UC San Diego Health

Polypharmacy and Deprescribing

a case of PPI-induced Secondary Hyperhidrosis

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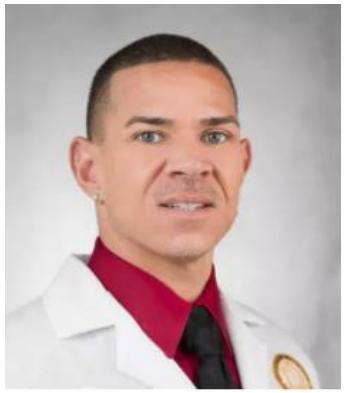
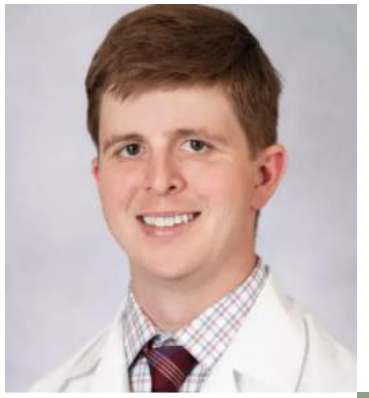
June 7th, 2022

Presentation Outline

- Review 4Ms of Age-Friendly Health System
- Recognize the importance of polypharmacy and impact in geriatric care
- Review existing clinical tools and frameworks that help with identify inappropriate prescription and assist with deprescribing
- Clinical case of Proton-Pump Inhibitors (PPI) -induced secondary craniofacial hyperhidrosis (HH)

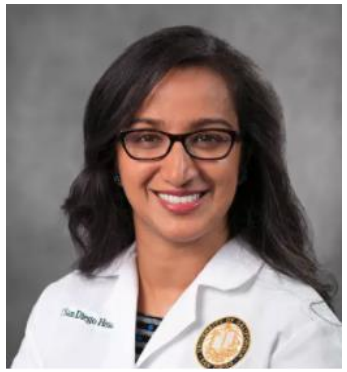
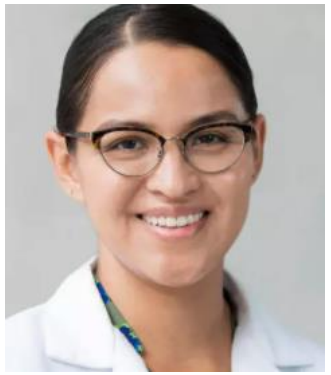
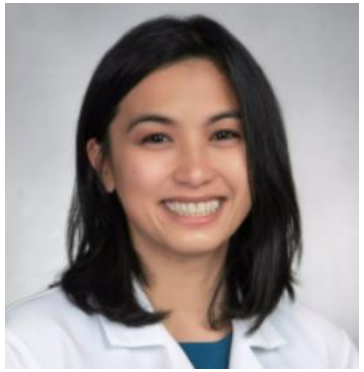



