Management of GERD and use of PPIs: Length of therapy and common side effects

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Disclosures

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Part 1.

49-year-old male computer programmer with hypertension complains of 2 years of persistent heartburn with occasional acid regurgitation to the mid-chest. His symptoms are worse after a big meal, eating spicy food, and sometimes with alcohol. He reports daytime symptoms 3-4 times per week, and occasionally at night. He takes Tums regularly. About 2.5 years ago, he was promoted at work to manager, which has been stressful and demanded longer hours. He has since exercised less and gained about 15 lbs. Recent labs drawn for his annual physical were normal, including a CBC.

Most GERD is diagnosed clinically

If it walks like a duck, and talks like a duck…

Typical symptoms:

- Heartburn
- Acid regurgitation

Mild symptoms ≥ 2 times per week, severe symptoms ≥ 1 time per week

Always start with lifestyle

Diet

- I always mention the classics
  - Coffee / caffeine
  - Alcohol
  - Red sauce
  - Chocolate
  - Citrus
  - Spicy / rich foods, etc…
- Patient's should assess for their own "trigger foods", consider keeping a diary
- For more generic advice, I offer the following…

Diet

Adherence to a predominantly Mediterranean diet decreases the risk of gastroesophageal reflux disease: a cross-sectional study in a South Eastern European population

I. Mone ✉, B. Kraja, A. Bregu, V. Duraj, E. Sadiku, J. Hyska, G. Burazeri

Diseases of the Esophagus, Volume 29, Issue 7, 1 October 2016, Pages 794–800,

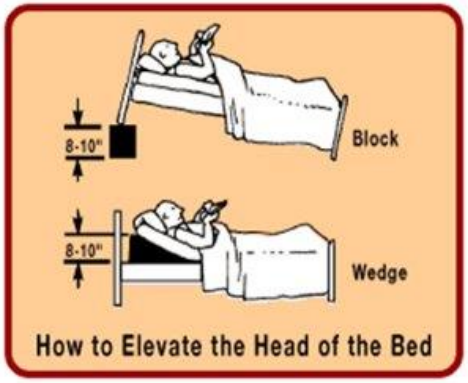
After controlling for demographics and lifestyle factors, including meal regularity, eating rate, and meal-to-sleep interval, the Non-Mediterranean diet was positively correlated with GERD (OR 2.3, 95% CI 1.2-4.5).

