The *voice* of the community pharmacist.

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Taking a Functional Medicine Approach to Medication Therapy Management

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Foodie Farmacist LLC

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Disclosure Statement

Lara Zakaria has a financial interest with Gaia Herbs and the relationship has been mitigated through peer review of this presentation.

There are no relevant financial relationships with ACPE defined commercial interests for anyone else in control of the content of the activity.

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Pharmacist and Technician Learning Objectives

1. Identify opportunities for your pharmacy team to leverage functional medicine during MTM encounters to optimize medication safety and efficacy.
2. Using principles of functional medicine, explain effective strategies for reducing side effects and improving outcomes for your patients taking commonly prescribed medication.
3. Review nutraceuticals, nutrition, and lifestyle principles that safely support medication efficacy to help patients to achieve their health goals.

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Today's Agenda

1. Define the terms
2. Spot the opportunity
3. Review a case

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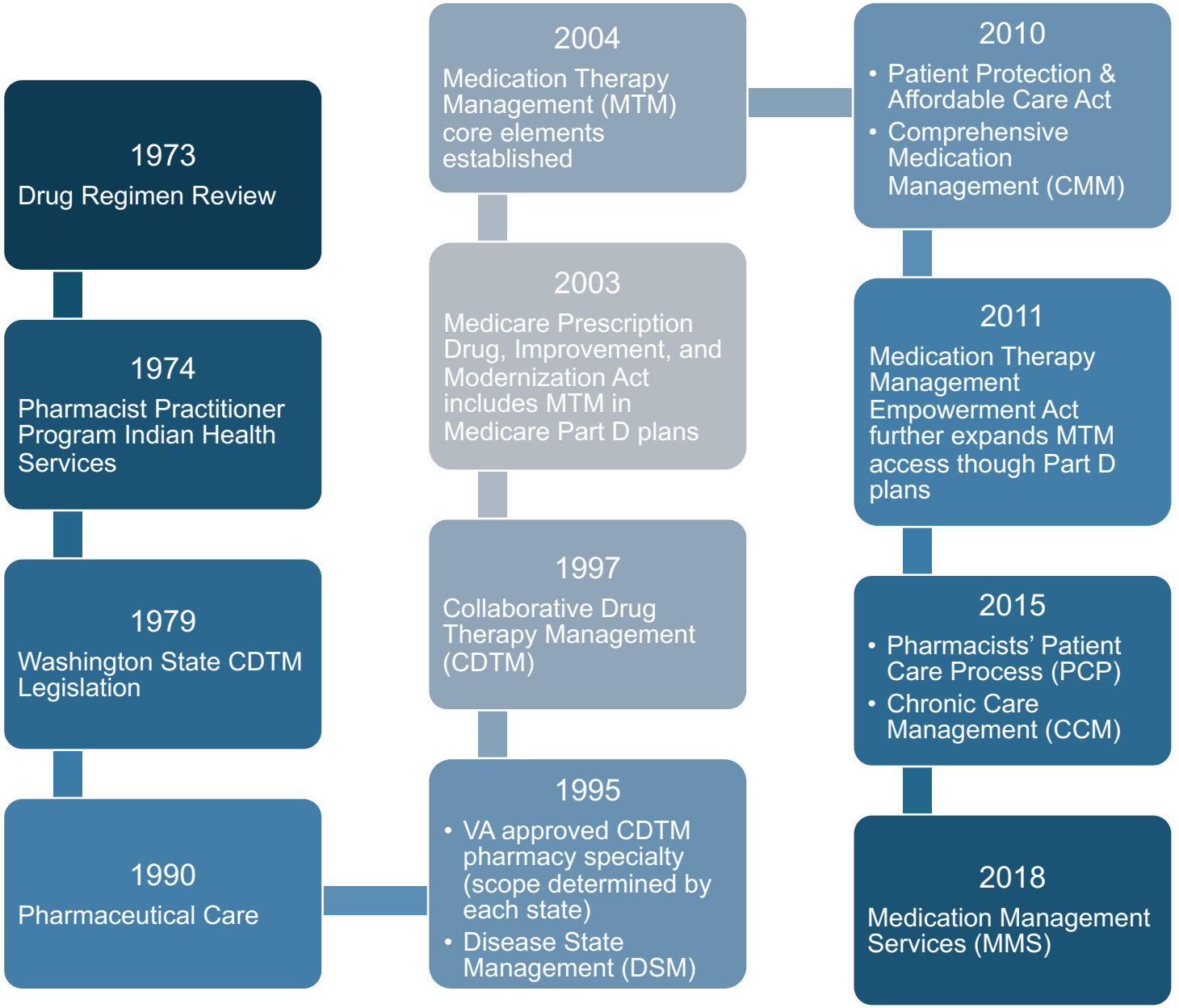
History of MTM



adapted from https://www.mpqhf.org/QIO/wp-content/uploads/2017/03/6.5.2018_MPQH-CMM_MTM-FINAL.pdf

Medication Management Services (MMS)

MMS are a spectrum of patient-centered, pharmacist provided, collaborative services that focus on

- Medication appropriateness
- Effectiveness
- Safety
- Adherence

The broader term encompass a variety of services, including

- Medication Therapy Management (MTM)
- Disease State Management (DSM)
- Comprehensive Medication Management (CMM)
- Collaborative Drug Therapy Management (CDTM)

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Disease management. AMCP.org. https://www.amcp.org/about/managed-care-pharmacy-101/concepts-managed-care-pharmacy/disease-management

Services/Collaborations Include

Disease State Management (DSM)

- A comprehensive, integrated approach to care and reimbursement based on the natural course of a disease
- Treatment designed to address an illness with maximum effectiveness and efficiency, high quality of care, and reduce healthcare costs

Collaborative (or coordinated) drug therapy management (CDTM)

- Practice involves developing a collaborative practice agreement (CPA) between health care provider and pharmacist

Collaborative practice agreement (CPA)

- Allows qualified pharmacists working within the context of a defined protocol to assume professional responsibility for performing patient assessments, counseling, and referrals
- Other services include ordering laboratory tests, medication management (selection, initiating, monitoring, and adjustments)

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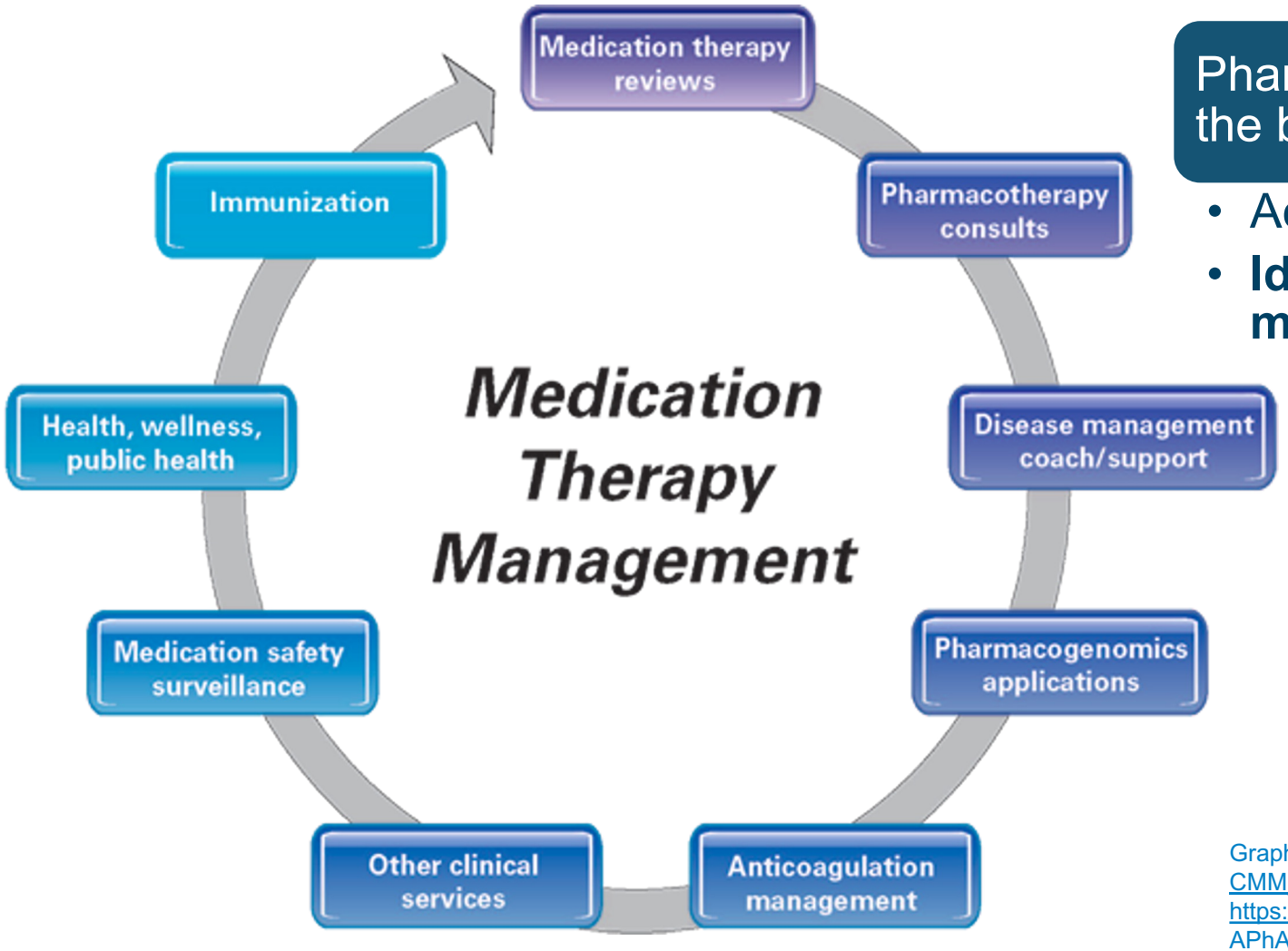
Disease management. AMCP.org. https://www.amcp.org/about/managed-care-pharmacy-101/concepts-managed-care-pharmacy/disease-management

What is MTM?



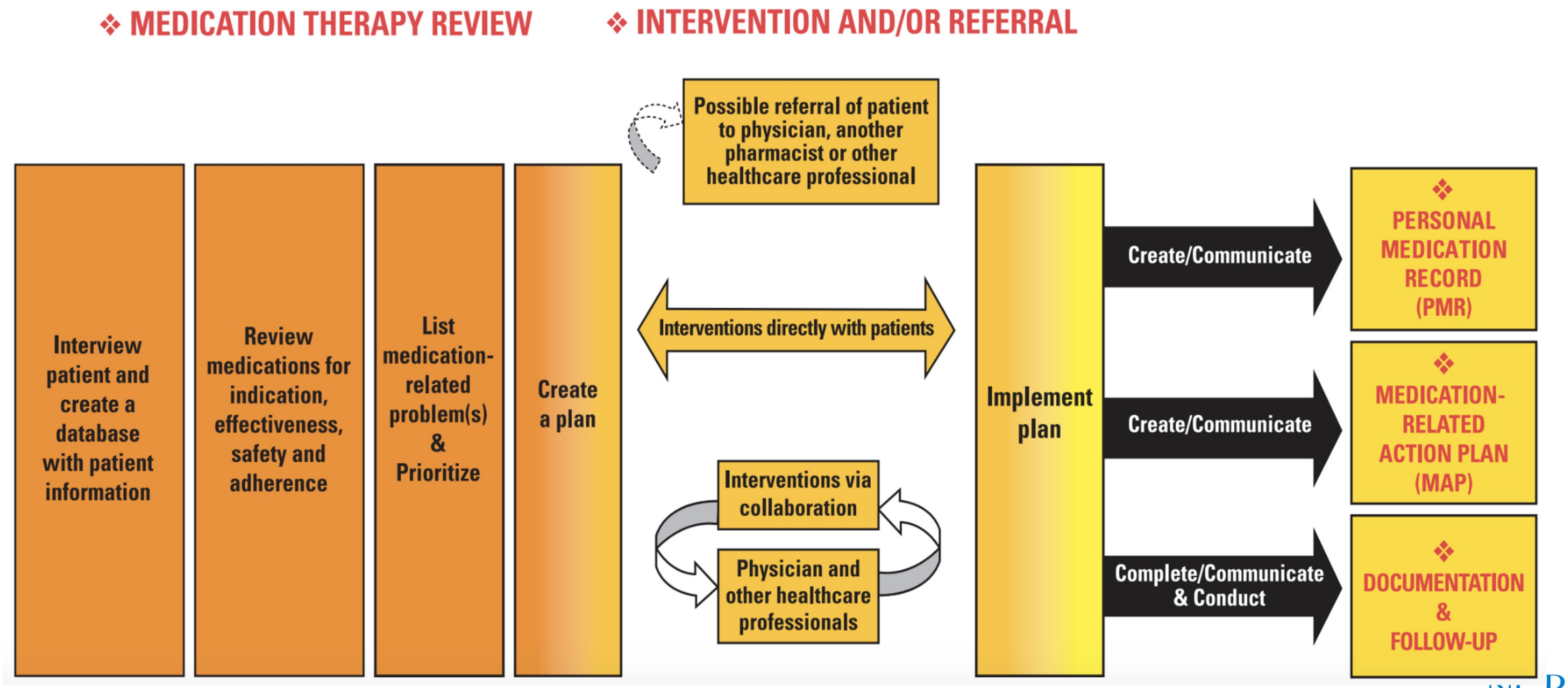
Patient-centric service that optimizes therapeutic outcomes

Pharmacists provide MTM to help patients get the best benefits from their medications by

