemorrhage or other bleeding-related harms. Grade B, consistent with 2014 recs.

US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Aspirin use to prevent preeclampsia and related morbidity and mortality: US Preventive Services Task Force recommendation statement. JAMA 2021;326(12):1186-1191.

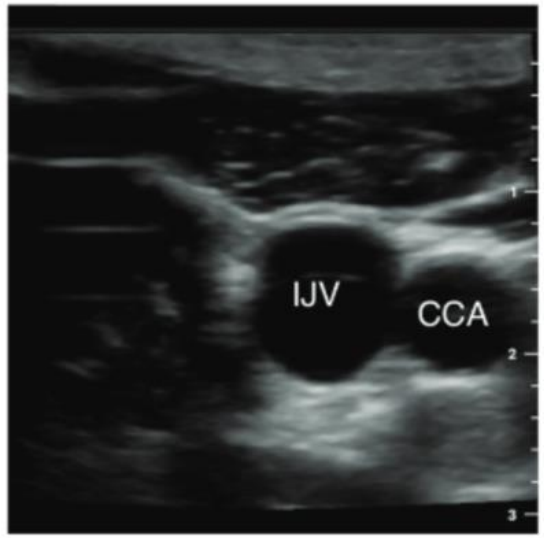
One cerumenolytic assists with in-office manual disimpaction of ear wax (vs saline) in one dose: chlorobutanol/Cerumol. Many others work after multiple applications

Sridharan K, Sivaramakrishnan G. Cerumenolytics with or without manual extraction for impacted earwax: A network meta-analysis of randomised clinical trials. Clin Otolaryngol 2021;46(3):464–473

And finally…

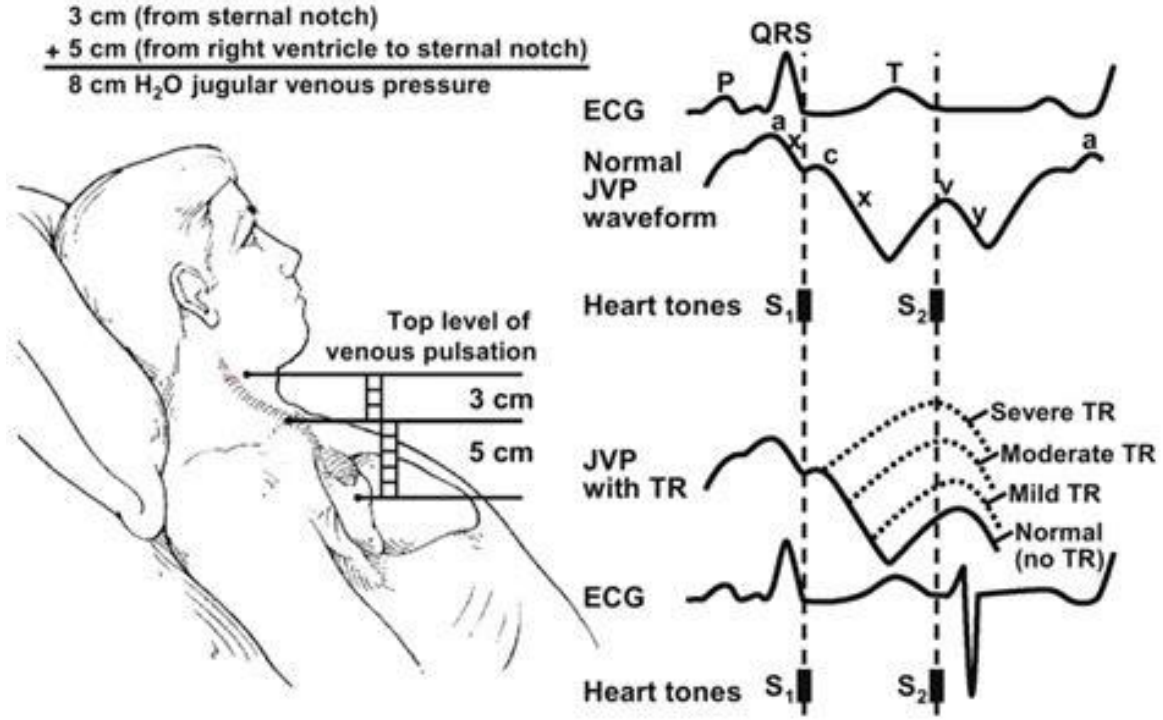
POCUS!