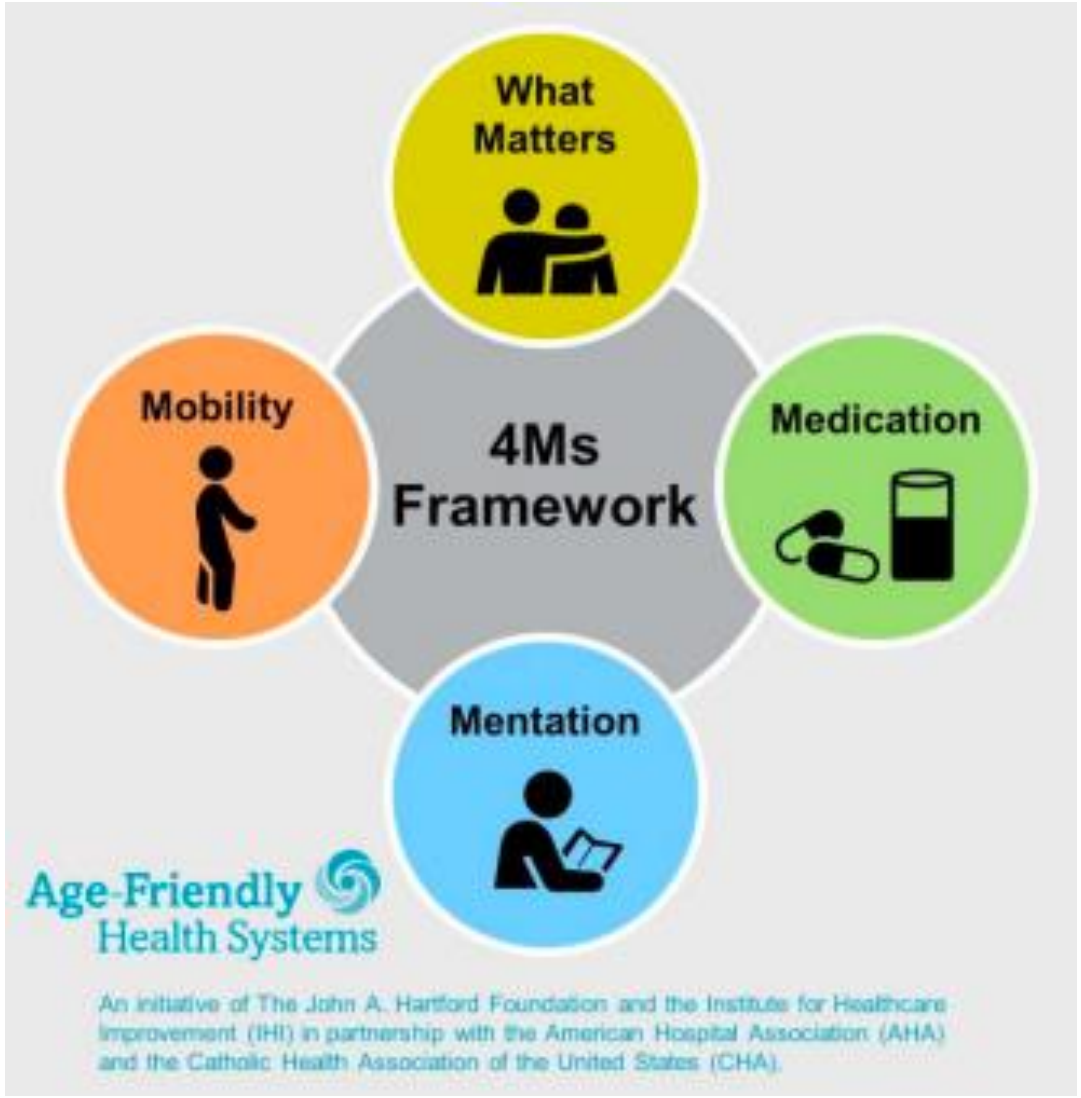




UC San Diego Health Part of National Initiative to Improve Senior Patient Care

First in San Diego to implement evidence-based approach to provide high quality of care to seniors