- Actively managing drug therapy
- **Identifying, preventing and resolving medication-related problems**

Graphic from https://www.mpqhf.org/QIO/wp-content/uploads/2017/03/6.5.2018_MPQH-CMM_MTM-FINAL.pdf
https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/mtm
APhA Medication Therapy Management Core Elements Service Model Version 2.0. 2008.
https://s3.amazonaws.com/filehost.pharmacist.com/CDN/PDFS/Practice/core_elements_of_an_mtm_practice.pdf?AWSAccessKeyId=AKIAYICBVAN2V7IWVG4T&Expires=1683339678&Signature=hUlSmXMOWFQ9hz%2BLSVPjZ6Hxr5g%3D

MTM Core Elements Service Model



APhA Medication Therapy Management Core Elements Service Model Version 2.0. 2008. https://s3.amazonaws.com/filehost.pharmacist.com/CDN/PDFS/Practice/core_elements_of_an_mtm_practice.pdf?AWSAccessKeyId=AKIAYICBVAN2V7IWVG4T&Expires=1683339678&Signature=hUlSmXMOWFQ9hz%2BLSVPjZ6Hxr5g%3D

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Comprehensive Medication Management (CMM)

CMM (2012) is defined as the standard of care that ensures each patient's medications, including

- Prescription and nonprescription
- Alternative and traditional

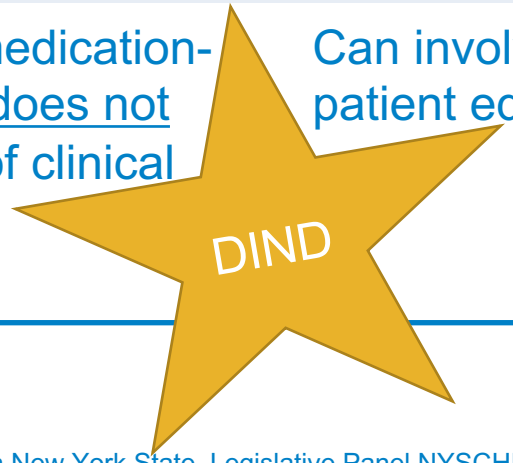
Everything is assessed to determine:

- Appropriateness for individual needs
- Compliance issues
- Effectiveness

ACCP. Comprehensive Medication Management in Team-Based Care https://www.accp.com/docs/positions/misc/CMM%20Brief.pdf

MTM vs. CMM

MTM	CMM	CDTM
2003 Established by CMS (Part D)	Pharmacy practice, not law	Legal agreement, not clinical practice
Not tied to filling prescriptions	Establish patient-centered plan	Collaborative agreement, protocol medicine
Does not require a CDTM agreement, covered under pharmacist scope of practice	Includes assessment, monitoring, and multi-disciplinary collaboration	Regulation of CMM (depending on level of agreement)
Involves identifying medication-related problem, but does not involve assessment of clinical status	Can involve laboratory review, patient education and counseling	Varies from state to state



Perspectives, Priorities, and Pharmacy in New York State. Legislative Panel NYSCHP Annual Assembly. 2017. https://slideplayer.com/slide/11852700/

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Pharmacists' Patient Care Process

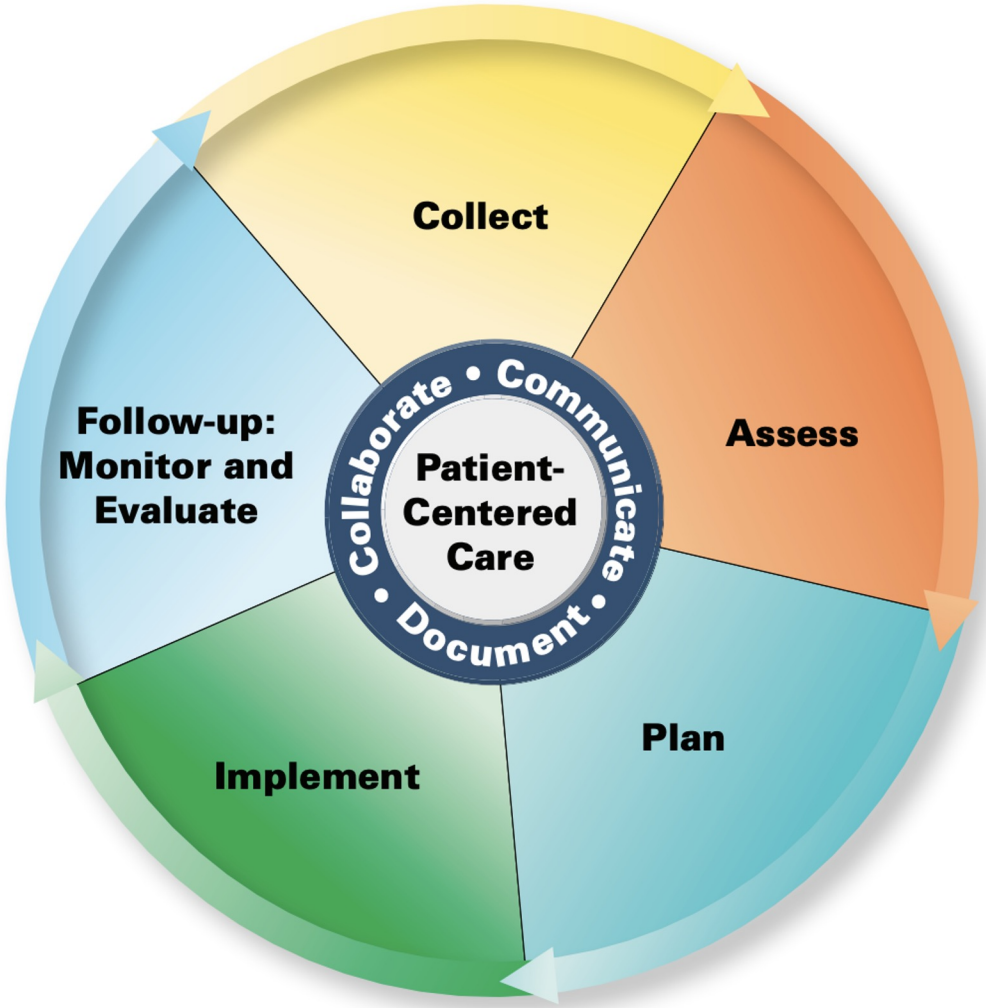

Figure 1: Pharmacists' patient care process

Pharmacists' Patient Care Process

Pharmacists use a patient-centered approach in collaboration with other providers on the health care team to optimize patient health and medication outcomes.

Using principles of evidence-based practice, pharmacists:

Collect
The pharmacist assures the collection of the necessary subjective and objective information about the patient in order to understand the relevant medical/medication history and clinical status of the patient.

Assess
The pharmacist assesses the information collected and analyzes the clinical effects of the patient's therapy in the context of the patient's overall health goals in order to identify and prioritize problems and achieve optimal care.

Plan
The pharmacist develops an individualized patient-centered care plan, in collaboration with other health care professionals and the patient or caregiver that is evidence-based and cost-effective.

Implement
The pharmacist implements the care plan in collaboration with other health care professionals and the patient or caregiver.

Follow-up: Monitor and Evaluate
The pharmacist monitors and evaluates the effectiveness of the care plan and modifies the plan in collaboration with other health care professionals and the patient or caregiver as needed.

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Joint Commission of Pharmacy Practitioners (JCPP) PCP https://jcpp.net/patient-care-process/

Functional Medicine Opportunities in MTMs

Drug-Induced Nutrient Depletions (DIND)

Opportunity to reduce ADR and improve clinical efficacy of medication through nutrient balance

Drug-Herb Interactions

As more and more patients start taking herbs, there's an increased risk for interactions, injury or possibly the opportunity to enhance drug efficacy

Drug-Nutrient Interactions

Reduce interactions and avoid subtherapeutic or supratherapeutic concretions as a result of nutrient interactions

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Drug Induced Nutrient Depletions (DIND)

Factors that impact significance of DIND

Let’s take a quick poll

- ❑ I’m just learning about DIND and haven’t been using it in practice
- ❑ I’ve heard of DIND but haven't been sure how to implement it
- ❑ I’ve been using DIND in some encounters (when medications are involved), but not all
- ❑ I use DIND in almost every patient encounter (when medications are involved)

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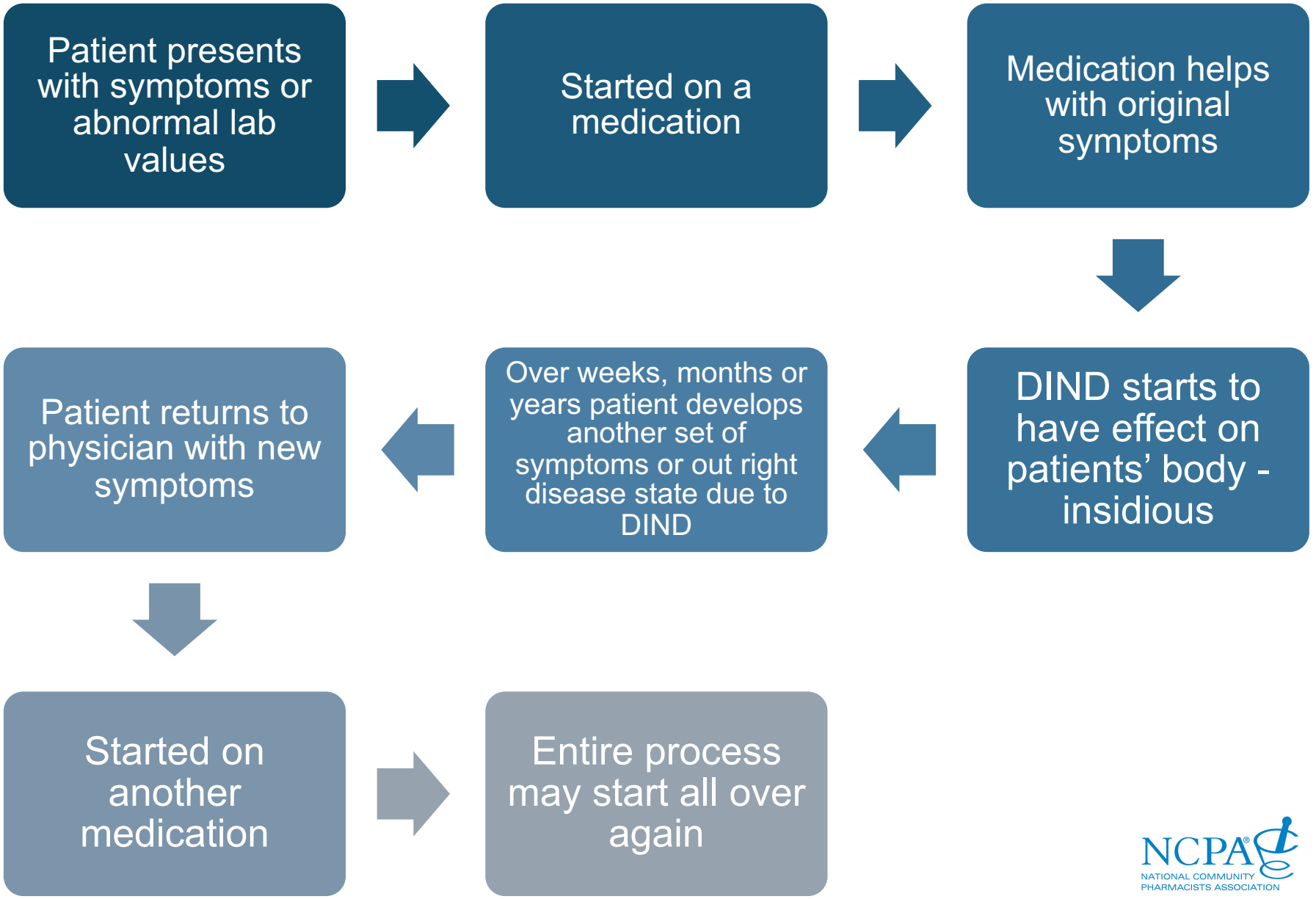
Drug Induced Nutrition Depletion (DIND)

- Medications block or impair the absorption, storage, metabolism, or synthesis of nutrients
- Include direct and indirect mechanisms *(more in a moment)*
- Requires some clinical assessment and interpretation