Meal timing and HOB elevation

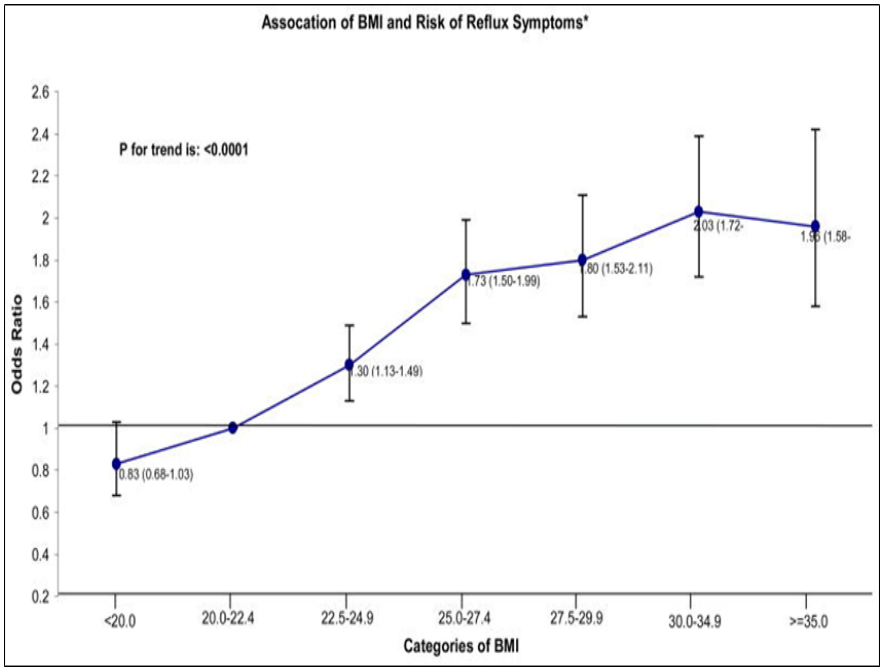
Don’t eat close to bedtime

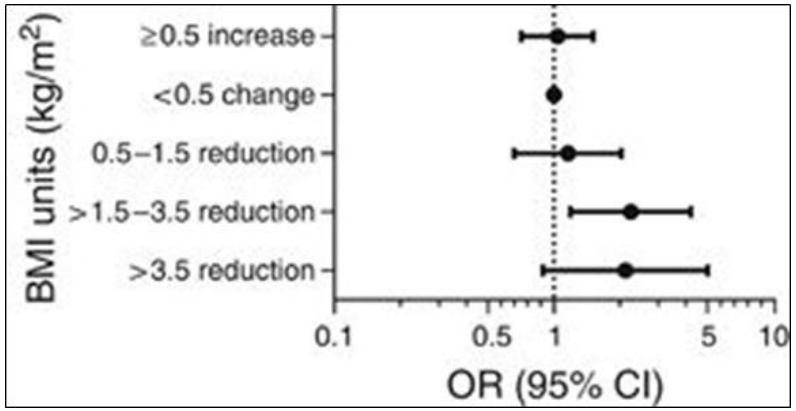
Piesman et al. AJG 2007

- RCT comparing early (6-hr before) vs. late (2-hr before) dinner meal
- Significantly more supine reflux after late meal



Weight loss





Jacobson et al. NEJM 2006.
Ness-Jensen et al. AJG 2013.

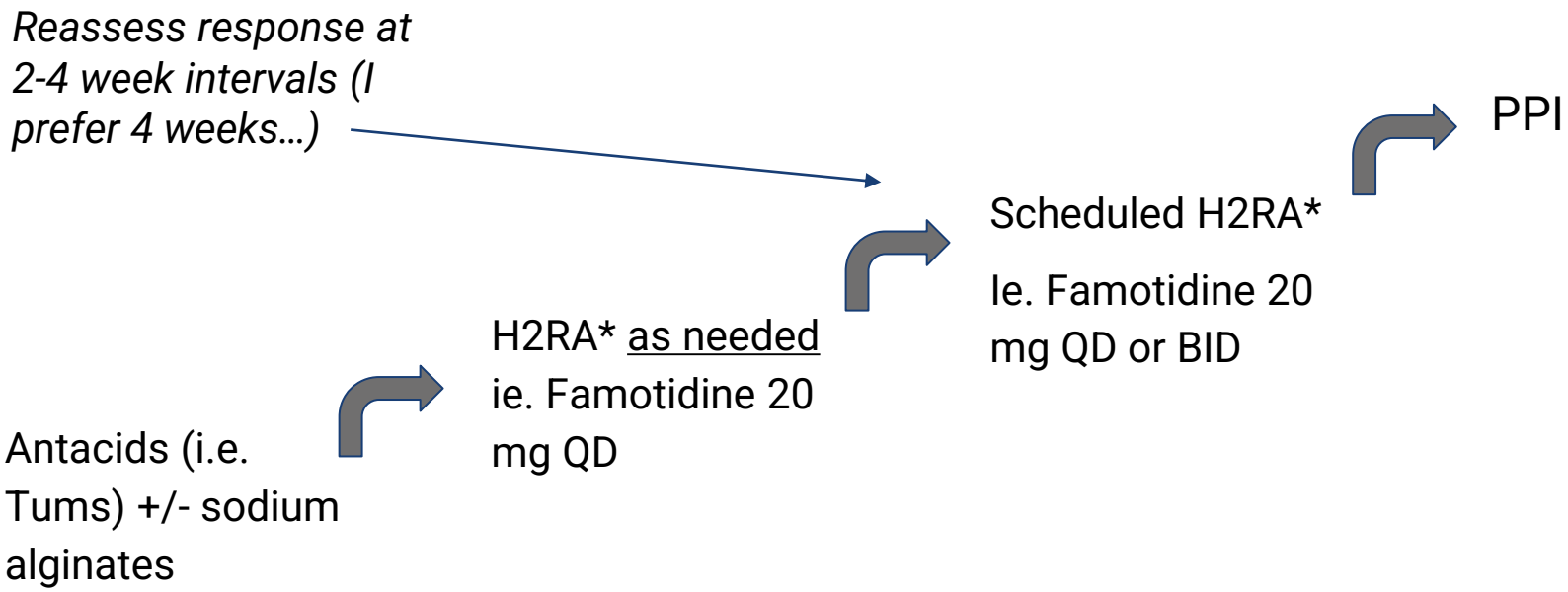
Part 1. Take-home Points

- Most GERD is diagnosed clinically
- Start with a diet and lifestyle discussion, tailor it to the patient

Part 2.