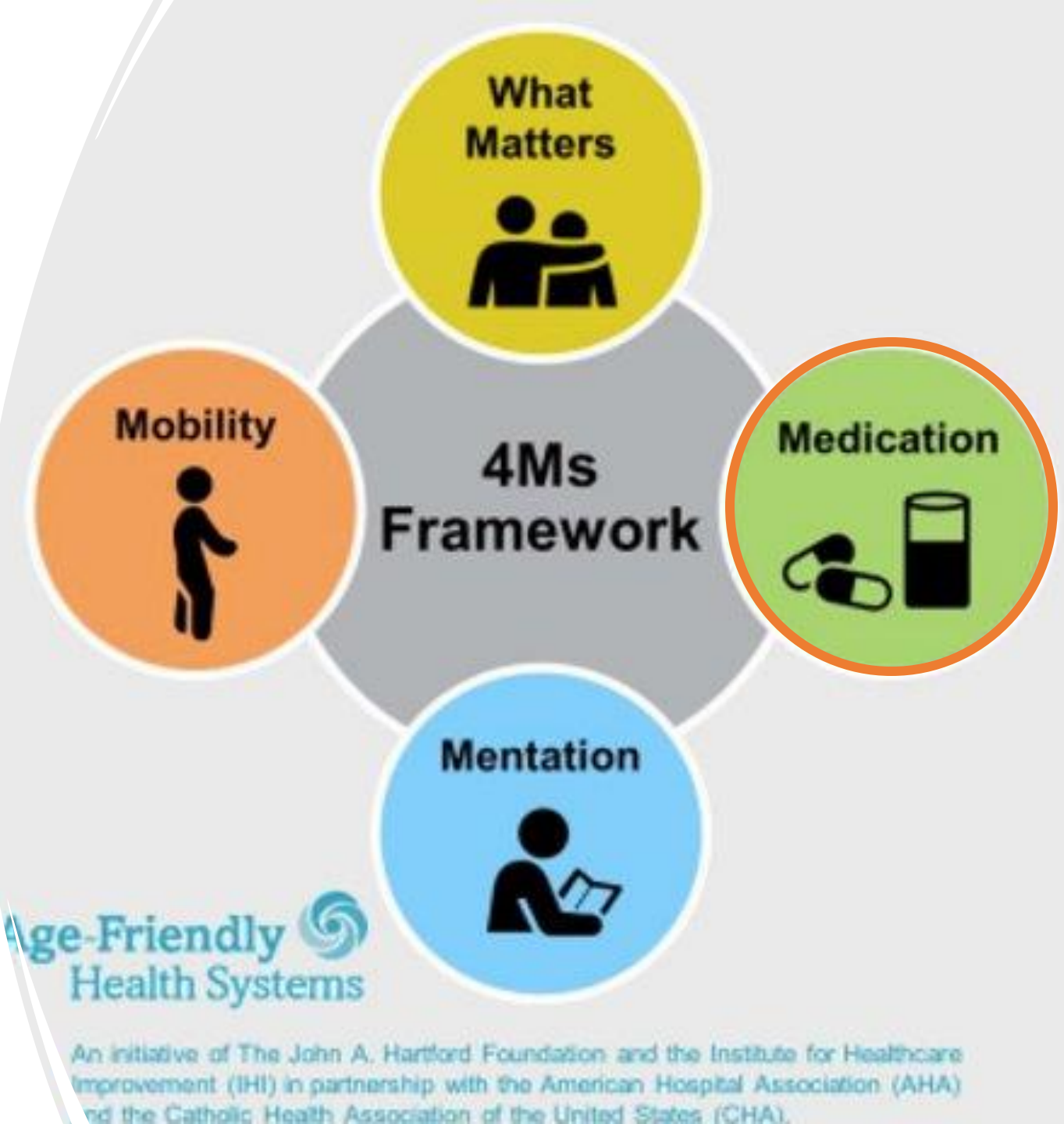




What constitutes the **4Ms** of Age-Friendly Health System?

Medication

- Polypharmacy or drug burden, side effects, drug-drug interaction, and food-drug interaction
- Does medication prescription align with patient's care goal?
- will the medication interfere with other 3Ms?