The DIND Cascade



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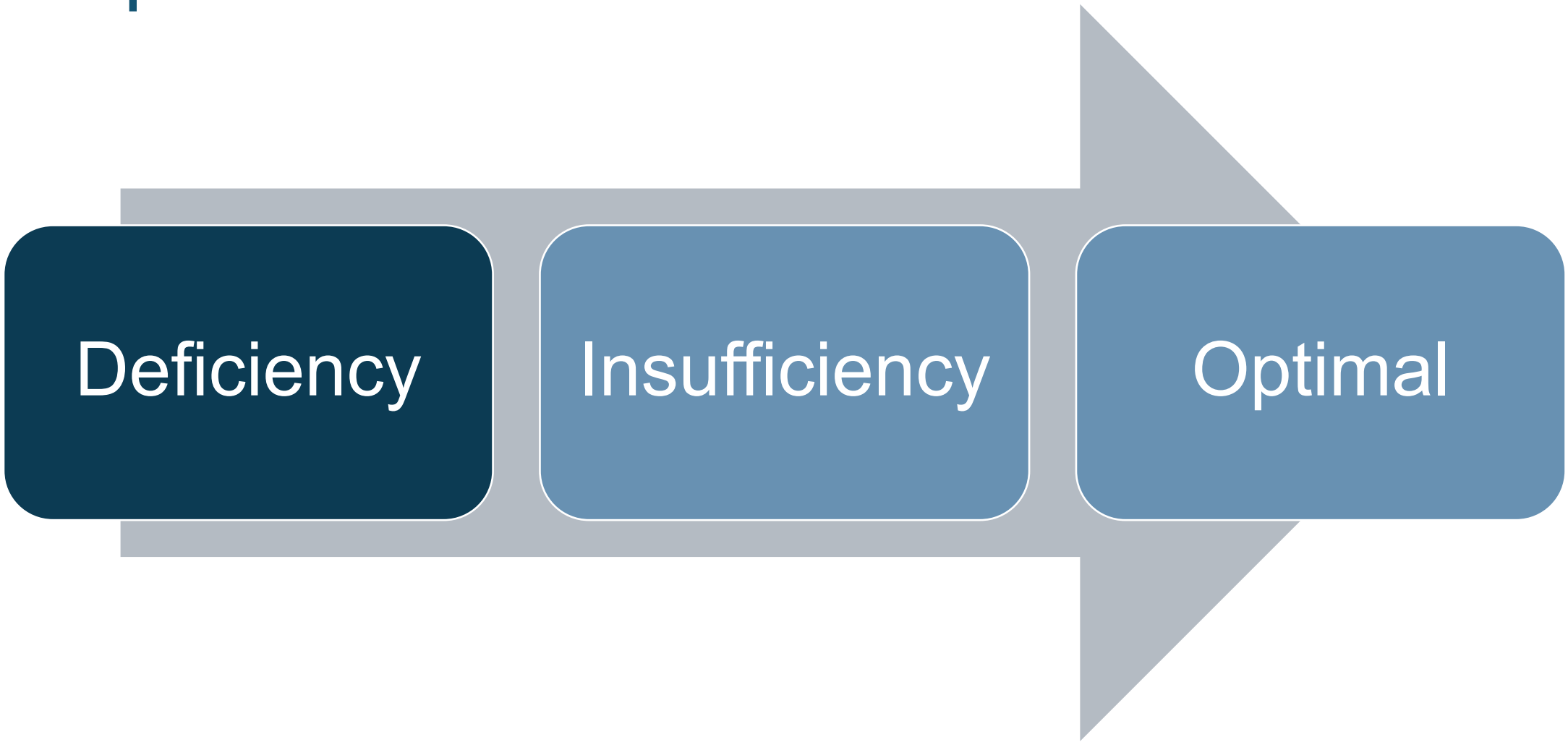
The Spectrum of Nutritional Status



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Factors that Influence DIND

- Patient on a lot of medications (polypharmacy)
- Elderly (altered pharmacokinetics)
- Poor initial nutritional status, deficiencies
- Chronic health conditions (increased physiological demand, altered metabolism)

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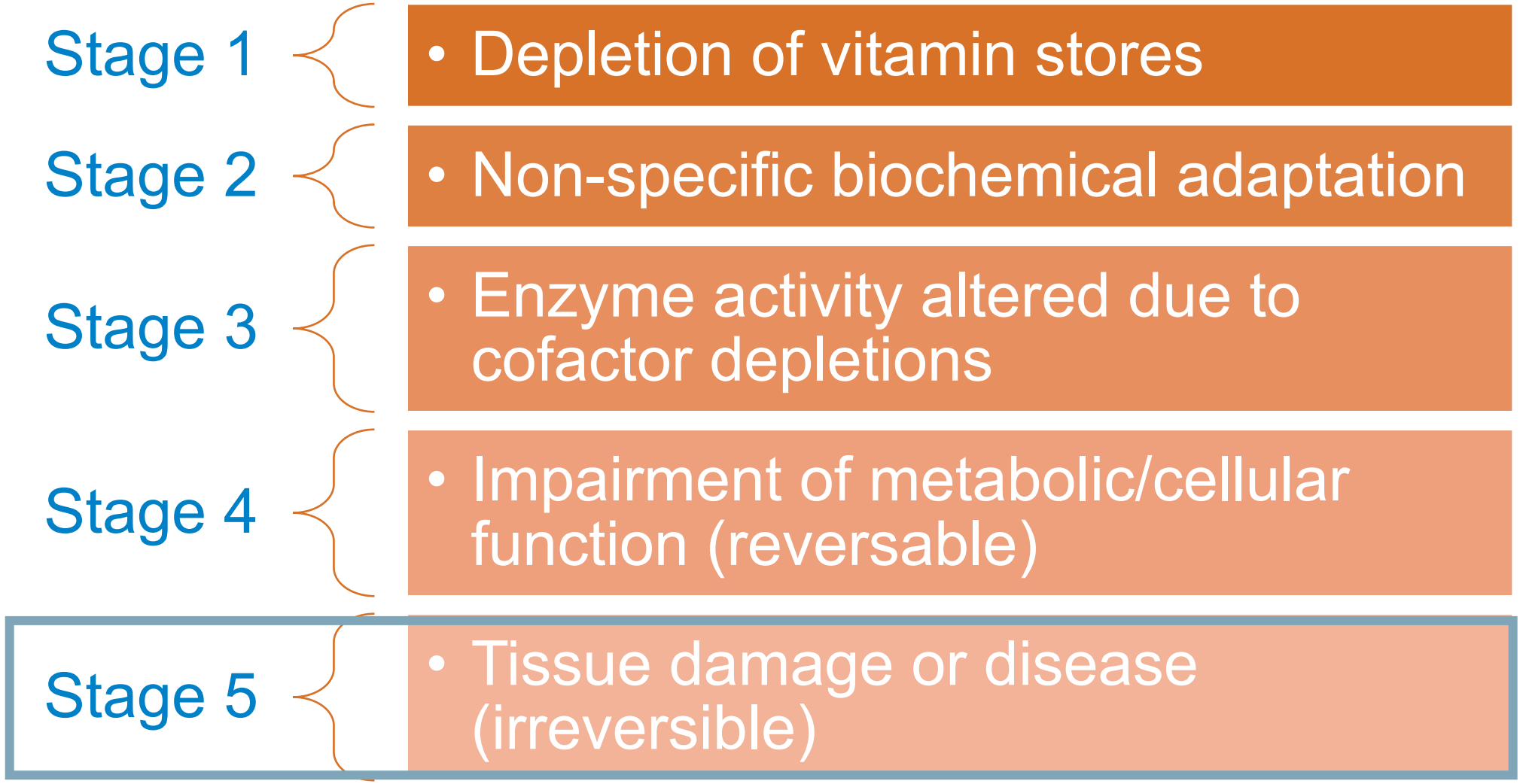
The Continuum of Nutritional Deficiency



J Int Med Res. May 2007:277-289

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Mechanism of Action: DIND

Inhibition of nutrient absorption	PPIs
Inhibition of nutrient synthesis	Statins
Alterations in transport of nutrients membranes across	Metformin
Increase or decrease in metabolism of nutrients	Estrogens
Increase or decrease in excretion of nutrients	ACE Inhibitors
Alteration in the body's ability to store nutrients	Caffeine, Alcohol

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Factors Impacting Nutritional Status

Biological

- Strenuous physical activity
- Chronic diseases
- Trauma or healing
- Metabolic disorders
- Maldigestion/malabsorption
- Genetics and biodiversity

External

- DIND
- Drug- or nutrient-nutrient interaction
- Diet quality
- Exposures
- Climate & geographic location

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DIND Resources

Review Article

Medications and Micronutrients: Identifying Clinically Relevant Interactions and Addressing Nutritional Needs

Journal of Pharmacy Technology
2018, Vol. 34(5) 216–230

DOI: 10.1177/8755122518780742
journals.sagepub.com/home/pmt
SAGE

Jeffery David Prescott, Pha
and Jan Frederik Stevens, P

Abstract

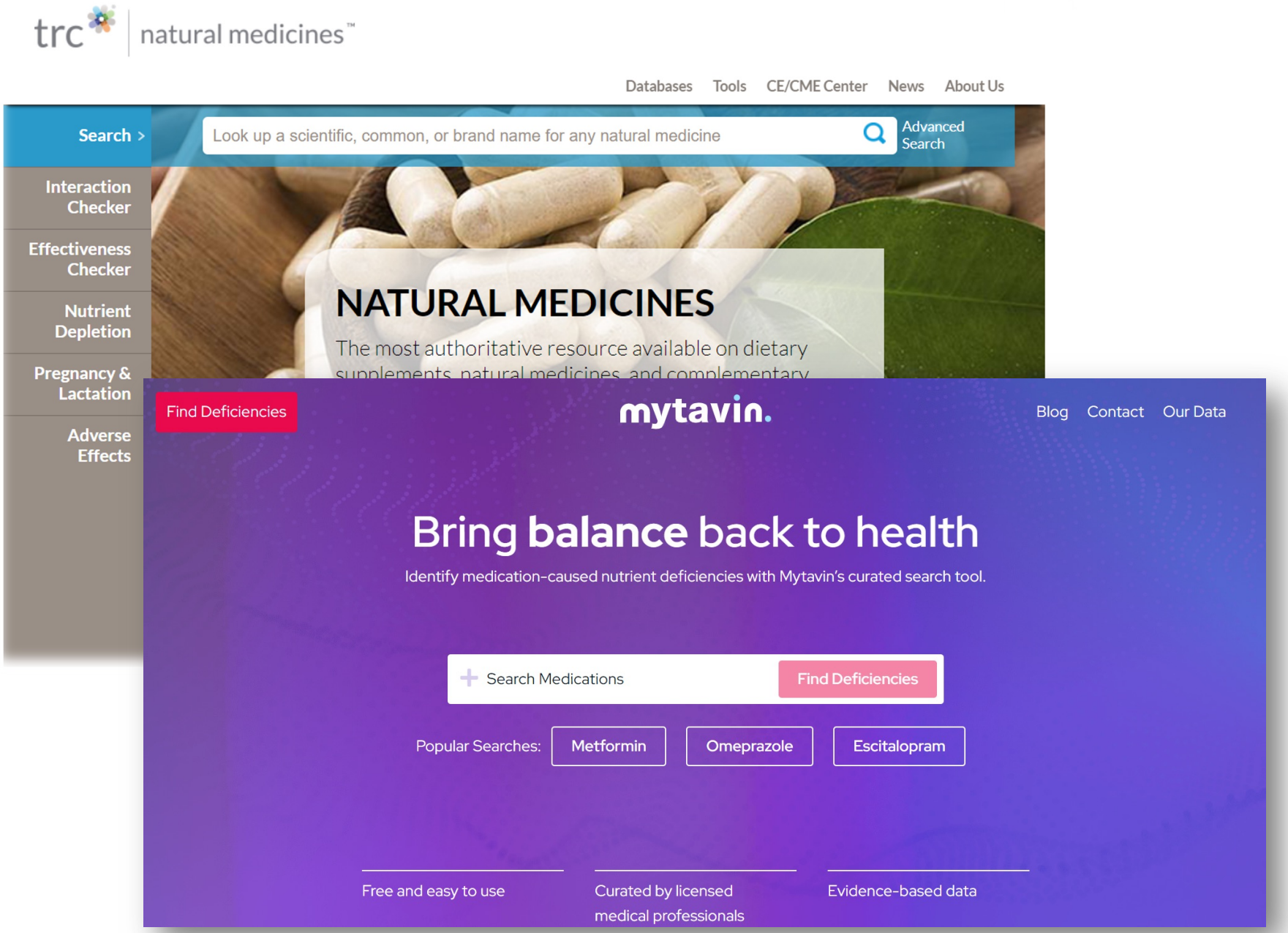
Objective: Prescription drug use is
States, more than half of all adults ta
are becoming an important consider
the literature to identify common ar
in practice. **Data Sources:** A MEDL
performed using search terms (and
Selection and Data Extraction: R
selected for inclusion. **Data Synthe**
even frank deficiencies, thereby neces
supplements. This most often occur
pump inhibitors and histamine-2 rec
may predispose patients to micronut
Drug-nutrient interactions can often
medication or the dietary supplemen
to be discontinued or monitored dur
nutrient interactions with patients an

Table 2. Common Drug-Micronutrient Interactions, Their MOAs, Consequences of the Interaction(s), and Potential Action(s) Required.[11,16,25-34]