Accuracy of Ultrasound Jugular Venous Pressure Height in Predicting Central Venous Congestion

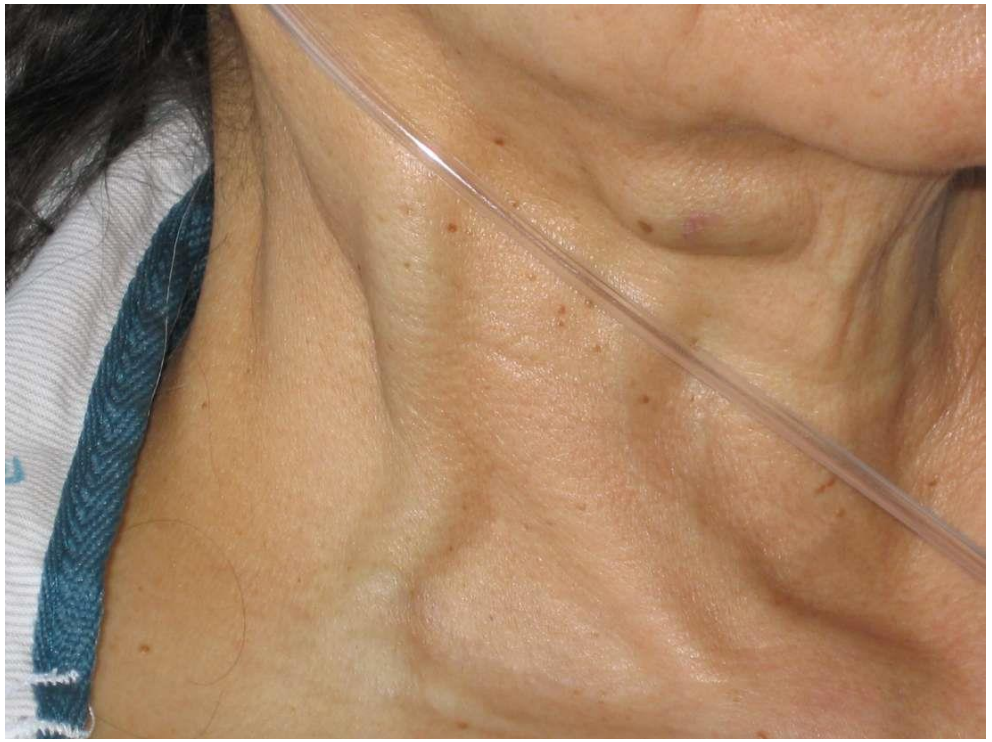


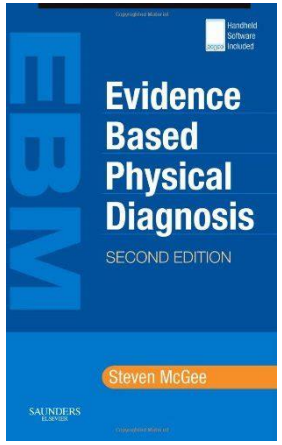
Annals of Internal Medicine

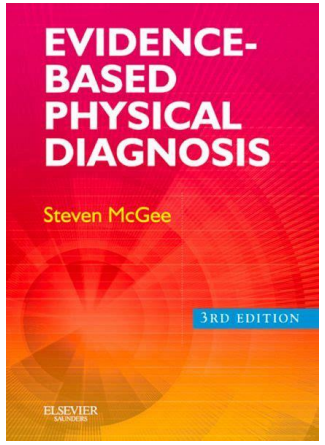
Accuracy of Ultrasound Jugular Venous Pressure Height inPredicting Central Venous Congestion. Ann Intern Med. 2022;175:344-351