Definitions

Polypharmacy: ≥ 5 prescribed or over-the counter (OTC) drug therapies

Excessive polypharmacy or **hyperpolypharmacy**: ≥ 10 prescription or OTC drug therapies

Problematic Polypharmacy

- Multiple drug therapies are used in a way that is not appropriate
  - Medication not provide an overall benefit
  - Unacceptable pill burden
  - Difficulty with medication adherence
- Prescribing cascade: drug side-effects are misinterpreted as a new medical condition resulting in additional medications being prescribed

Inappropriate prescribing tools

- Beers criteria
- STOPP and START criteria
- STOPP Frail
- Medication Appropriateness Index
- Anticholinergic Risk Scale
- PRISCUS criteria
- Inappropriate prescribing for the elderly
- French consensus panel list
- Drug Burden INdex

Beers Criteria

- First created in 1991 by an expert consensus panel led by geriatrician Mark Beers and colleagues in the US
- Undergone multiple updates including the most recent (6th edition) published in 2019 under the sponsorship of the American Geriatric Society (AGS)
- Initially designed to assist researchers in identifying quality of prescribing in long-term care homes
- Provides a list of medications are considered potentially inappropriate, medications to avoid in certain conditions, medications to use with caution, specific drug-drug interactions , and medications that require dose-adjustment related to kidney function

STOPP/START and STOPPFrail criteria

- **STOPP** = Screening Tool of Older Persons' Prescription
- **START** = Screening Tool to Alert providers to the Right Treatment
- Developed in Ireland by a group of expert lead by Dr. O'Mahony
- first published in 2008, updated in 2015.
- Identified medications that were potentially inappropriate for older adults, organized by physiological system. Also include drug-drug interactions and duplications of meds within a class.
- **STOPPFrail criteria** *was published in 2017 and updated in 2021. Attempt to discontinue inappropriate medications in older adults who are frail with limited life expectancy.*

Medication Appropriateness Index

- Created by Hanlon and colleagues in 1992
- Series of 10 questions that helps to identify potential drug-related problems associated with a specific medications.
- Strength of this tool: assesses a range of issues that important to consider when evaluating on-going need for a medication

QUESTIONS	SCORE
Is there an indication for the drug?	3
Is the medication effective for the condition?	3
Is the dosage correct?	2
Are the directions correct?	2
Are the directions practical?	2
Are there clinically significant drug-drug interactions?	2
Are there clinically significant drug-disease/condition interactions?	1
Is there unnecessary duplication with other drugs?	1
Is the duration of therapy acceptable?	1
Is this drug the least expensive alternative available compared with others of equal utility?	1
Max Score of Inappropriateness	18

Anticholinergic Risk Scale (ARS)

- Medications with anticholinergic properties are prescribed to at least of 20% of American seniors 65 and older. Anticholinergic medication is known to be associated with increased risk for fall, delirium, and cognitive impairment in geriatric patients.
- Developed by Rudolph and Colleagues from the US in 2008
- To assess the burden & risk of adverse events, associated with use of anticholinergic medications.
- The higher ARS scores are associated with increased risk of anticholingergic adverse effects.