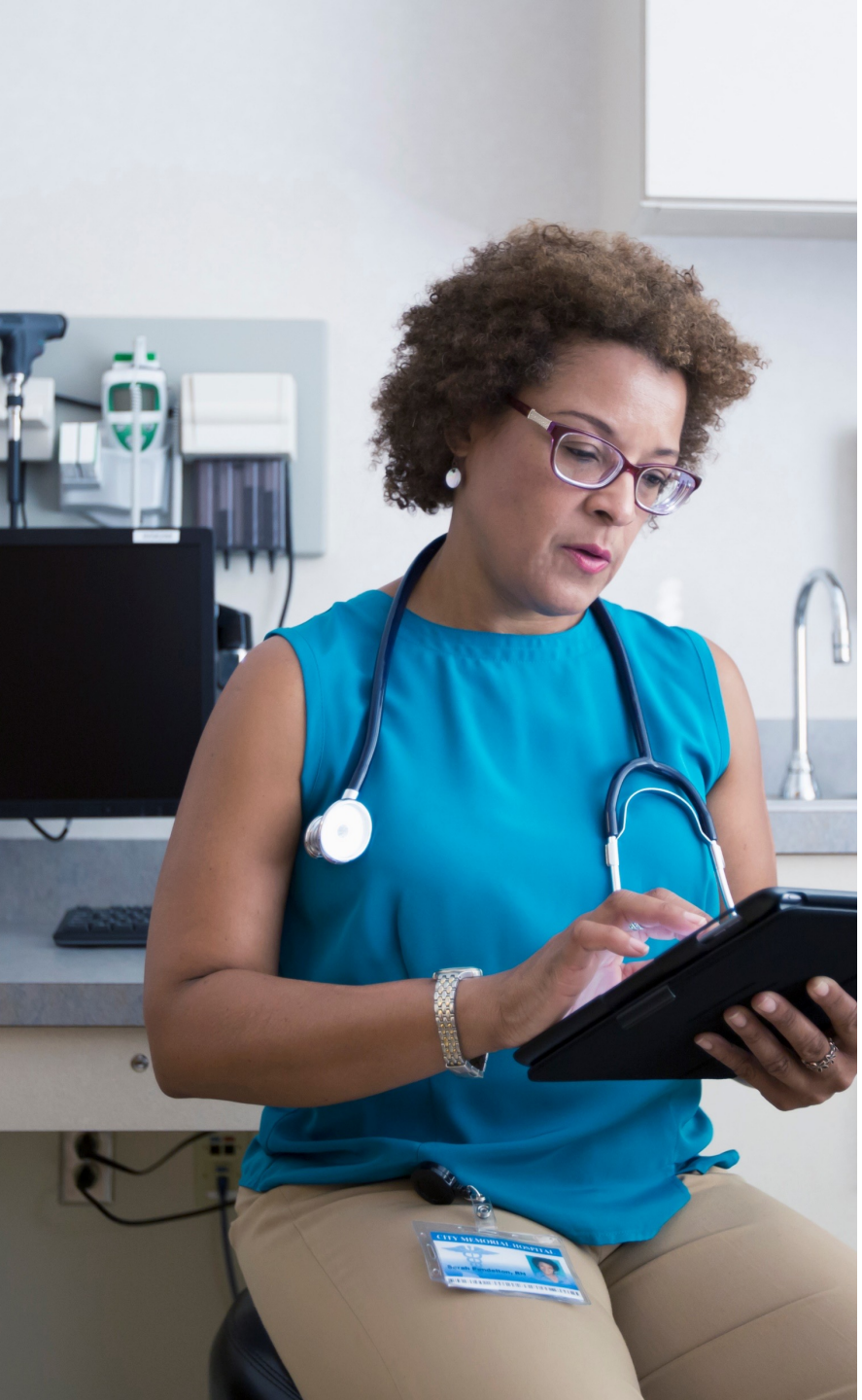
Drug	Micronutrient	MOA	Consequence(s)	Potential Action(s) Required
Antacids and acid reducers				
Antacids containing aluminum/ magnesium hydroxide	Folate, iron, phosphorus	Decreased absorption of folate, iron, and phosphorus	Potential decreased effect of iron or folic acid supplementation if administered concurrently; hypophosphatemia	Take iron or folic acid separately by 2 hours; take calcium citrate separately by 3 hours
Proton-pump inhibitors	Vitamin B_{12}	Increased gastric pH, decreased release of vitamin B_{12} from R-protein, decreased absorption of dietary, but not supplemental, vitamin B_{12}	Vitamin B_{12} deficiency (megaloblastic anemia), hyperhomocysteinemia	Monitor vitamin B_{12} status, supplementation may be needed
	Calcium	Decreased solubility of calcium due to higher gastric pH, potential decreased absorption of insoluble calcium	Reduced bioavailability of insoluble calcium salts	Ensure recommended daily intake of calcium (via diet and/or supplementation) Take calcium carbonate supplements with meals to improve bioavailability Consider use of soluble calcium salts (calcium citrate)
	Iron	Decreased absorption of carbonyl iron	Reduced bioavailability of carbonyl iron-containing supplements	Use an alternative iron supplement
Histamine-2 receptor antagonists	Vitamin B_{12}	Bacterial colonization, decreased absorption of dietary, but not supplemental, vitamin B_{12}	Vitamin B_{12} deficiency	Monitor vitamin B_{12} status with long-term use
	Iron	Iron absorption decreased	Iron status decreased	Take ⩾2 hours before or after iron
Antibiotics				
Penicillins	Biotin, vitamin K	Inhibition of intestinal biotin and vitamin K synthesis	Adverse effects on biotin and vitamin K status	Caution with vitamin K supplementation
	Zinc	Decreased zinc absorption	Zinc status decreased	May need to increase zinc intake
Cephalosporins	Vitamin K	Inhibition of endogenous vitamin K synthesis	Decreased vitamin K status, potentially leading to bleeding abnormalities	May need to increase vitamin K intake
Fluoroquinolones	Calcium, magnesium, zinc, iron	Decreased absorption and bioavailability of drug	Decreased antibiotic efficacy	Take calcium, magnesium, zinc, iron, or MVM supplement at least 2 hours before or 6 hours after
Tetracyclines	Calcium, iron, magnesium, zinc	Formation of complex, decreased absorption of antibiotic	Decreased antibiotic efficacy	Take calcium, iron, magnesium, zinc, or MVM supplement separately by 3 hours before or 1 hour after drug
	Vitamin C	Increased renal vitamin C excretion	Decreased WBC vitamin C status	Take vitamin C supplement
Trimethoprim-sulfamethoxazole	Folate	Inhibitory effect on dihydrofolate reductase	Folate deficiency	May need folic acid supplementation, particularly pregnant women
Antidiabetics				
Metformin	Vitamin B_{12}	Inhibition of calcium-dependent receptor-mediated endocytosis of the IF-B_{12} complex (impaired absorption)	Vitamin B_{12} deficiency (megaloblastic anemia), hyperhomocysteinemia	Monitor vitamin B_{12} status

J Pharm Technol. 2018;34(5):216-230
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6109862/pdf/10.1177_8755122518780742.pdf

More DIND Resources



https://naturalmedicines.therapeuticresearch.com/
https://mytavin.com/



The *art* of DIND assessment

- Lack of research/data *(especially on newer drugs)*
- Bio-individual variables
- Just because someone is on a medication, we can't assume they're depleted (it's a function of many factors)

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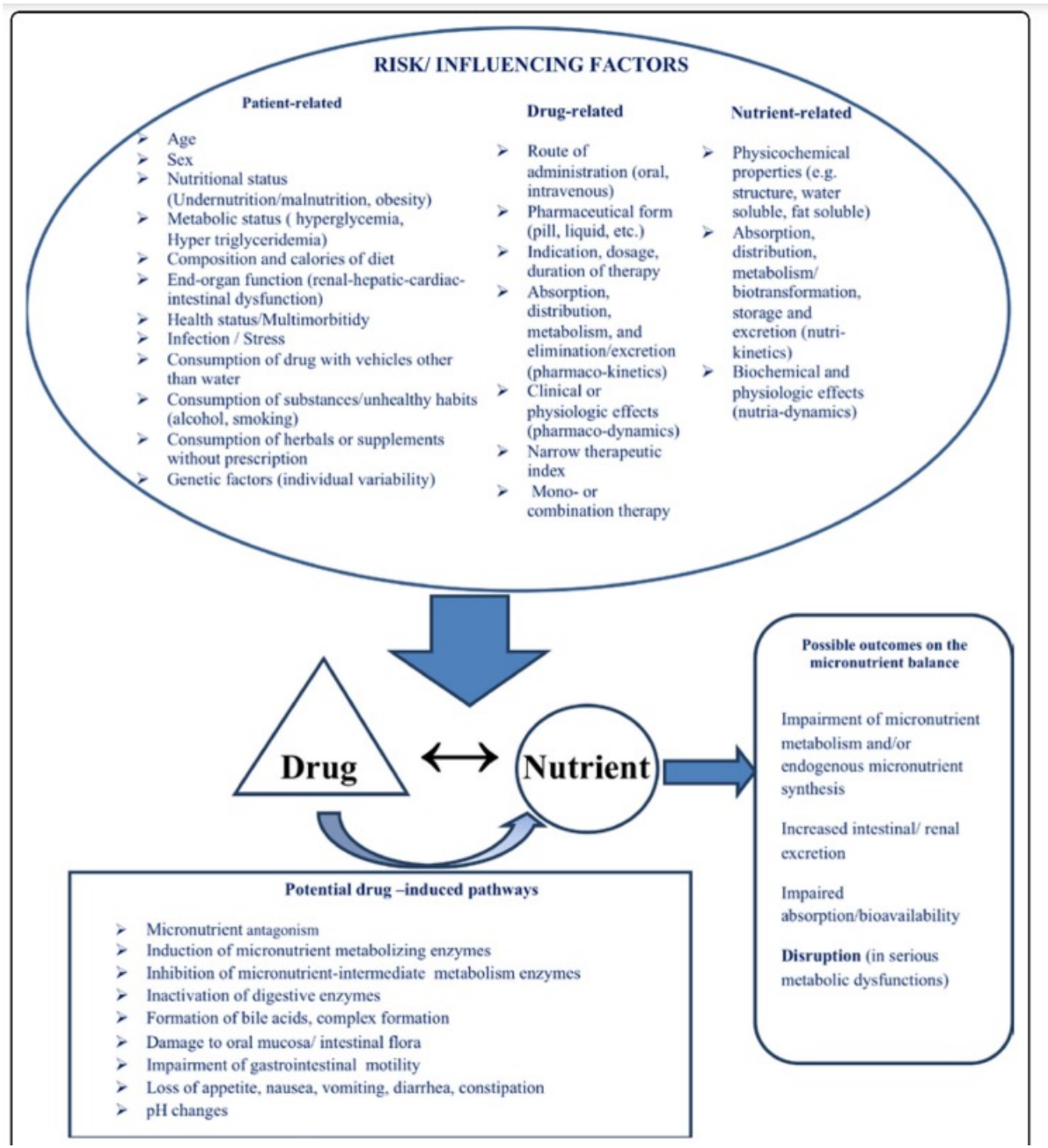
DNI

Drug-Nutrient Interactions

Relationship of drug-nutrient interactions (DNI)

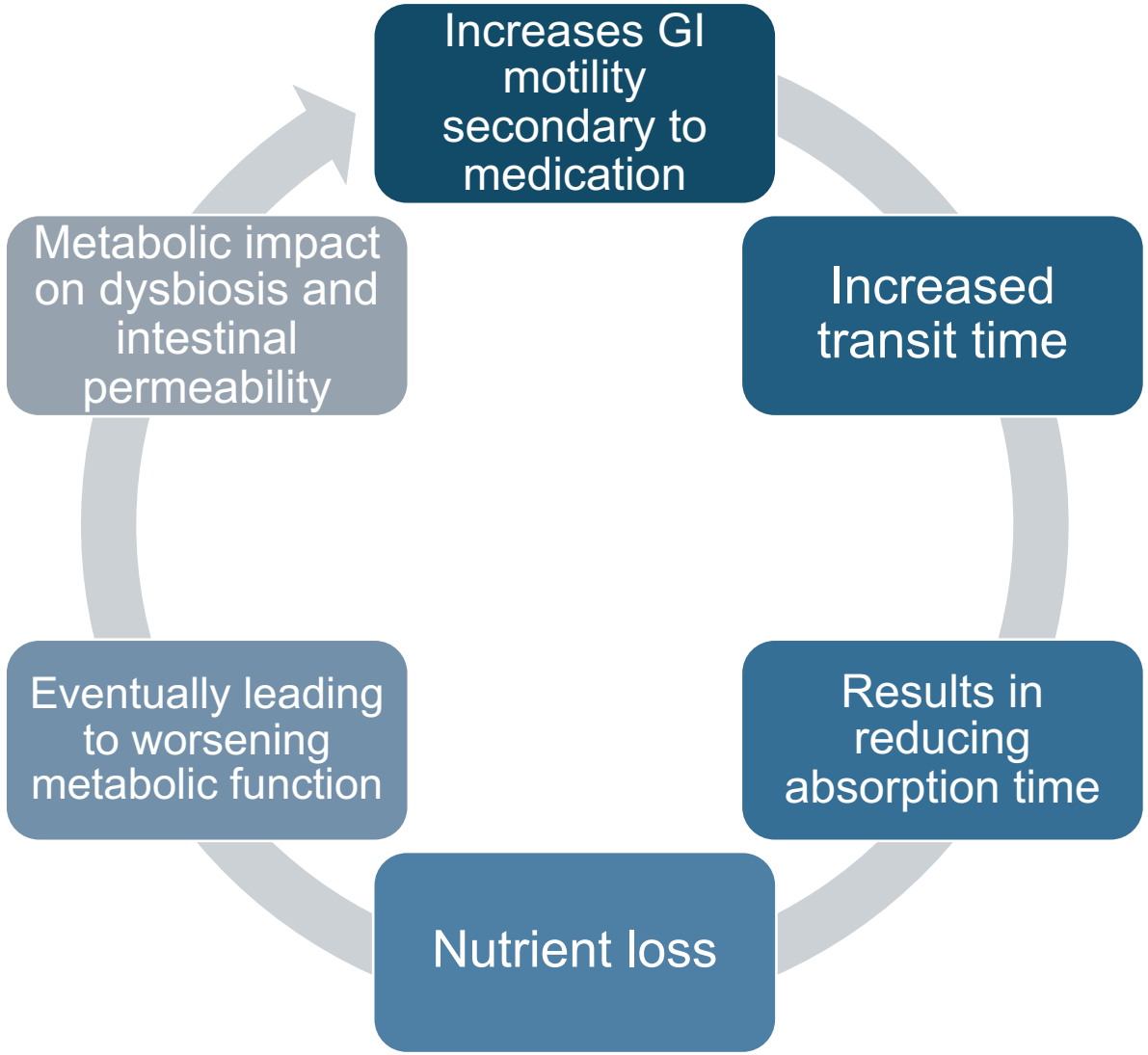
Bidirectional in their outcomes

Drugs influence intestinal absorption, cellular bioavailability



J Pharm Technol. 2018;34(5):216-230

Example of drug-nutrient interaction: **Metoclopramide**



J Pharm Technol. 2018;34(5):216-230

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Mechanisms & Examples of DNI