I'm trying, but I still have symptoms... what can I take?

"Step up" approach



*H2RA = histamine H2 receptor antagonist

Assess for alarm features

- Dysphagia / odynophagia
- Vomiting / PO intolerance
- New symptoms in older patient (>60)
- Evidence of bleeding (melena, hematochezia, +FOBT)
- Anemia
- Weight loss
- Anorexia
- Family history of esophageal or gastric cancer in FDR

Atypical symptoms

- Chest pain
- Nausea
- Globus
- Water brash

- Extra-esophageal symptoms
  - Cough
  - Hoarse voice
  - Sore throat

When to consider endoscopy

GERD with alarm features

Refractory and atypical symptoms

Evaluation of abnormal imaging

Barrett's screening

- GERD for >5 years AND at least one of the following:
  - Age over 50, male, Caucasian, obese, hiatal hernia, smoker (current or former), +FHx of Barrett's or esophageal cancer

The "Step Down" Approach

Indications: Failed H2RA therapy, known esophagitis, severe symptoms.

- Start with standard dose PPI x 8 weeks
  - ie. Omeprazole 20 mg once daily
  - Take on empty stomach, first thing in AM, 30 minutes before eating or drinking (!!!)
- If persistent symptoms, increase to BID dosing
- For known esophagitis, GI often involved, may specify higher dosing and need for repeat endoscopy
- When patient not responding, consider GI referral

The "Step Down" Approach

- Reassess need for PPI after ~8 weeks
- Consider tapering off PPI for patient's on >3 months
- No magic to the taper, I recommend decreasing by 50% of the dose every 2 weeks (ie take QOD for 2 weeks, then stop)

Part 2. Take-home Points

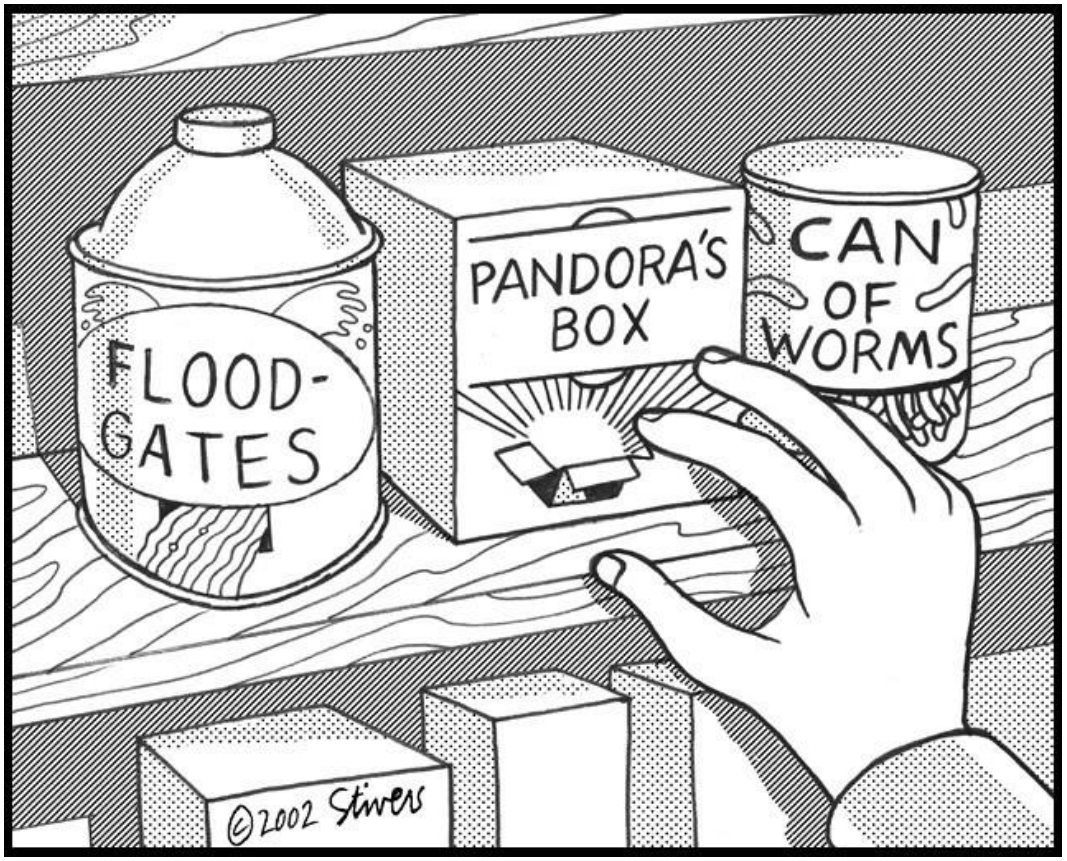
- “Step Down” therapy is indicated for
  - Non-response to H2RA agonists
  - Known esophagitis
  - Severe symptoms up-front
- Consider GI referral for alarm symptoms, atypical symptoms, non-response