SCORE 1		SCORE 2	SCORE 3	
Antianxiety medications		**Skeletal muscle relaxers**	**Skeletal muscle relaxers**	
Alprazolam (*Xanax*) Clorazepate (*Tranxene*)	Diazepam (*Valium*)	Cyclobenzaprine (*Flexeril*)	Methocarbamol (*Robaxin*)	Orphenadrine (*Norflex*)
Antipsychotic medications		**Antipsychotic medications**	**Antipsychotic medications**	
Aripiprazole (*Abilify*) Asenapine (*Saphris*) Haloperidol (*Haldol*)	Iloperidone (*Fanapt*) Paliperidone (*Invega*) Risperidone (*Risperdal*)	Loxapine (*Loxitane*) Pimozide (*Orap*) Molindone (*Moban*)	Clozapine (*Clozaril*) Olanzapine (*Zyprexa*) Perphenazine (*Trilafon*)	Quetiapine (*Seroquel*) Thioridazine (*Mellaril*)
Antidepressants		**Anticonvulsants**	**Antidepressants**	
Bupropion (*Wellbutrin*) Venlafaxine (*Effexor*)	Fluvoxamine (*Luvox*) Trazodone (*Desyrel*)	Carbamazepine (*Tegretol*) Oxcarbazepine (*Trileptal*)	Amitriptyline (*Elavil*) Clomipramine (*Anafranil*) Desipramine (*Norpramin*) Doxepin (*Sinequan*)	Imipramine (*Tofranil*) Nortriptyline (*Pamelor*) Paroxetine (*Paxil*)
Antihistamines (2nd Generation)		**Antihistamine (1st Generation)**	**Antihistamines (1st Generation)**	
Cetirizine (*Zyrtec*) Desloratadine (*Clarinex*)	Loratadine (*Claritin*) Levocetirizine (*Xyzal*)	Cyproheptadine (*Periactin*)	Brompheniramine Chlorpheniramine Clemastine (*Tavist*) Dimenhydrinate (*Dramamine, etc*)	Diphenhydramine Doxylamine (*Unisom, etc*) Hydroxyzine (*Atarax/Vistaril*) Meclizine (*Antivert*) Promethazine (*Phenergan*)
Gastrointestinal (GI) antispasmodic		**GI antispasmodic**	**GI antispasmodics**	
Clidinium (*Librax*)		Belladonna	Dicyclomine (*Bentyl*) Hyoscyamine (*Levsin*)	Scopolamine (*Transderm Scop*)
Opioid or opioidlike		**Opioid or opioidlike**	**Urinary Anticholinergics**	
Codeine (*various*) Fentanyl (*Duragesic, Actiq*) Morphine (*MS Contin, Avinza*)		Meperidine (*Demerol*)	Darifenacin (*Enablex*) Fesoterodine (*Toviaz*) Flavoxate (*Urispas*) Oxybutynin (*Ditropan*)	Solifenacin (*Vesicare*) Tolterodine (*Detrol*) Trospium (*Sanctura*)
Antidiarrheal (nonopioid)		**Parkinson's disease**	**Parkinson's disease**	
Loperamide (*Imodium, others*)		Amantadine (*Symmetrel*)	Benztropine (*Cogentin*)	Trihexyphenidyl (*Artane*)
Blood thinner			**Prototypical anticholinergic**	
Warfarin (*Coumadin*)			Atropine	
Blood pressure medications		**Example Scoring:**		
Captopril (*Capoten*) Atenolol (*Tenormin*) Metoprolol (*Lopressor, Toprol*) Chlorthalidone (*Diuril, Hygroton*) Furosemide (*Lasix*) Nifedipine (*Procardia, Adalat*) Hydralazine (*Apresoline*) Isosorbide (*Isordil, Ismo*)		Warfarin – Score 1 Fentanyl – Score 1 Carbamazepine – Score 2 Chlorpheniramine – Score 3 Paroxetine – Score 3 Oxybutynin – Score 3 Total Anticholinergic Burden Score = 13	**Possible Changes to Reduce Anticholinergic Burden:** • Discontinue medications where possible, reduce doses, or change to alternatives. • Discontinuation of chlorpheniramine would reduce score by 3. • Changing to loratadine (Score 1) and would reduce score by 2. • Changing paroxetine to escitalopram would reduce score by 3. • If changing these medications, score would decrease from 13 to 8	
Glucocorticosteroids				
Hydrocortisone	Prednisone			
Gout	**Asthma**			
Colchicine (*Colcrys*)	Theophylline			
Atrial Fibrillation/CHF	**Antiarrhythmic**			
Digoxin (*Lanoxin*)	Quinidine			

Art of Deprescribing

When less is more!

When should deprescribing be considered?