Alteration in digestive environment

- Fatty foods → increase drug absorption of some lipid soluble drugs
- Stimulating/ increasing bile or splanchnic blood flow
- E.g. Some antiretroviral protease inhibitors (e.g., saquinavir and atazanavir)

Altering the gut flora

- Through mechanical or physiological mechanisms
- E.g. Vitamin K deficiency with antibiotic use
- E.g. Beneficial impact of pre/probiotics with antibiotics

Forming irreversible or insoluble complex

- Resulting in reduced bioavailability
- E.g. Phenytoin is bound by proteins in food products
- E.g. Tetracyclines and fluoroquinolones can bind to divalent cations
- E.g. Levofloxacin with iron and magnesium

Alteration in gastrointestinal pH

- Gastric pH is elevated due to buffering and diluting effect of the food
- Bioavailability of many drugs altered including drug release, solubility, chemical stability, charge state, and/or intestinal permeability
- E.g. Ciprofloxacin should be taken on an empty stomach and Griseofulvin should be taken with food (fat-soluble)

Enzyme induction/ inhibition (CYP450 enzymes)

- 6 main CYP enzymes: 1A2, 2C9, 2C19, 2D6, 2E1, and 3A4
- E.g. Statins and grapefruit inhibits CYP3A4, CYP1A2 is induced by cruciferous vegetables and barbecued or charbroiled food, and CYP3A4 is inhibited by grape juice

Am J Ther. 2018;25(4):e423-e433. | Alan RG; A-Z Guide to Drug-Herb-Vitamin Interactions

Nutritional Compounds with Significant

Tyramine – containing foods

- Cheese, wine, sausages, salami, soy sauces
- Indirectly acting sympathomimetic agent degraded by MAO
- In the presence of monoamine oxidase inhibitors (MAOIs) it can lead to a hypertensive crisis

Vitamin K – rich foods

- Green leafy vegetables, spring onions, brussels sprouts, kale, spinach, parsley, and broccoli
- Affect vitamin K metabolism and elevate the risk of bleeding or clot formation
- Large quantities of or sudden changes to vitamin K intake not advised for those taking warfarin

Dairy products

- Rich sources of divalent ions, such as calcium and magnesium that complex with some drugs
- Impacts
  - Antibiotics – fluoroquinolones, tetracycline
  - Mercaptopurine
  - Laxatives

Grapefruit (juice)

- Furanocoumarins in grapefruit have a major inhibitory effect on the CYP450 enzyme system
- Drug Interactions:
  - Statins
  - Calcium Channel Blockers
  - Oral contraceptives
  - Estrogen
  - Anti-psychiatric meds

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Am J Ther. 2018;25(4):e423-e433.

It’s all about timing

Timing medications on an empty stomach or away from food/supplements

TRE/IF – use shorter window to eat (challenge with Rx that must be taken with food)

J Pharm Technol. 2018;34(5):216-230.

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DHI

Drug-Herb Interactions

Herbal Dietary Supplement Sales

In 2020 US Consumers **spent $11 billion** on supplements

In 2021 supplement market grew 7.5%, adding $4.15 billion in sales → **at $59.91 billion** (over $5 billion more than pre-COVID projections from 2019)

The industry is expected to add nearly another $10 billion through 2025

The global market for Dietary Supplements is estimated at $155.2 billion in 2022 and is projected to grow at a CAGR of 7.3% to reach $220.8 billion by 2027

American Botanical Council's (ABC's) 2020 Herb Market Report https://www.herbalgram.org/news/press-releases/2021/record-breaking-us-herbal-supplement-sales-increase-in-2020/
Nutrition Business Journal's Supplement Business Report 2022 https://www.prnewswire.com/news-releases/supplement-market-more-than-5b-higher-than-pre-pandemic-expectations-according-to-nutrition-business-journals-2022-supplement-business-report-301563200.html

We have to ask the right questions

30% of Americans are using at least one herbal supplement

25% of herbal supplement users regularly take prescribed drugs

40% of patients disclose using herbal supplement to their health care providers

Medicines (Basel). 2021;8(8):44.
Pharmaceutics. 2021;13(5):610.
Front Pharmacol. 2012;3:69.

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Herbal Active Constituents

Phenolics (tannins, lignins, quinolones, salicylates)	Phenolic glycosides (flavonoids, cyanogens, glucosinolates)	Terpenoids (sesquiterpenes, steroids, carotenoids, saponins, iridoids)	Alkaloids
Peptides	Polysaccharides (gums, mucilage)	Resins	Essential oils

Front Pharmacol. 2012;3:69
Altern Ther Health Med. 2022;28(2):70-77.

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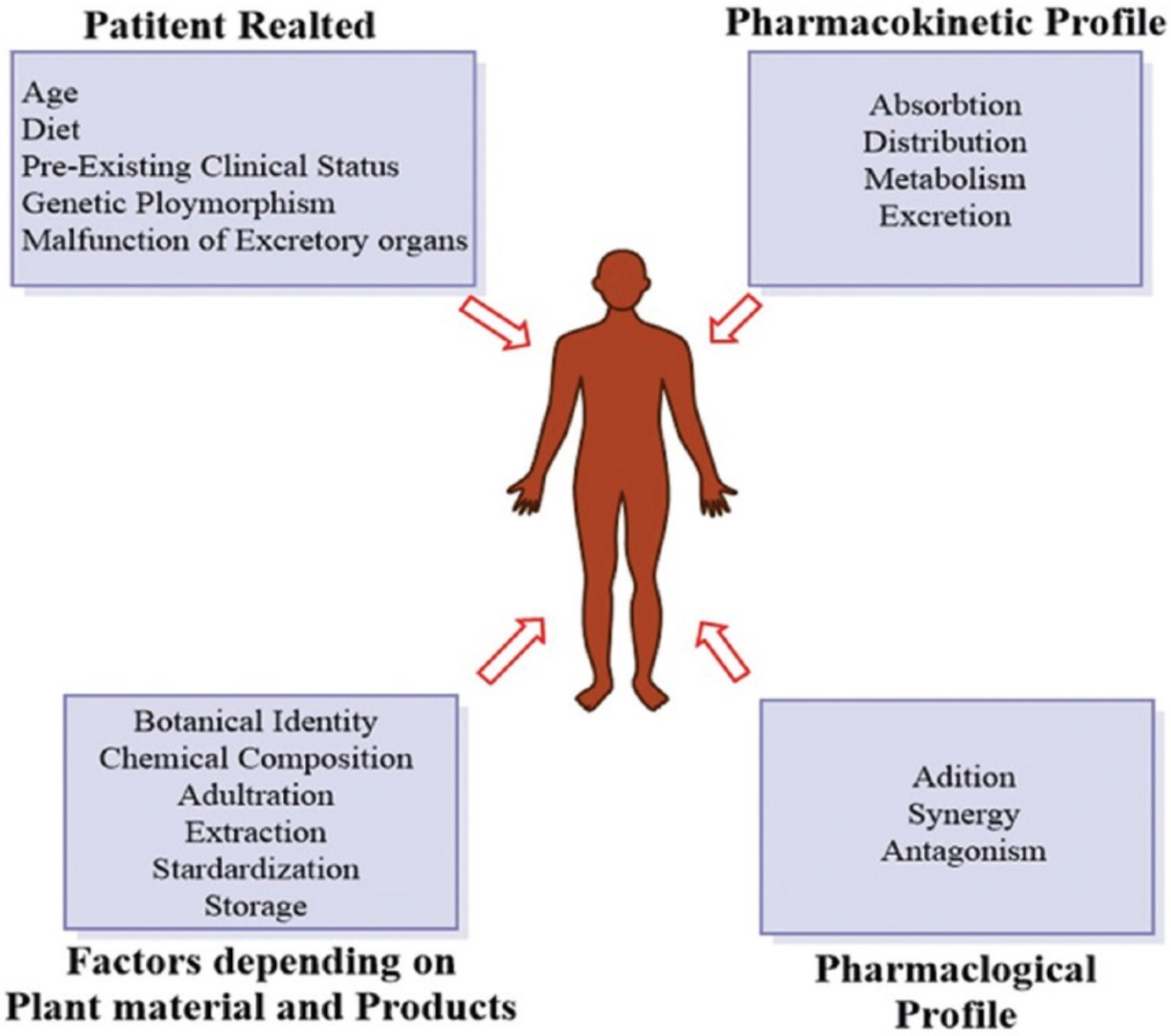
Risk factors that increase risk for DHI

Figure 1. Important risk Factors involved in Occurrence of Herbal-Drug interactions.



Altern Ther Health Med. 2022;28(2):70-77

Biotransformation Considerations in DHI

Most common mechanism

- Herbs can alter pharmacokinetic or pharmacodynamic (PK/PD) of a drug
- PK = What the body does to drugs and how fast it does it
- PD = what a drug does to the body

Herbs can increase drug metabolism

- Might result in therapeutic failure
- Impact depends on drug's therapeutic window

Herbs that decrease a drug's metabolism

- Leads to more adverse effects to elevated medication
- Also depends on therapeutic window
- Pro-drugs: Might also cause therapeutic failure (inhibit pro-drugs activation)

Many herbs induce or inhibit CYP450 enzymes

- Phase I detoxification
- Heavily concentrated in the liver and intestines (think site of detoxification)

Australas Med J. 2015;8(10):315-319.
Front Pharmacol. 2012;3:69.

DHI Mechanisms

- Induction or inhibition of metabolic enzymes
- Inhibition or induction of transport and efflux proteins
- Alteration of gastrointestinal functions
- Alteration in renal or hepatic elimination
- Pharmacodynamics: Synergy, addition, and antagonism

The literature on herb-drug interactions

- Lacking in sufficient clinical studies
- In vitro doesn't always translate to clinical practice
- Most of the human data available are case reports (weak sources) and often skewed towards risk (introducing bias)
- Seldom include perspective outside of current medical culture

Medicines (Basel). 2021;8(8):44.

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St. John's wort *(Hypericum perforatum)*

Potent inducer of CYP3A4 and P-glycoprotein

- Can reduce the AUC of a CYP450 substrate by up to 80%

Reduces the plasma concentration of MANY drugs

- **Antidepressants**
- Antihypertensives
- Bronchodilators
- NSAIDs
- Oral contraceptives
- Statins
- Benzodiazepines
- Immunosuppressants
- HIV protease inhibitors

https://www.nccih.nih.gov/health/ginkgo

Australas Med J. 2015;8(10):315-319.

Front Pharmacol. 2012;3:69

J Food Drug Anal. 2018;26(2S):S26-S31.

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Example Potential DHI: St John's Wort

Table 4. Potential drug-HDS and non-HDS interactions

Herb	Interacting drug	No. of interactions	Interaction severity[a]	Quality of documentation regarding interaction[a]	Description of interaction
St. John's wort	SSRIs	1	*MAJOR*	*Fair*	Increased risk of serotonin syndrome
	Oral contraceptives	2	*MAJOR*	*Good*	Decreased contraceptive effectiveness
	Benzo-diazepines	1	*Minor*	*Fair*	Reduced benzodiazepine effectiveness
	Statins	1	*Moderate*	*Fair*	Reduced atorvastatin & simvastatin effectiveness

Advances in Patient Safety: New Directions and Alternative Approaches (Vol. 4: Technology and Medication Safety)
https://www.ncbi.nlm.nih.gov/books/NBK43772/

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Clinical Considerations

“Thinking Outside the Vial”

Can we capitalize on therapeutic DHI?

Positive synergy

- Interactions could be used to reduce cost and ADR
- Can have synergistic pharmacodynamic benefit, reducing dose or need for medications
- Can modify CYP clearance leading to reduce drug dose (increase efficacy at lower dose due to reduced clearance)

Examples

- NSAIDs and polyphenols like resveratrol and curcumin
- Black pepper in g-glycation may reduce drug resistance, enhance effectiveness, and bioavailability of certain chemo agents

Front Cell Dev Biol. 2018;6:10
J Med Food. 2018;10.1089/jmf.2017.4176
Council for International Organizations of Medical Science

Resveratrol Enhances pain relief **in combination** with meloxicam (double-blind RCT)

110 men and women (45–75 years old) diagnosed with mild to moderate knee OA were treated with 15 mg per day meloxicam and either 500 mg per day resveratrol or placebo for 90 days in a double-blind, randomized control trial

Pain severity was evaluated at the beginning and at the end of treatment using Visual Analogue Scale-100 scores. Fasting blood was collected to determine serum IL-1β and IL-6, TNF-α, hsCRP, and complement proteins C3 and C4.