Part 3.

Hey Doc, my symptoms are typical, I don't have any alarm features, and my endoscopy was clean… but I can't stop taking these PPIs!

What do I do?

Chronic proton pump inhibitor use is bad for my health – myth or fact?



The short answer is… myth.

The longer answer is…

- Chronic PPI use has been associated with several risks, including enteric infections and C. diff, bone fracture, renal dysfunction, dementia and others.
- Majority of evidence is observational only
- Association ≠ causation

Leonard et al. 2007; Kwok et al. 2012; Khalili et al. 2012; Klatte et al. 2017; Khan et al. 2020

The longer answer is…

	Strength	Consistency	Plausibility	MY TAKE
Enteric infections	RR 2.9 (campylobacter, salmonella) OR 1.99 (C. diff)	✓	✓	
Fracture	OR 1.25 - 1.5	–	?	
Renal dysfunction	HR 1.28 - 1.5 (CKD) Idiosyncratic risk of AIN	–	?	
Dementia	HR 0.78 - 1.44	✗	?	

The longer answer is…

Randomized Controlled Trial > Gastroenterology. 2019 Sep;157(3):682-691.e2.
doi: 10.1053/j.gastro.2019.05.056. Epub 2019 May 29.

Safety of Proton Pump Inhibitors Based on a Large, Multi-Year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin

- Participants randomized to pantoprazole 40 mg QD or placebo
- Medical records reviewed and participants interviewed every 6 months, out to 3 years
- Analyzed “safety outcomes of special interest” (ie. PPI side effects)

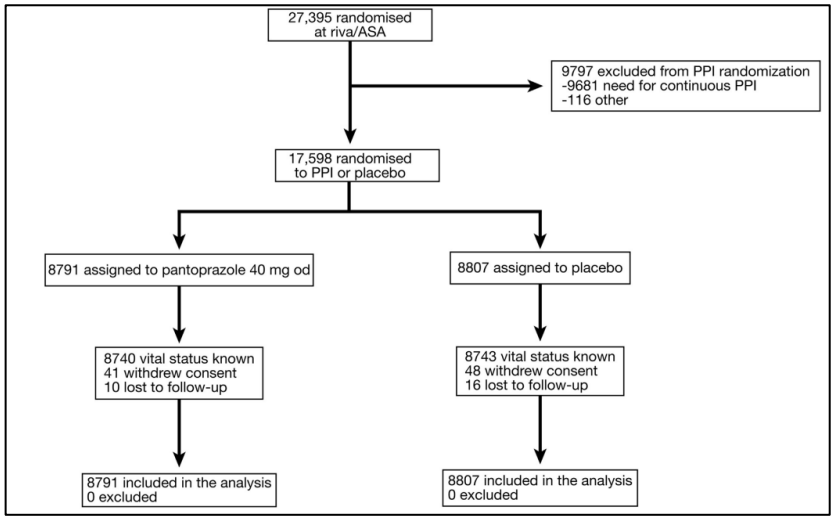


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Table 3. Other Prespecified Safety Outcomes