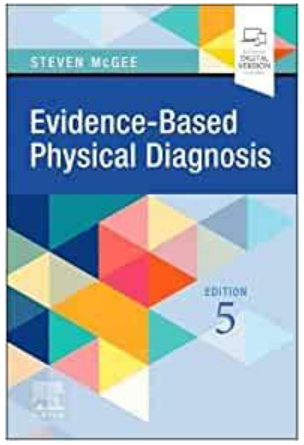


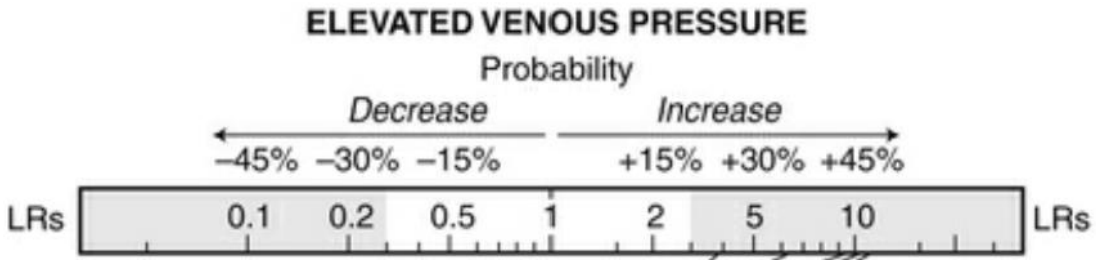
luation of jugular venous pressure (JVP). ECG, electrocardiogram; TR, tricuspid regurgitation.