- Any geriatric patient:
  - Presenting with a new symptom or clinical syndrome suggestive of adverse drug effects
  - Manifesting advanced or end-stage disease, terminal illness, dementia, extreme frailty, or full dependence on others for all care
  - Receiving high-risk drug(s) or drug combinations
  - Receiving preventive drugs for scenarios associated with no increased disease risk despite drug cessation

Good Palliative-Geriatric Practice Algorithm

- Developed in 2007 by Garfinkel and colleagues in Israel
- Uses a series of questions to guide the process of deprescribing process
- Patients of interest, based on VOCODFLEX status
  - Very Old age
  - extent of Comorbidities
  - Dementia
  - Frailty
  - Limited life EXpectancy
- Settings:
  - Nursing home: ~3 drugs were discontinued per individual residents
  - Community-dwelling: only 2% of 256 discontinued medications in 64 patients were restarted due to reoccurrence of original indication. 88% of 64 patients report overall improved health

Deprescribing Protocol

- Five-step approach to aid in deprescribing
- Published by Scott and colleagues from Australia in 2015.
- CEASE Algorithm
  - Current medicines
  - Elevated risk
  - Assess
  - Sort
  - Eliminate

DRUG guide: a systematic approach to deprescribe

	DRUGS guide to optimising medication safety for older adults
D	**DISCUSS goals of care and what matters most to the patient** • Include patients and caregivers in deprescribing discussions to ensure decisions focus on goals of care

R	**REVIEW medications**
	• Encourage patients to bring all prescribed and over-the-counter medications to their appointment
	• Review medications on an ongoing basis and when clinical conditions or goals of care change
	  • Discontinue potentially unnecessary drugs
	  • Consider drug side-effects as a potential cause for a new symptom
	  • Consider non-pharmacological options
	  • Change for safer alternatives
	  • Lower the dose
	• To identify possible prescribing cascades, determine when the medication was started and why

U	**USE tools and frameworks**
	• Identify drugs from the inappropriate prescribing tools, including Beers criteria or STOPP criteria
	• Use the STOPPFrail list when the individual is extremely frail and approaching the end of life
	• Consider whether the new or existing medical condition could be the result of a prescribing cascade and ask:
	  • Is a new drug being prescribed to manage a side-effect from another prescribed drug?
	  • Could the initial drug be replaced with a safer drug or could the dose be reduced?
	  • Does the patient need the first drug or could this drug be stopped?
	• Pay attention to older people who are receiving so-called good drugs with narrow therapeutic windows that might no longer be needed or for whom dose reduction might be beneficial

G	**GERIATRIC medicine approach** • Geriatricians carefully consider how multiple medical problems, frailty, cognitive impairment, and limited life expectancy reduce medication benefit, increase adverse events, or interfere with medication adherence
S	**STOP the medications** • Consider the algorithm created by Scott[65] or the Good Palliative–Geriatric Practice algorithm to guide deprescribing

Rochon PA, Petrovic M, et al. Polypharmacy, inappropriate prescribing, and deprescribing in older people: through a sex and gender lens. The Lancet Healthy Longevity. 2021; 2 (5): 290-300.

Clinical Case

71-year-old women with new onset excessive sweating

71-year-old woman with excessive sweating

- PMHx: Hypertension, Hyperlipidemia, GERD, Osteoarthritis
- Med list: total of 5 medications, including Pantoprazole.
- No family history of primary hyperhidrosis
- Symptoms: drenching sweat on face and scalp. Each episode last for 20-30min, occurs once or twice daily. Not associated with activity, food or temperature change.
- Impact on daily function: embarrassed with symptom of excessive sweating, patient feels uncomfortable to leave her home and to carry out normal social interactions
- Prior to referral to Geriatric's clinic, numerous work-up by PCP, cardiologist and endocrinologist were inconclusive...

71-year-old woman with excessive sweating

- During Geriatric eval, a comprehensive history collected, and her medications reviewed
  - Pantoprazole was held
- After three days of medication discontinuation, patient's sweating symptom resolved with no recurrence while patient not on the medication.
- Within 4 days of restartng pantoprazole, patient's symptom returns in full vengeance...
- Concerned for **Pantoprazole-induced secondary craniofacial hyperhidrosis**, the medication was deprescribed.