Outcome	Incident events, n (%)		Pantoprazole, 40 mg od, vs placebo	
	Pantoprazole, 40 mg od (n = 8791)	Placebo (n = 8807)	OR (95% CI)	*P* value
Gastric atrophy	19 (0.2)	26 (0.3)	0.73 (0.40–1.32)	.30
Clostridium difficile	9 (0.1)	4 (<0.1)	2.26 (0.70–7.34)	.18
Other enteric infection	119 (1.4)	90 (1.0)	1.33 (1.01–1.75)	.04
Chronic kidney disease	184 (2.1)	158 (1.8)	1.17 (0.94–1.45)	.15
Dementia	55 (0.6)	46 (0.5)	1.20 (0.81–1.78)	.36
Pneumonia	318 (3.6)	313 (3.6)	1.02 (0.87–1.19)	.82
Fracture	203 (2.3)	211 (2.4)	0.96 (0.79–1.17)	.71
COPD	146 (1.7)	124 (1.4)	1.18 (0.93–1.51)	.17
Diabetes mellitus	513 (5.8)	532 (6.0)	0.96 (0.85–1.09)	.56

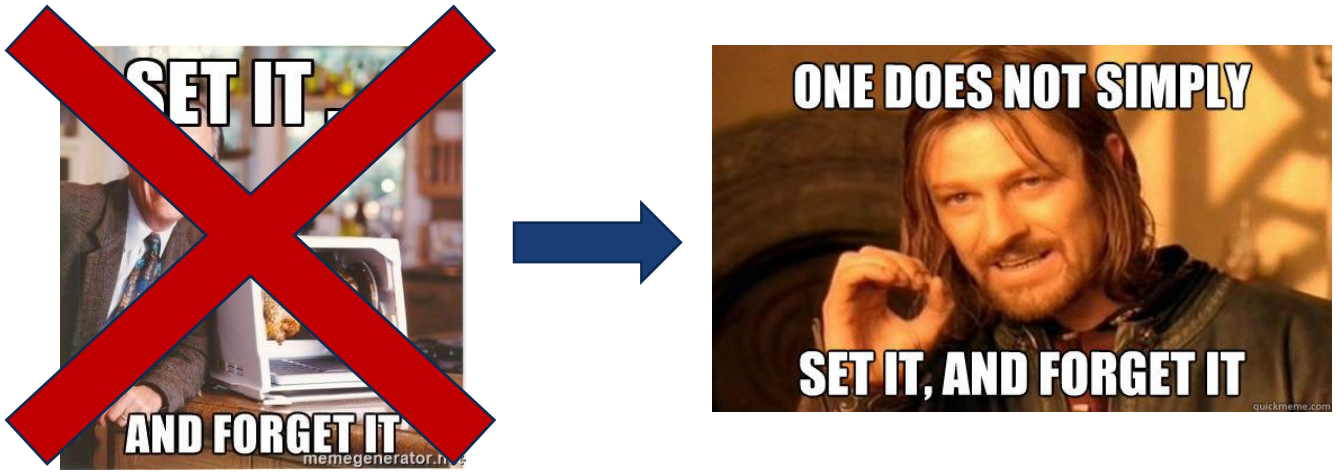
COPD, chronic obstructive pulmonary disease; od, once daily.

For certain indications, the benefit clearly outweighs the risk.

- GERD with esophagitis
- Barrett's esophagus
- Peptic ulcer disease
- NSAID-associated ulcer disease
- Zollinger-Ellison syndrome

For patients without a definitive indication for chronic PPI:

- Be clear about reason for use
- Consider diet / lifestyle interventions FIRST
- If still symptoms, aim for lowest necessary dose
- Reassess periodically, consider dose decrease or discontinuation