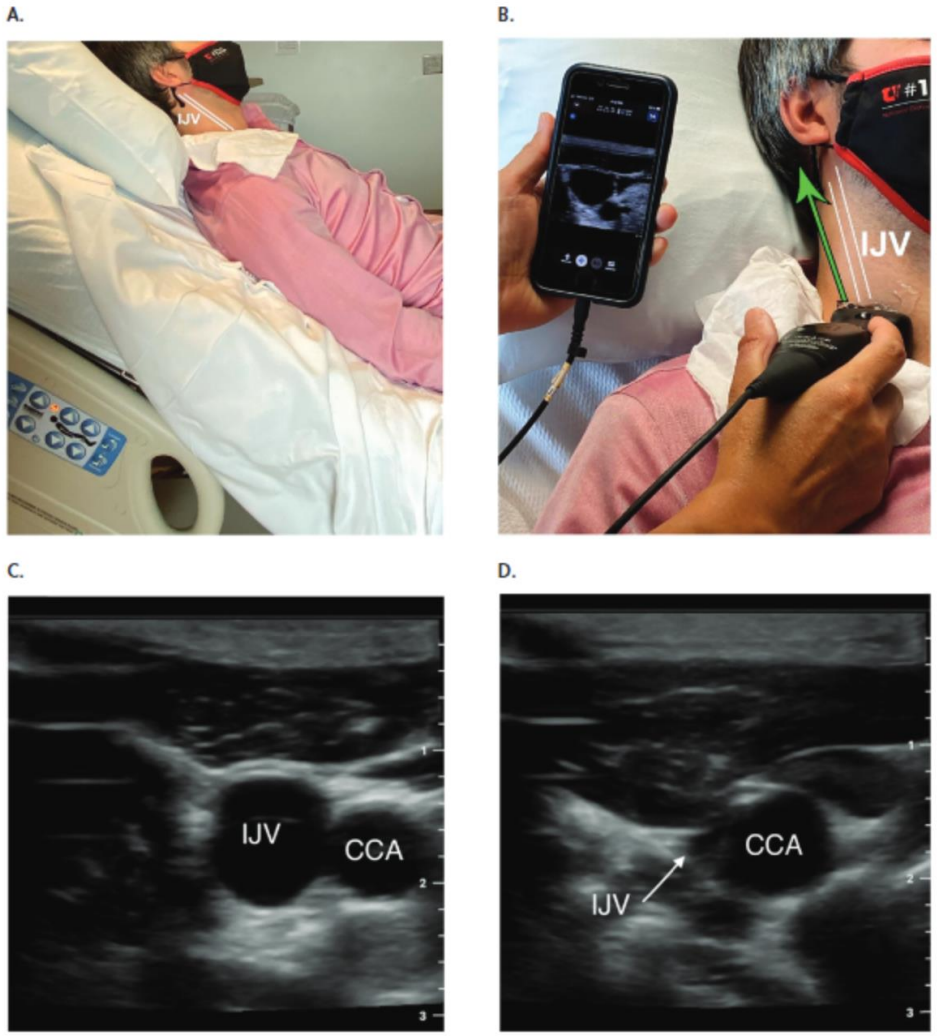




Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Estimated Venous Pressure Elevated				
Detecting measured CVP >8 cm water[22,30–32]	47-92	93-96	9.7	0.3
Detecting measured CVP >12 cm water[22,30]	78-95	89-93	10.4	0.1
Detecting elevated left heart diastolic pressures[33–35]	10-58	96-97	3.9	NS
Detecting low LV ejection fraction[36–38]	7-25	96-98	6.3	NS
Detecting myocardial infarction (if chest pain)[39]	10	96	2.4	NS
Predicting postoperative pulmonary edema[40,41]	19	98	11.3	NS
Predicting postoperative MI or cardiac death[40,41]	17	98	9.4	NS
Estimated Venous Pressure Low				
Detecting measured CVP ≤5 cm water[32]	90	89	8.4	0.1

Accuracy of Ultrasound Jugular Venous Pressure Height inPredicting Central Venous Congestion. Ann Intern Med. 2022;175:344-351

Figure 1. Demonstration of the uJVP technique.



CCA = common carotid artery; IJV = internal jugular vein; uJVP = ultrasound jugular venous pressure. **A.** The patient is reclined with the head of bed at 30° to 45°. **B.** The linear (or "vascular") ultrasound probe (setting) is used. Probe orientation is in parallel to the floor and in transverse orientation to the CCA and IJV. Starting at the base of the neck above the clavicle, the probe is moved from caudal to cranial, tracking the IJV. **C.** Demonstration of a dilated IJV adjacent to the CCA. **D.** A collapsed IJV just superior to the height of the uJVP collapse point, where the IJV is both smaller than the adjacent CCA and at its smallest point across the respiratory cycle.

Findings

100 participants undergoing right heart catheterization for HF indications

Visualization of the uJVP was possible in 100%, vs 61% of patients examined via traditional visualization

uJVP similar to traditional physical examination technique, similar threshold for elevated filling pressure of greater than 3 cm of vertical height from the sternal angle (greater than 8 cm from the right atrium)

The uJVP well correlated with a range of RAP measured on right heart catheterization