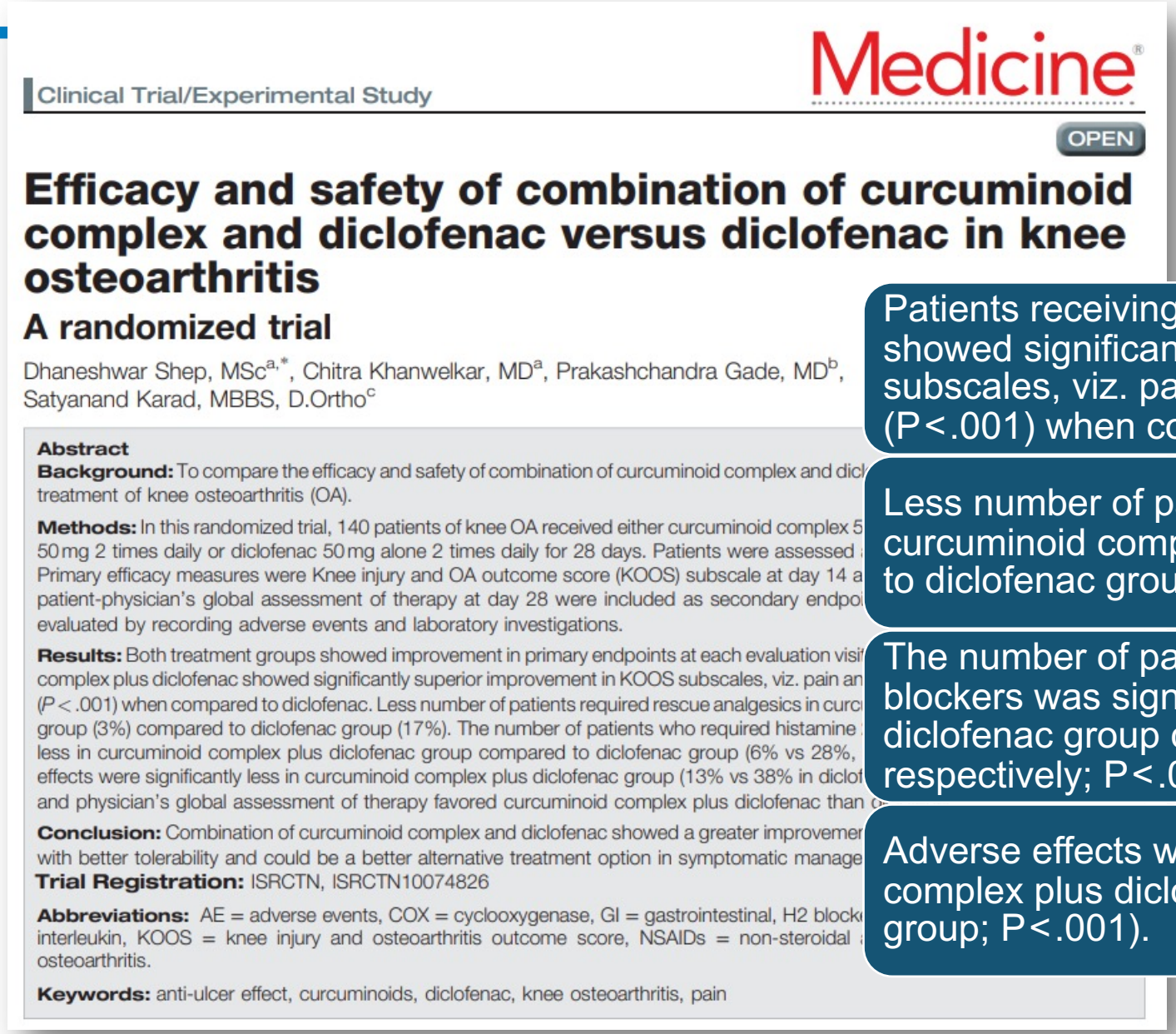
500 mg of resveratrol enhanced NSAID (meloxicam) to reduce pain and inflammation compared to control with statistical significance. Resveratrol mechanism of action involves the inhibition of production of COX-2 and PGE2

J Med Food. 2018;10.1089/jmf.2017.4176. doi:10.1089/jmf.2017.4176

Impact on Inflammatory Markers

TNF-α	Resveratrol significantly decreased serum levels of the pro-inflammatory cytokine TNF-α in patients with knee OA treated with meloxicam for 12 weeks ($P < .05$). TNF-α in the group treated with meloxicam alone showed nonsignificant elevation ($P > .05$).
IL-1β and IL-6	Treatment with resveratrol in supplementation with meloxicam also resulted in a significant reduction in the serum levels of IL-1β and IL-6 after 90 days
C3/C4	Combination of resveratrol + meloxicam significantly decreased the serum levels of complement proteins C3 and C4 ($P < .05$) after 12 weeks of treatment compared with the baseline values of the same group and the values of the group treated with meloxicam alone
CRP	90-day treatment with resveratrol + meloxicam significantly decreased serum hs-CRP levels compared with both the baseline values and the levels of the corresponding group that used meloxicam alone ($P < .05$).
VAS-100 Score	Patients reported significant decreases in pain severity after 30 days of using resveratrol, reaching maximum improvement after 60 days compared with baseline.

J Med Food. 2018;10.1089/jmf.2017.4176. doi:10.1089/jmf.2017.4176



Clinical Trial/Experimental Study

Medicine

OPEN

Efficacy and safety of combination of curcuminoid complex and diclofenac versus diclofenac in knee osteoarthritis

A randomized trial

Dhaneshwar Shep, MSc[a,*], Chitra Khanwelkar, MD[a], Prakashchandra Gade, MD[b], Satyanand Karad, MBBS, D.Ortho[c]

Abstract

Background: To compare the efficacy and safety of combination of curcuminoid complex and dicl treatment of knee osteoarthritis (OA).

Methods: In this randomized trial, 140 patients of knee OA received either curcuminoid complex 5 50 mg 2 times daily or diclofenac 50 mg alone 2 times daily for 28 days. Patients were assessed Primary efficacy measures were Knee injury and OA outcome score (KOOS) subscale at day 14 a patient-physician's global assessment of therapy at day 28 were included as secondary endpo evaluated by recording adverse events and laboratory investigations.

Results: Both treatment groups showed improvement in primary endpoints at each evaluation visi complex plus diclofenac showed significantly superior improvement in KOOS subscales, viz. pain an ($P < .001$) when compared to diclofenac. Less number of patients required rescue analgesics in curc group (3%) compared to diclofenac group (17%). The number of patients who required histamine less in curcuminoid complex plus diclofenac group compared to diclofenac group (6% vs 28%, effects were significantly less in curcuminoid complex plus diclofenac group (13% vs 38% in diclof and physician's global assessment of therapy favored curcuminoid complex plus diclofenac than

Conclusion: Combination of curcuminoid complex and diclofenac showed a greater improvemer with better tolerability and could be a better alternative treatment option in symptomatic manage

Trial Registration: ISRCTN, ISRCTN10074826

Abbreviations: AE = adverse events, COX = cyclooxygenase, GI = gastrointestinal, H2 block interleukin, KOOS = knee injury and osteoarthritis outcome score, NSAIDs = non-steroidal osteoarthritis.

Keywords: anti-ulcer effect, curcuminoids, diclofenac, knee osteoarthritis, pain

Patients receiving curcuminoid complex plus diclofenac showed significantly superior improvement in KOOS subscales, viz. pain and quality of life at each study visit (P<.001) when compared to diclofenac.

Less number of patients required rescue analgesics in curcuminoid complex plus diclofenac group (3%) compared to diclofenac group (17%).

The number of patients who required histamine 2 (H2) blockers was significantly less in curcuminoid complex plus diclofenac group compared to diclofenac group (6% vs 28%, respectively; P<.001).

Adverse effects were significantly less in curcuminoid complex plus diclofenac group (13% vs 38% in diclofenac group; P<.001).

Medicine (Baltimore). 2020;99(16):e19723.

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In your MTM a patients reports insufficient pain management on NSAID

Positive DHI/DNI*

- Combine with polyphenols like resveratrol and/or curcumin
- Council on anti-inflammatory diet including …
- Sources of anti-inflammatory fats and microbiome-modulating fiber-dense, colorful f/v

**Short list of examples*

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Clinical Considerations

- Education on the mechanisms of herbs and potential drug interactions
- Prioritizing patient education – *limit our own bias!*
- Bio-individual variations and environmental factors
- Weight clinical significance
- Build collaborative are teams (prescriber/clinician + Nutrition professional + pharmacist relationships)
- More (and better) studies on herbal-drug interactions are needed - for both positive as well as safety data

Resources for DHI/DNI

Natural Medicine Database https://naturalmedicines-therapeuticresearch-com

Alan R. Gaby, MD *A-Z Guide to Drug-Herb-Vitamin Interactions* – available on Amazon https://www.amazon.com/Guide-Drug-Herb-Vitamin-Interactions-Revised-Expanded/dp/0307336646

Integrative Pro Drug-Nutrient Interaction Checker https://www.integrativepro.com/drug-nutrient-interaction-checker

Lexicomp https://www.wolterskluwer.com/en/solutions/lexicomp/lexicomp

Memorial Sloan Kettering Cancer Center- AboutHerbs website

Stokely's Herbal Drug Interactions text https://www.pharmpress.com/product/9780857110268/stockleys-herbal-medicines-interactions

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De-escalation Case Study: PPI

Case: Ms Goodgut

Proton Pump Inhibitors (PPIs)

Available PPIs Rx and OTC (various potencies)

- Omeprazole
- Pantoprazole
- Lansoprazole
- Dexlansoprazole
- Esomeprazole
- Rabeprazole

Uses:

- GERD
- Peptic ulcers
- Dyspepsia
- Stress ulcer prophylaxis

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Consequences of chronic PPI use

Microbiome Changes

- Increased risk of *C. difficile* infection
- Small Intestinal Bacterial/Fungal Overgrowth (SIBO/SIFO)

Micronutrient malabsorption

- **Most significant**
  - **Magnesium**
  - **B12**
- Less significant/lower level of evidence
  - Calcium
  - Folate
  - Iron
  - Zinc (important for mucosal integrity)

Other complications

- Increased risk of demineralization and bone fracture
- Increased CV risks
- Increased risk of dementia
- Increased risk of IBD
- Increased risk of community acquired pneumonia (CAP) and COVID-19 infection
- Rebound acid hypersecretion (RAHS)
- Various ADRs (ranging in significance from GI symptoms to acute nephritis)

DIND

Ther Adv Drug Saf. 2018;10:2042098618809927
TRC Natural Medicine Database
Guiliams TG. Supplementing Dietary Nutrients. Point Institute 2017

PPI Deprescribing Framework Through a FxMed Lens

Assess and address

- Assess potential risks of both continuation and escalation
- Address nutritional gaps (including DIND) and DHI/DNI if appropriate

Apply foundational support

- If the patient expresses interest in de-escalation or deprescribing, assess willingness to adhere to lifestyle changes
- Introduce nutraceuticals to support GI based on assessment

Initiate De-escalation

- Slow taper PPI over 2-6 weeks (higher dose, longer duration of therapy requires longer taper)
- Consider step-down to lower dose PPI and/of H2A and other antacids for symptom control
- Use clinical judgment to determine if it's appropriate to initiate 5R protocol

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Start with Nutrition & Lifestyle

Eliminate triggers

- Focus on a nutrient-dense, anti-inflammatory “rainbow” diet
- Caffeine, alcohol, spicy food, garlic, onions, fried foods are common triggers in GERD and GI irritants
- Elimination diet (consider IgG sensitivities, IgE-mediated triggers, FODMAPs)

Review meal habits

- Avoid multitasking
- Avoid large meals, especially too close to bedtime
- Slow down and chew
- Avoid drinking water with meals

Lifestyle modifications

- Smoking cessation
- Stress management
- Support the Migrating Motor complex (MMC) and vagal nerve
- Work on sleep and circadian rhythm

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Factors That Might Aggravate GERD

Medications	Supplements	Foods/beverages	Lifestyle factors
• Anticholinergics • Benzodiazepines • TCAs • Theophylline • Prostaglandins • Calcium channel blockers • Alpha-adrenergic blockers, beta-blockers • Nitrates • Phosphodiesterase inhibtors • Progesterone • Steroids • NSAIDs • Bisphosphonates • SR potassium	• Arginine (NO2 stimulation) • Carmitive herbs (peppermint, spearmint)	• Alcohol • Chocolate • Coffee/caffeine/tea • Milk • Fatty foods/fried foods • Acidic juice (orange, tomato) • Spicy food	• Stress (anxiety) • Smoking

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Consider a comprehensive 5R GI Protocol

Remove	• Food sensitivities, alcohol, aspirin, NSAIDS from the diet. • Use antimicrobials for dysbiosis, infection, and/or parasites.
Replace	• Digestive support to improved nutrient absorption and metabolism • May include digestive enzymes, or agents that promote improved motility and regular bowel movements.
Reinoculate	• Provide an environment where good bacteria can thrive and where bad ones cannot • Use pre- and probiotics.
Repair	• Support of the cellular repair process by providing specific nutritional support for the regeneration of the GI protective barrier • GI mucosa with healing nutrients and botanicals
Rebalance	• Lifestyle factors that influence the gut bacteria such as stress, sleep, exercise and relationships and assure ongoing gut health

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PPI Support Considerations

Gastric secretion/LES	• **Melatonin** • **5-HTP, or Tryptophan** (melatonin precursor) + B6 for activation
Bitters/motility agents	• **Globe Artichoke leaf** (least bitter), **Yarrow, Gentian, Wormwood** (most bitter, antimicrobial activity) • **Iberagast** 1 ml TID
Digestive enzymes	• **Betaine HCL** tapper 500mg-2000mg with meals (protein) • Broad spectrum digestive enzymes with bromelain and papain
Nutrients	• Evaluate and rebalance DIND like **B12** and **magnesium** • **Zinc carnosine** (PepZinGI®) especially useful for GERD and barrier integrity repair dosed at 150mg/day (2 divided doses)
Microbiome & barrier integrity	• **Glutamine** 5-10 grams QD-TID • **Serum Bovine-derived immunoglobulins** 5-15 gm daily or **Whey protein with concentrated immunoglobulins**: 15-30 grams daily • Prebiotics and polyphenols • Probiotics (*Lactobacillus* and *Bifidobacterium* most commonly studied)
Demulcents	• **Deglycyrrhizinated licorice (DGL)** 150-300mg as needed for symptom management [500-1000mg/day TID to QID] • **Slippery elm** (*Ulmus fulva*) 2-4 grams TID • **Marshmallow** (*Althaea officinalis*) 2-5 grams daily in divided doses • **Mastic gum** 1-3g/day in divided doses between meals • **Bismuth citrate** 250mg/day in divided doses
Bioflavonoids	• **Quercitin** 200-1000 mg TID • **Rutin** 200-1000 mg TID
Anti-inflammatory herbs	• **Chamomile** (Matricaria recutita) prepared as a hot water infusion of 1-3g of the flower, QID • **Ginger** (Zingiber officinale) standardized to gingerols 200-500 mg TID • **Turmeric** (Curcuma longa) standardized to curcuminoids 200-1000 mg TID • **Green tea** (Camellia sinensis) standardized to catechins 100-300 mg TID • **Boswellia** (Boswellia serrata) standardized to boswellic acids 300-400 mg TID

Guilliams, TG. *Functional Strategies for the Management of Gastrointestinal Disorders*. 2016. The Roadmap Series. Point Institute.