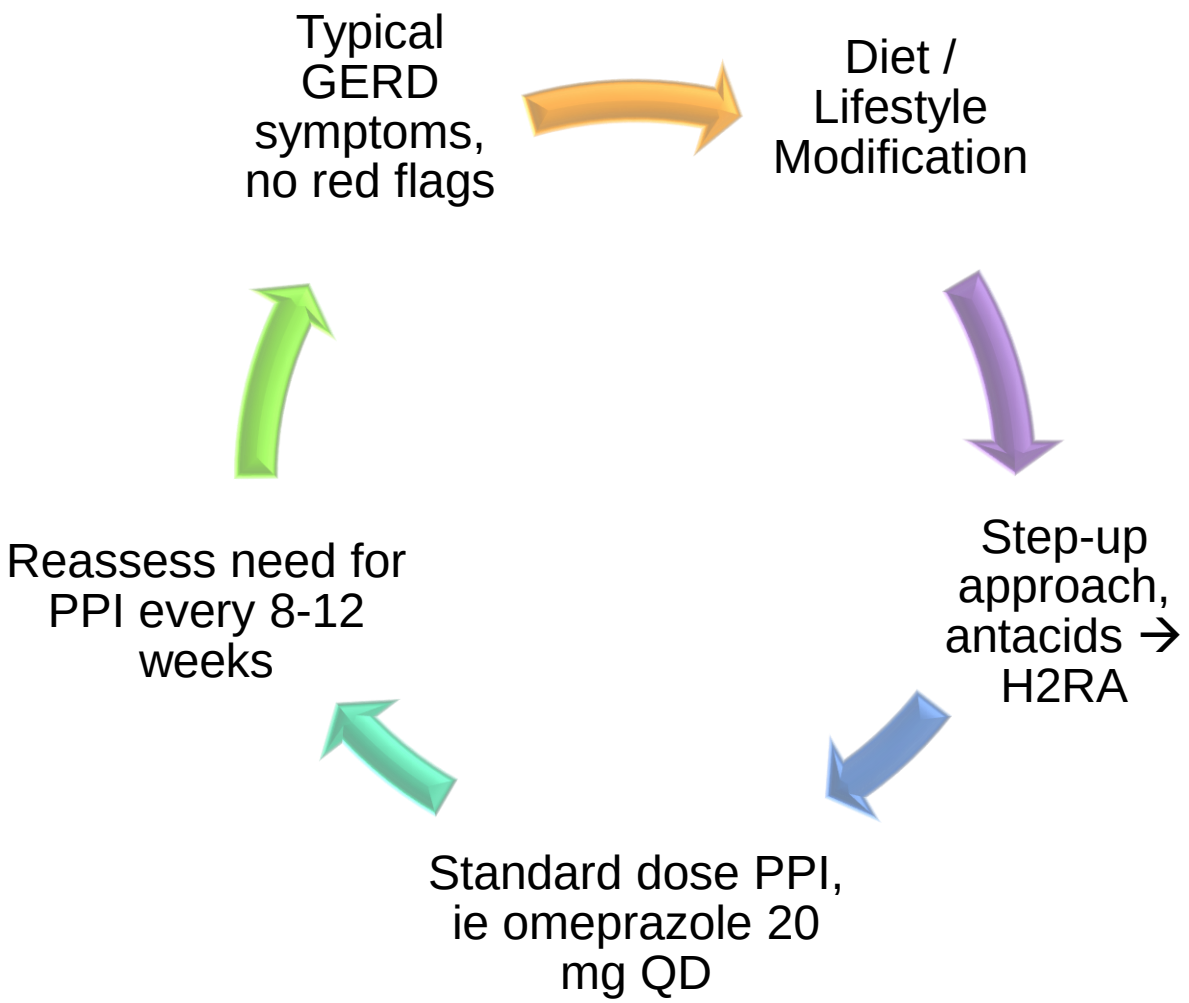


Targownik et al. 2022
Yadlapati et al. 2022

Part 3. Take-home points

- Chronic PPI use is probably NOT bad for your health.
- Most reported risks are based on observational data only, and association ≠ causation.
- Best available data (RCT) supports modestly increased risk of enteric infection.
- However, PPI stewardship is still important.
- Periodically reassess need for use, and aim for lowest necessary dose.

Uncomplicated GERD Life Cycle



Bonus slide - PCABs

- Potassium-competitive Acid Blockers (PCABs) are an alternative to PPI
- FDA approved in US for treatment of H pylori (May 2022), erosive esophagitis (Nov 2023), and recently non-erosive esophagitis (July 2024)
- Benefits:
  - Rapid onset of action, long half-life
- Cons:
  - Cost, not available OTC
  - Less data available

Thank you

Mount Auburn Hospital

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TEACHING HOSPITAL

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