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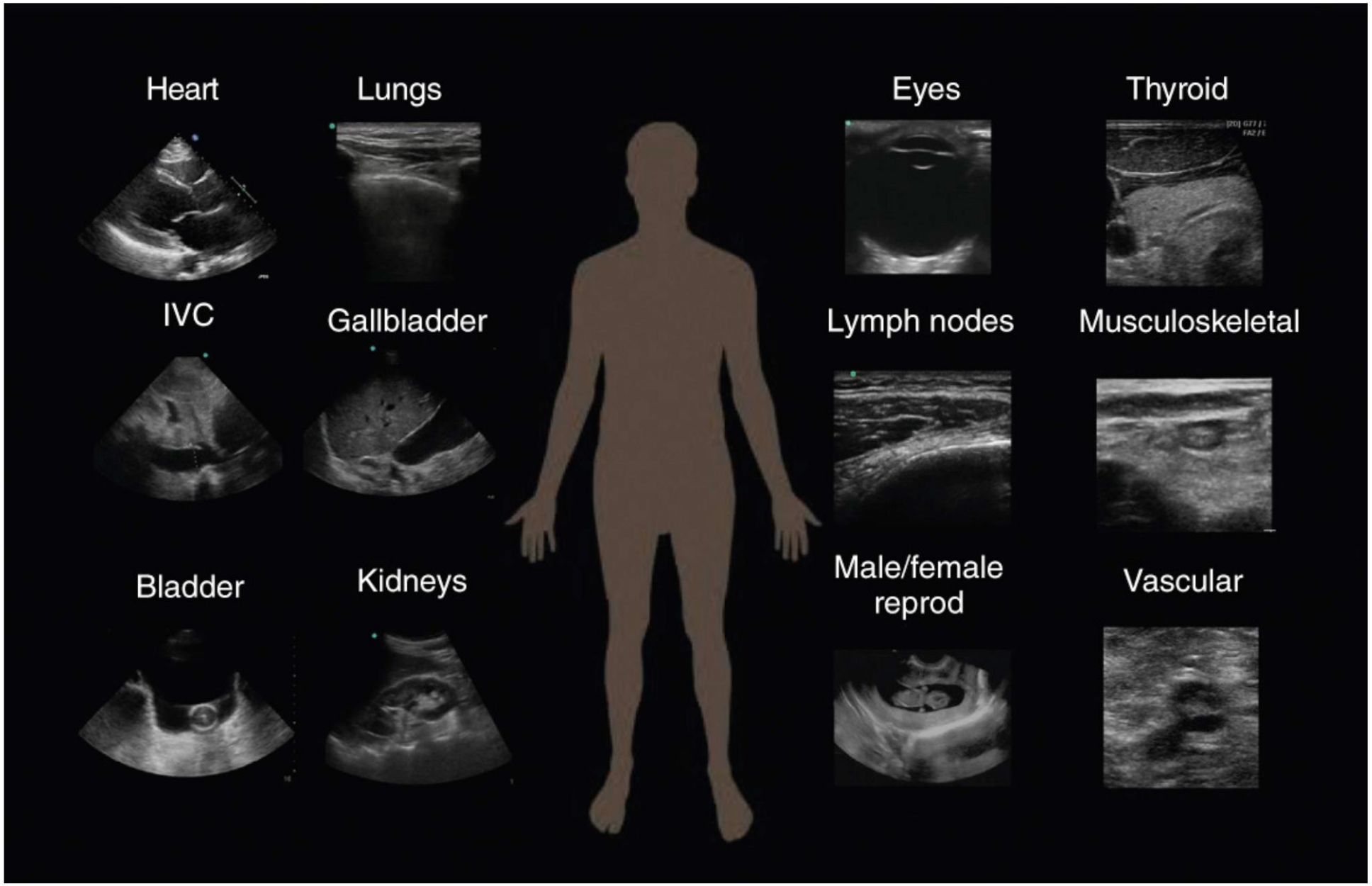
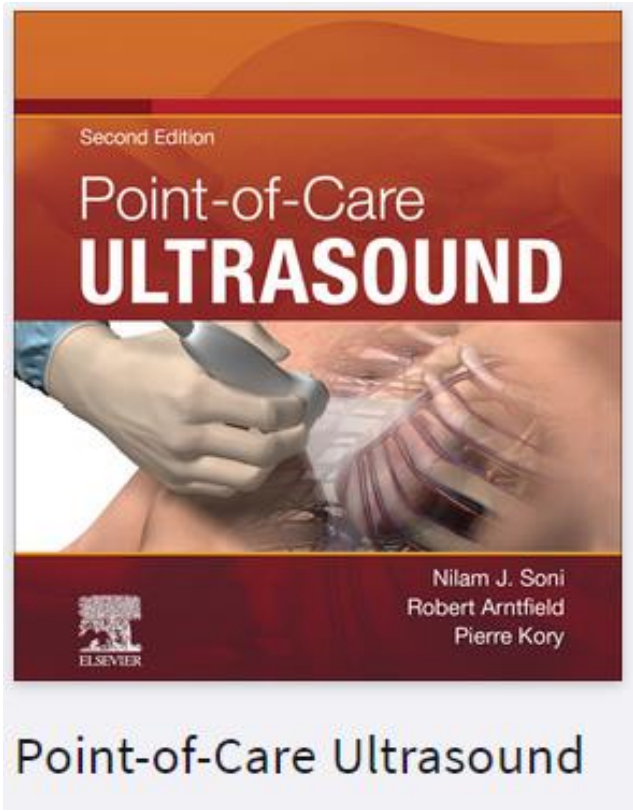

Heart
Lungs
Eyes
Thyroid
IVC
Gallbladder
Lymph nodes
Musculoskeletal
Bladder
Kidneys
Male/female reprod
Vascular

https://sm.stanford.edu/archive/sonodoc/#/home



Point-of-Care Ultrasound

How to Stay Current?

Staying Current

Read everything….? *(good luck)*

Journal clubs with your colleagues

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

Podcasts (including Frank Domino's)

Teach and Precept.

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

Do a talk like this!

Thanks!

Creating a health network that
practices, teaches, and researches
WITH our communities
so that we can all flourish.