Rakel, & Minichiello, V. J. (2023). Integrative medicine (Rakel & V.Minichiello, Eds.; Fifth edition.). Elsevier.

Wolf MM. Proton pump inhibitors: Overview of use and adverse effects in the treatment of acid related disorders. UpToDate July 2022.

Nutrients. 2020;12(3):665

Initiate PPI Taper: Consider

Indications for remaining on PPIs

- Grade C/D erosive gastritis
- Barrett's esophagus
- Esophageal strictures from GERD
- Zollinger-Ellison syndrome
- Gastroprotection in those at high risk for GI bleeding
- Prevention of idiopathic pulmonary fibrosis
- Eosinophilic esophagitis

Other considerations

- Hiatal Hernia (> 3 cm)
- Gastrin (>300 pg/mL)
- Gastroparesis
- Uncontrolled Stress

Potency, Duration & Frequency

- Higher potency PPI
- Duration of use >5 years
- Frequency of PPI use (e.g., BID vs QD vs PRN)

Gradual reduction/taper seems to yield best outcomes for successful discontinuation

- Allows for adaptation for cells controlling HCL production
- H2a antacids might be useful for reflux symptom control during this period
- DGL might be helpful for managing symptoms PRN

Guilliams, TG. *Functional Strategies for the Management of Gastrointestinal Disorders*. 2016. The Roadmap Series. Point Institute
Rakel D. *De-prescribing Proton Pump Inhibitors*. Clinical Practice Update. 2022.

PPI Deprescribing guide (Canadian Family Physician)

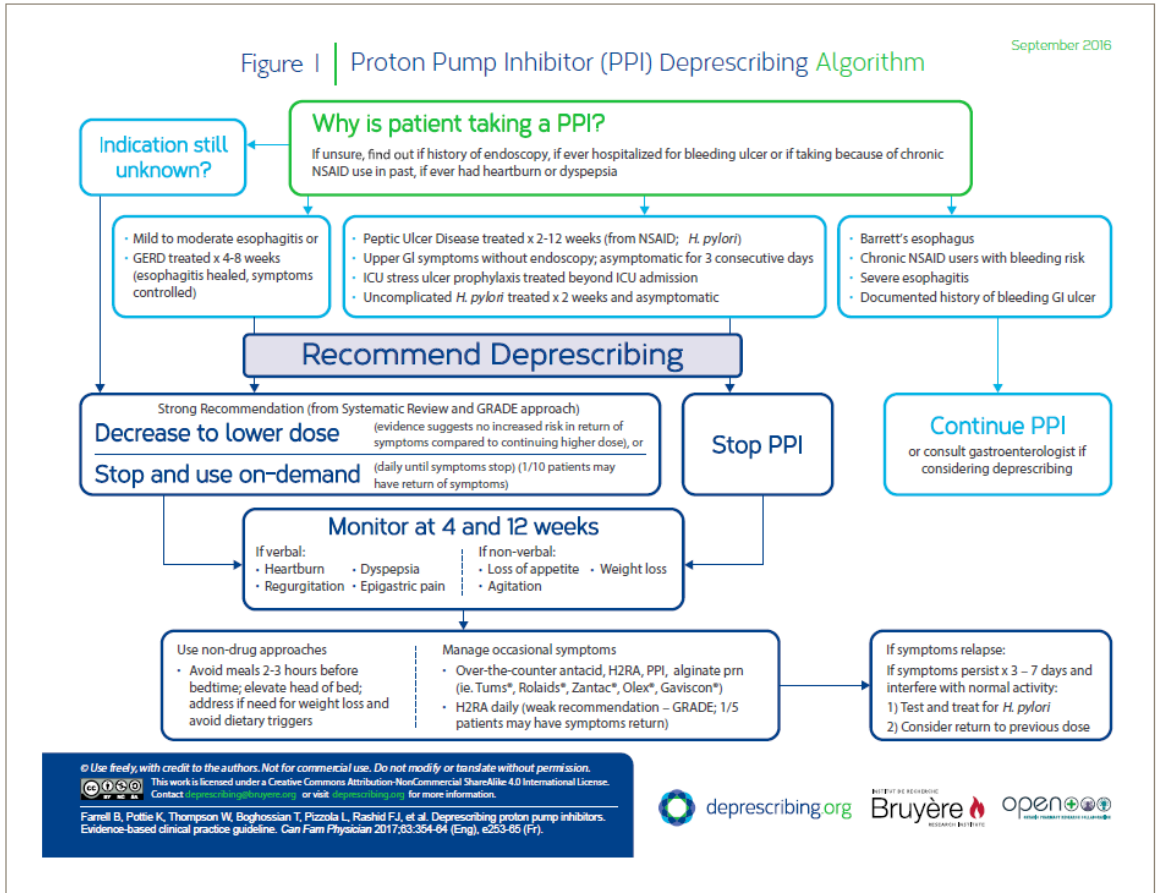


Figure 1 | Proton Pump Inhibitor (PPI) Deprescribing Algorithm

September 2016

Why is patient taking a PPI?

If unsure, find out if history of endoscopy, if ever hospitalized for bleeding ulcer or if taking because of chronic NSAID use in past, if ever had heartburn or dyspepsia

Indication still unknown?

- Mild to moderate esophagitis or
- GERD treated x 4-8 weeks (esophagitis healed, symptoms controlled)

- Peptic Ulcer Disease treated x 2-12 weeks (from NSAID; *H. pylori*)
- Upper GI symptoms without endoscopy; asymptomatic for 3 consecutive days
- ICU stress ulcer prophylaxis treated beyond ICU admission
- Uncomplicated *H. pylori* treated x 2 weeks and asymptomatic

- Barrett's esophagus
- Chronic NSAID users with bleeding risk
- Severe esophagitis
- Documented history of bleeding GI ulcer

Recommend Deprescribing

Strong Recommendation (from Systematic Review and GRADE approach)

Decrease to lower dose (evidence suggests no increased risk in return of symptoms compared to continuing higher dose), or

Stop and use on-demand (daily until symptoms stop) (1/10 patients may have return of symptoms)

Stop PPI

Continue PPI

or consult gastroenterologist if considering deprescribing

Monitor at 4 and 12 weeks

If verbal:
- Heartburn
- Dyspepsia
- Regurgitation
- Epigastric pain

If non-verbal:
- Loss of appetite
- Weight loss
- Agitation

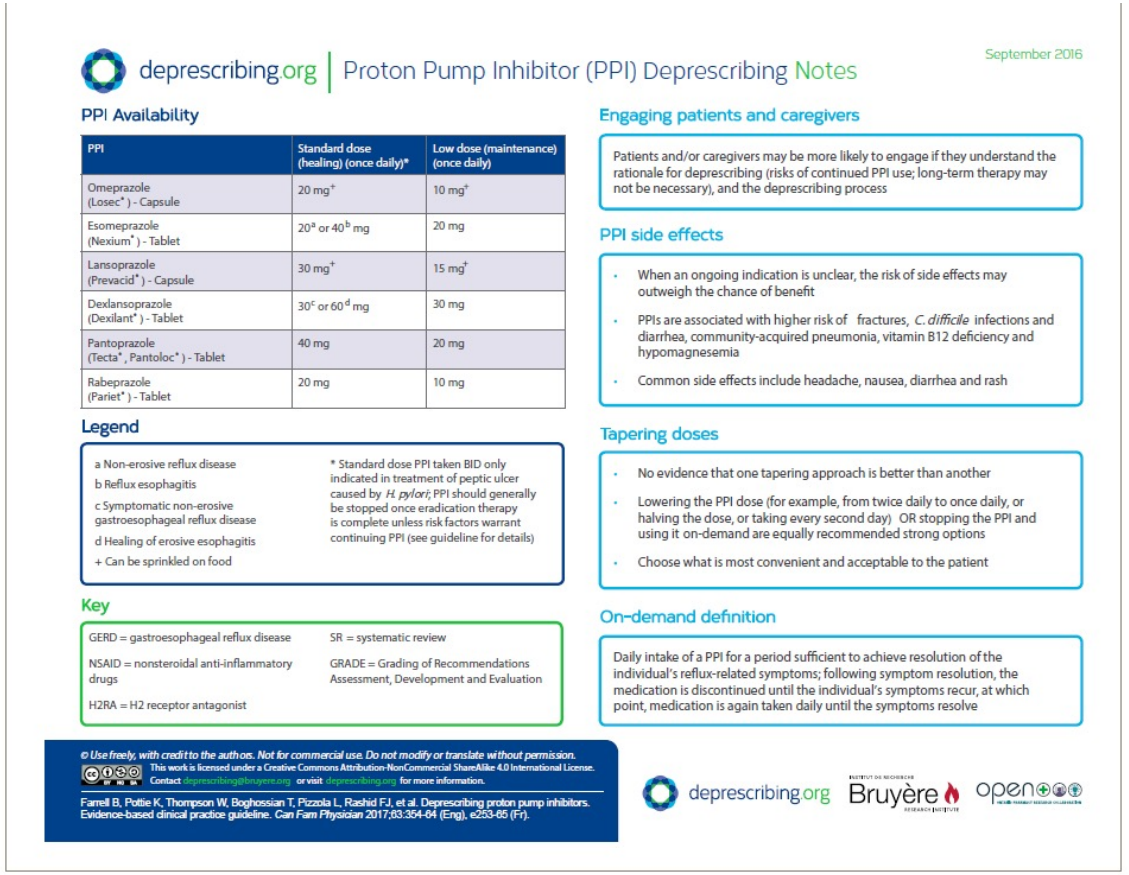
Use non-drug approaches
- Avoid meals 2-3 hours before bedtime; elevate head of bed; address if need for weight loss and avoid dietary triggers

Manage occasional symptoms
- Over-the-counter antacid, H2RA, PPI, alginate prn (ie. Tums®, Rolaids®, Zantac®, Olex®, Gaviscon®)
- H2RA daily (weak recommendation – GRADE; 1/5 patients may have symptoms return)

If symptoms relapse:
If symptoms persist x 3 – 7 days and interfere with normal activity:
1) Test and treat for *H. pylori*
2) Consider return to previous dose

Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. Deprescribing proton pump inhibitors. Evidence-based clinical practice guideline. *Can Fam Physician* 2017;63:354-64 (Eng), e253-65 (Fr).

deprescribing.org Bruyère RESEARCH INSTITUTE



deprescribing.org | Proton Pump Inhibitor (PPI) Deprescribing Notes

September 2016

PPI Availability

PPI	Standard dose (healing) (once daily)*	Low dose (maintenance) (once daily)
Omeprazole (Losec®) - Capsule	20 mg+	10 mg+
Esomeprazole (Nexium®) - Tablet	20[a] or 40[b] mg	20 mg
Lansoprazole (Prevacid®) - Capsule	30 mg+	15 mg+
Dexlansoprazole (Dexilant®) - Tablet	30[c] or 60[d] mg	30 mg
Pantoprazole (Tecta®, Pantoloc®) - Tablet	40 mg	20 mg
Rabeprazole (Pariet®) - Tablet	20 mg	10 mg

Legend

a Non-erosive reflux disease
b Reflux esophagitis
c Symptomatic non-erosive gastroesophageal reflux disease
d Healing of erosive esophagitis
+ Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

Key

GERD = gastroesophageal reflux disease
NSAID = nonsteroidal anti-inflammatory drugs
H2RA = H2 receptor antagonist
SR = systematic review
GRADE = Grading of Recommendations Assessment, Development and Evaluation

Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing (risks of continued PPI use; long-term therapy may not be necessary), and the deprescribing process

PPI side effects

- When an ongoing indication is unclear, the risk of side effects may outweigh the chance of benefit
- PPIs are associated with higher risk of fractures, *C. difficile* infections and diarrhea, community-acquired pneumonia, vitamin B12 deficiency and hypomagnesemia
- Common side effects include headache, nausea, diarrhea and rash

Tapering doses

- No evidence that one tapering approach is better than another
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options
- Choose what is most convenient and acceptable to the patient

On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual's reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual's symptoms recur, at which point, medication is again taken daily until the symptoms resolve

Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. Deprescribing proton pump inhibitors. Evidence-based clinical practice guideline. *Can Fam Physician* 2017;63:354-64 (Eng), e253-65 (Fr).

deprescribing.org Bruyère RESEARCH INSTITUTE

Canadian Family Physician May 2017, 63 (5) 354-364
Available here: https://www.cfp.ca/content/63/5/354

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DEPRESCRIBING GUIDE FOR PROTON PUMP INHIBITORS (PPIs)

(including omeprazole, pantoprazole, esomeprazole, lansoprazole, rabeprazole)

This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

GO TO SECTION:

CONSIDER TWO STEPS WHEN DEPRESCRIBING:

1 Should I deprescribe?

2 How do I deprescribe?

NSW GOVERNMENT | NSW Health Translational Research Grant Scheme 274

Monitor short term (within days to weeks)

Monitor for rebound symptoms

In daily PPI exposure > 4 weeks, rebound acid hypersecretion within ~2-8 weeks after discontinuation is likely.[6] See Alternative management recommendations.