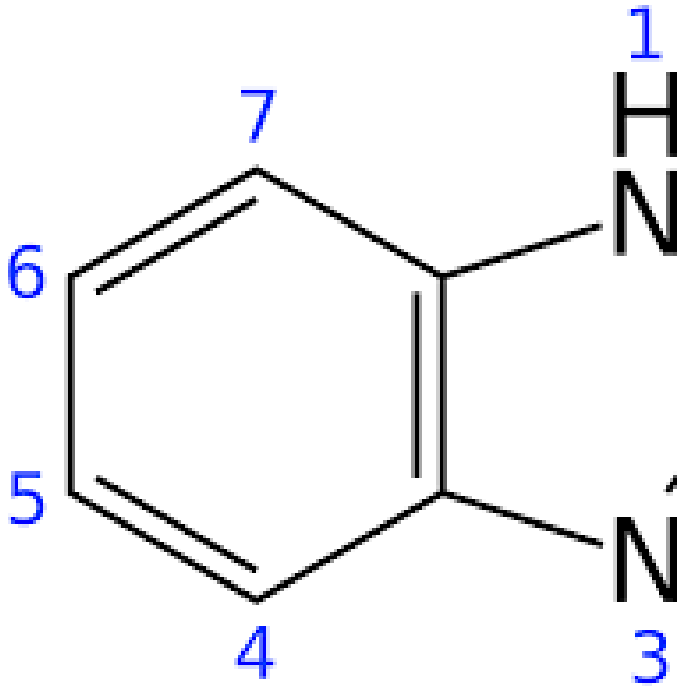
Proton-Pump Inhibitor (PPI) induced Secondary Craniofacial Hyperhidrosis

Hyperhidrosis (HH) and PPI

- Hyperhidrosis is a dermatological disorder that causes excessive sweat production beyond thermoregulatory needs.
- Approximately 2.8% of the US population is affected by it.
- Primary (idiopathic) vs Secondary HH
  - Primary HH - constitutes 93% of all HH cases, diagnosis of exclusion
  - Secondary HH – less prevalent compared to primary. Causes are more frequently related to an underlying medical condition or iatrogenic causes.
- Craniofacial HH
  - A subtype of secondary focal HH, affects face and/or scalp
  - PPI-induced 2nd craniofacial HH is an under-recognized side-effects of the medication

Proton-Pump Inhibitors (PPIs)

Proton Pump Inhibitors



- Class of medications that are chemically benzimidazole derivatives
  - Membrane permeable, acid-labile weak bases
- Mechanism of Action:
  - Irreversible inhibition of H/K ATPase, a proton pump located in gastric parietal cells, that regulates gastric acid production
  - Inhibits acid secretion until replacement pumps are resynthesized
- Available PPIs out in the market:
  - Pantoprazole, Omeprazole, Lansoprazole, Dexlansoprazole, Esoprazole, and Rabeprazole

PPI Indications

Best Practice Guidelines Regarding Use of PPIs[3–5,20]

Clinical Indication	Goals of Care and Duration of Use
GERD, acid-related: erosive esophagitis, peptic stricture[20]	• Short term for healing • Long term for symptom control
Uncomplicated GERD, for those who respond to short-term PPIs[20]	• Stop or reduce the PPI • If not possible, further evaluation before long-term therapy
Barrett esophagus and symptomatic GERD[20]	• Consider long-term PPI
Asymptomatic Barrett esophagus[20]	• Consider long-term PPI for symptom relief
High risk for ulcer bleeding while on NSAIDs[20]	• Use a PPI while the patient is on NSAIDs
Formulation of PPI[20]	• Do not choose a specific formulation based on potential risk
Patients on long-term PPIs[20]	• Need periodic reevaluation to determine lowest effective dose • Should not routinely use probiotics to prevent infection • Should not routinely increase calcium, vitamin B12, or magnesium intake above recommended dietary allowance • Do not routinely screen for bone density, serum creatinine, B12
Additional indications[3]	• Maintenance of healed EE • Nonerosive reflux disease (NERD) • Treatment of *Helicobacter pylori* infection in combination with antibiotics • Hypersecretory syndromes, including Zollinger Ellison syndrome • Critically ill patients on prolonged mechanical ventilation • Short term (with regular review) for functional dyspepsia
Gastroprotection[5]	• Steroid use not an indication, unless combined with NSAIDs
Refractory steatorrhea[5]	• PPIs may be added to pancreatic enzyme replacement
Appropriateness of PPI use and duration of therapy[4]	• Long-term use appropriate for Barrett esophagus, Zollinger Ellison syndrome PPI responsive eosinophilia, idiopathic peptic ulcer disease • Short-term therapy (4–12 weeks) for stress ulcer prophylaxis, *H. pylori* eradication, treatment of peptic ulcer disease, before endoscopy for acute upper GI bleeding, following endoscopy for upper GI bleeding
Inappropriate use of PPIs[4]	• Stress ulcer prophylaxis in non–critically ill patients • Corticosteroid use without concomitant NSAID use • Acute prophylaxis
Uncertain benefit[4]	• Nonresponsive GERD