Monitor long term (4-12 weeks)

Monitor for rebound or new symptoms

Recurrence of previous or new symptoms (e.g. heartburn, regurgitation, dyspepsia, epigastric pain, weight loss, loss of appetite, agitation) may occur 2 weeks after dose reduction.

- Common rebound symptoms (e.g. heartburn, regurgitation, dyspepsia) are usually mild, highly variable and can last up to several days to weeks, depending on the duration of PPI exposure.
- If severe symptoms (e.g. epigastric pain, weight loss, loss of appetite, agitation, blood in vomit, black tarry stools, anaemia) occur, restart at lowest effective dose.

AJGP. 2022. doi: 10.31128/AJGP-07-22-6497

Available here: https://www.nswtag.org.au/wp-content/uploads/2018/06/1.9-Deprescribing-Guide-for-Proton-Pump-Inhibitors-PPIs.pdf

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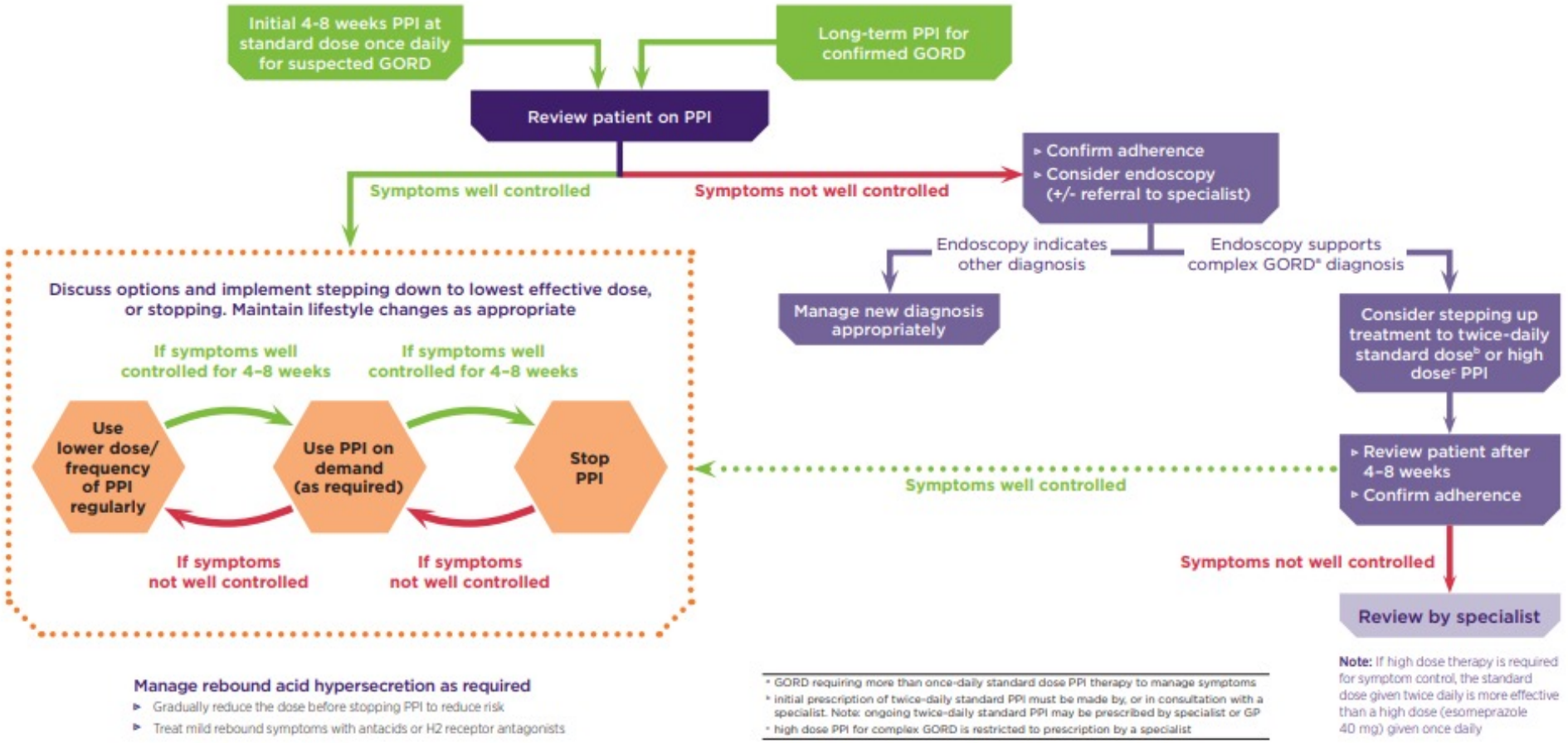
Reviewing proton pump inhibitors (PPIs) for gastro-oesophageal reflux disease (GORD)



Manage rebound acid hypersecretion as required

- Gradually reduce the dose before stopping PPI to reduce risk
- Treat mild rebound symptoms with antacids or H2 receptor antagonists

[a] GORD requiring more than once-daily standard dose PPI therapy to manage symptoms
[b] initial prescription of twice-daily standard PPI must be made by, or in consultation with a specialist. Note: ongoing twice-daily standard PPI may be prescribed by specialist or GP
[c] high dose PPI for complex GORD is restricted to prescription by a specialist

Note: If high dose therapy is required for symptom control, the standard dose given twice daily is more effective than a high dose (esomeprazole 40 mg) given once daily

nps.org.au
Independent. Not-for-profit. Evidence-based.
This program is funded by the Australian Government Department of Health.
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One more consideration:

Small Intestinal Bacterial/Fungal Overgrowth

- SIBO/SIFO Considerations (dietary, lifestyle, and nutraceutical recommendations)
- Common risk factors include PPIs, H. Pylori infection, IBS and gluten sensitivity/Celiac
- GI symptoms as well as non-GI symptoms (brain fog, fatigue, inflammation/pain)
- Dysbiosis incidence is high in patients with GERD. Independently, SIBO may be a contributory factor to refractory reflux symptoms

Clin Transl Gastroenterol. 2018;9(6):162
Surg Endosc. 2021;35(12):7112-7119

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Case Vignette: Ms Goodgut

Your patient is a 49 y/o woman with a history of IBS and reflux

- She's been taking pantoprazole 40mg daily for 2.5 years
- She's interested in stopping it because she's heard *it's not good to be on it a long time*

You ask her about her GI symptoms

- She reports some mild bloating after meals
- Certain foods still trigger her symptoms
- She's tried to quit taking the PPI – reports rebound heart burn

You ask her about her bowel movements

- "OK" goes at least every other day – occasionally every 3 days; hard packed.
- Occasionally floating BM

You ask her about her other symptoms

- Anxiety and restless sleep
- She "doesn't sleep great" – waking up around 3AM every day having trouble falling back asleep so sleep feels disjointed

You ask her about her diet

- "Lots" of vegetables, eggs or oatmeal for breakfast most days; dinner usually a starch, veggies and a protein (meat or fish)
- Not hungry when she wakes up, so she eats breakfast late and skips lunch most days
- Sugar and caffeine cravings. Carbohydrate (especially mid afternoon) when she gets tired

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Intestinal Health

Digestion	Result		Normal
Steatocrit	**9 %**		<15 %
Elastase-1	120	Low	>200 ug/g

GI Markers	Result	Normal
b-Glucuronidase	**913**	<2486 U/mL
Occult Blood - FIT	**7**	<10 ug/g

Immune Response	Result		Normal
Secretory IgA	2517	High	510 - 2010 ug/g
Anti-gliadin IgA	**144**		0 - 157 U/L

What might you expect to show up in a patient on chronic PPI?

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Normal Bacterial Flora			
	Result		Normal
Bacteroides fragilis	**1.83e10**		1.60e9 - 2.50e11
Bifidobacterium spp.	**2.88e9**		>6.70e7
Enterococcus spp.	**9.19e4**	Low	1.9e5 - 2.00e8
Escherichia spp.	**1.48e7**		3.70e6 - 3.80e9
Lactobacillus spp.	**5.49e4**	Low	8.6e5 - 6.20e8
Clostridia (class)	**7.12e5**	Low	5.00e6 - 5.00e7
Enterobacter spp.	**1.38e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**<dl**		1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**1.39e4**		1.00e3 - 5.00e8

Phyla Microbiota	Result		Normal
Bacteroidetes	**2.64e11**	Low	8.61e11 - 3.31e12
Firmicutes	**1.27e9**	Low	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.00**		<1.00

Pattern of low commensal bacteria

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Opportunistic Bacteria			
Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**9.52e4**		<1.50e5
Enterococcus faecalis	**4.02e5**	**High**	<1.00e4
Enterococcus faecium	**3.53e2**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**4.09e5**	**High**	<1.00e4
Pseudomonas aeruginosa	**<dl**		<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**3.68e2**		<5.00e2
Streptococcus spp.	**4.30e3**	**High**	<1.00e3
Methanobacteriaceae (family)	**5.04e7**		<5.00e9

Dysbiosis: Combination of diet, lifestyle, and PPI use

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PPI Taper: Apply the foundations

Assess

- Patient's understanding of medication use and interested in Deprescribing PPI
  - Determine she's eligible – *no associated risk factors for Ms Goodgut*
  - Discuss and assess willingness to change current lifestyle habits (decide on a starting date)

Address nutritional gaps/needs (including DIND)

1. Magnesium + L-theonine (sleep/anxiety)
2. Multi-mineral
3. B-complex and B12

Apply foundational dietary and lifestyle interventions

1. Council on foundational anti-inflammatory diet (with a focus on good protein sources, blood sugar stability and phytonutrients)
2. We might need to intervene with an elimination diet if appropriate

Guilliams, TG. *Functional Strategies for the Management of Gastrointestinal Disorders*. 2016. The Roadmap Series. Point Institute.

Rakel, & Minichiello, V. J. (2023). Integrative medicine (Rakel & V.Minichiello, Eds.; Fifth edition.). Elsevier.

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AJGP. 2022. doi: 10.31128/AJGP-07-22-6497
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PPI Taper:
Initiate de-escalation

Maintain acid-suppression with while bridging with nutraceutical

Start with Reducing dose from Pantoprazole 40mg to 20mg

Instructed her to try using DGL PRN for occasional reflux

Monitor for rebound reflux

After 2-4 weeks reduce to every-other-day in the AM

Continue to monitored for rebound reflux for 4 weeks before further de-escalation

After 4 weeks, only a handful of reflux episodes,

Continue de-escalation

Continued DGL

Before discontinuing PPI, we switched her to omeprazole 20mg every 2-3 days

Extra cautious before discontinuing (with instruction take PRN if needed)

Guilliams, TG. *Functional Strategies for the Management of Gastrointestinal Disorders*. 2016. The Roadmap Series. Point Institute.
Rakel, & Minichiello, V. J. (2023). Integrative medicine (Rakel & V.Minichiello, Eds.; Fifth edition.). Elsevier.
Canadian Family Physician May 2017, 63 (5) 354-364
Available here: https://www.cfp.ca/content/63/5/354
AJGP. 2022. doi: 10.31128/AJGP-07-22-6497
Available here: https://www.nswtag.org.au/wp-content/uploads/2018/06/1.9-Deprescribing-Guide-for-Proton-Pump-Inhibitors-PPIs.pdf

PPI Taper: Correct underlying pathophysiology

Put on training wheels…

Diet

- GF/DF anti-inflammatory diet (after a couple of weeks, was feeling more confident for a full elimination diet with careful challenge after 6 weeks)
- Increase intake of diverse fibers and polyphenol sources
- Balanced intake of protein and inflammatory fat sources
- Replaced coffee with green tea and hot mushroom beverage

Nutraceuticals

- Melatonin 1mg at bedtime
- Combo product with Zinc L-Carnosine, mastic gum, bismuth citrate
- Blend of L-glutamine, quercetin, and marshmallow root
- Digestive enzymes
- DGL as needed
- Berberine

Lifestyle

- Chewing and meal habits
- Address motility and MMC vagal nerve support
- Meal timing
- Evening walk
- Circadian rhythm and stress management

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Summary

Using a holistic approach to medication management within the context of a functional medicine framework can help us improve outcomes, minimize ADRs, and reduce risk

Functional MTM includes screening for interactions, including drug-herb and drug-nutrient interactions (DHI/DNI), as well as drug-induced nutrient depletions (DIND)

Deprescribing guidelines have been created by several international societies for safe reduction of polypharmacy risk, but more research is needed to guide safe and effective deprescribing; until then use clinical prudence *(the "art")*

The bottom line when determining if initiating a deprescribing protocol is appropriate: weigh risk vs benefit, determine patient's willingness to make changes and adherence, decide if there's a need for tapering or step-down protocol before medication withdrawal

"Put on the training wheels" - Address any nutritional imbalances, foundational nutrition and lifestyle, initiate nutraceuticals (screening for potential DHI or DNI)

Collaboration between the patient, prescriber, and pharmacist can help ensure safe and positive outcomes

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