Commonly known PPI Adverse Reactions

Related to acid inhibition:

- Small intestinal bacterial overgrowth
- Clostridium difficile infection
- Pneumonia
- Spontaneous bacterial peritonitis
- Nutrient deficiency: vitamin B12, iron, calcium, and/or magnesium
- Fracture

Unrelated to acid inhibition:

- Renal: Acute interstitial nephritis, CKD
- Cardiovascular: MI and mortality
- Allergic reaction
- Dementia
- Drug-interactions (I.e. plavix, reduce the blood thinning effect)

Beers criteria, 2019

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Androgens Methyltestosterone Testosterone	Potential for cardiac problems; contraindicated in men with prostate cancer	Avoid unless indicated for confirmed hypogonadism with clinical symptoms	Moderate	Weak
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women Evidence indicates that vaginal estrogens for the treatment of vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to nonhormonal therapies are advised to discuss the risks and benefits of low-dose vaginal estrogen (dosages of estradiol <25 µg twice weekly) with their healthcare provider	Avoid systemic estrogen (eg, oral and topical patch) Vaginal cream or vaginal tablets: acceptable to use low-dose intravaginal estrogen for management of dyspareunia, recurrent lower urinary tract infections, and other vaginal symptoms	Oral and patch: high Vaginal cream or vaginal tablets: moderate	Oral and patch: strong Topical vaginal cream or tablets: weak
Growth hormone	Impact on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	Avoid, except for patients rigorously diagnosed by evidence-based criteria with growth hormone deficiency due to an established etiology	High	Strong
Insulin, sliding scale (insulin regimens containing only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin)	Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting. Avoid insulin regimens that include only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin. This recommendation does not apply to regimens that contain basal insulin or long-acting insulin.	Avoid	Moderate	Strong
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong
Sulfonylureas, long acting Chlorpropamide Glimepiride Glyburide (also known as glibenclamide)	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH Glimepiride and glyburide: higher risk of severe prolonged hypoglycemia in older adults	Avoid	High	Strong
Gastrointestinal				
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults and with prolonged exposure	Avoid, unless for gastroparesis with duration of use not to exceed 12 weeks except in rare cases	Moderate	Strong
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong
Proton-pump inhibitors	Risk of *Clostridium difficile* infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk patients (eg, oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (eg, because of failure of drug discontinuation trial or H2-receptor antagonists)	High	Strong

Choosing wisely Canada recommendation on PPI therapy

" Don't maintain long-term PPI therapy for GI symptoms without an attempts to stop/reduce the PPI at least once per year in most patients"

Barrett esophagitis and gastrointestinal bleeding are exceptions

Deprescribing.org

Official website: https://deprescribing.org/resources/deprescribing-guidelines-algorithms/

PPI Algorithm white board: https://www.youtube.com/watch?v=EH2vEGJYqVI

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Thank you!

The End