

# KNOW YOUR MEDICATIONS: STEPS TOWARD SAFER MEDICATION USE

## APDA Oklahoma Chapter

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# Outline for Today

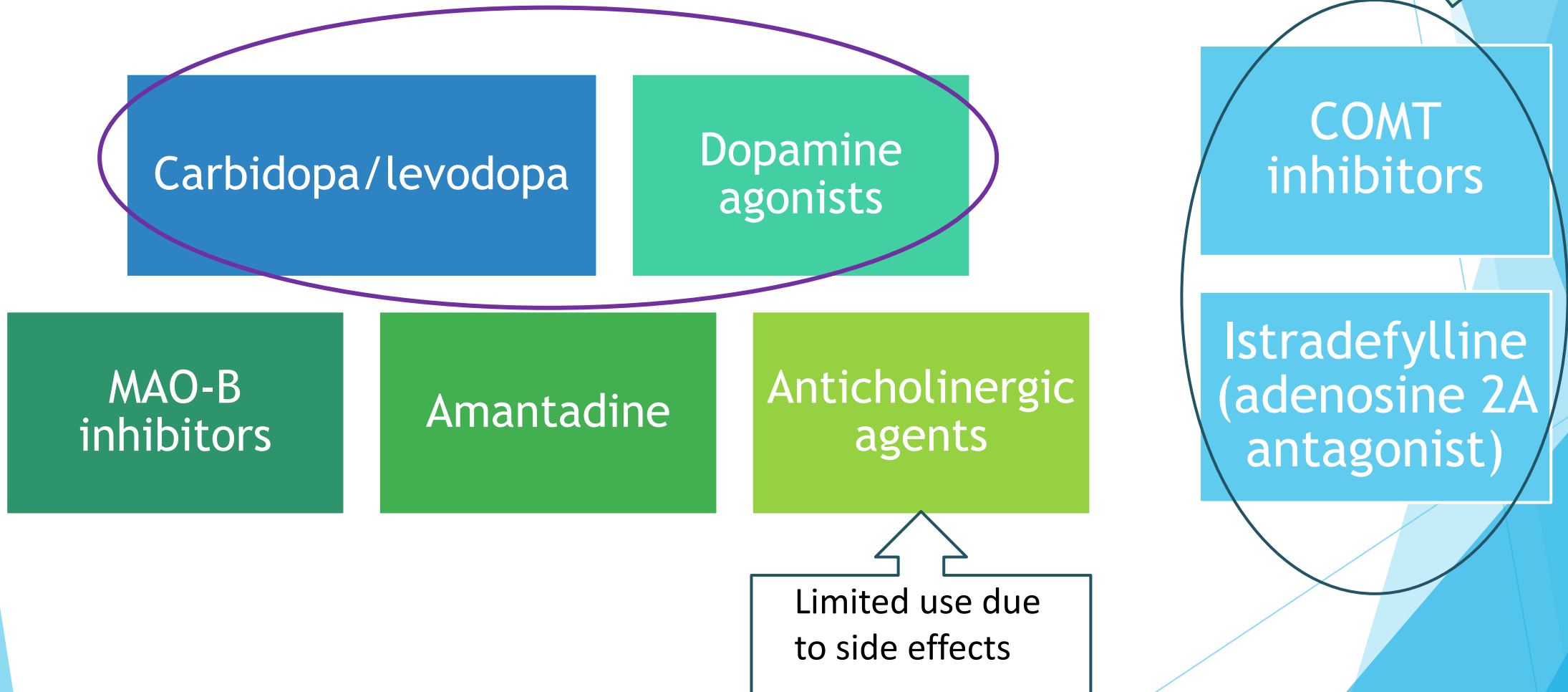
Medications for managing motor and selected nonmotor symptoms of Parkinson's Disease

Dietary supplement use

Non-drug interventions & management strategies

Safe medication use concepts: principles & strategies

# Drug therapy options for managing motor symptoms



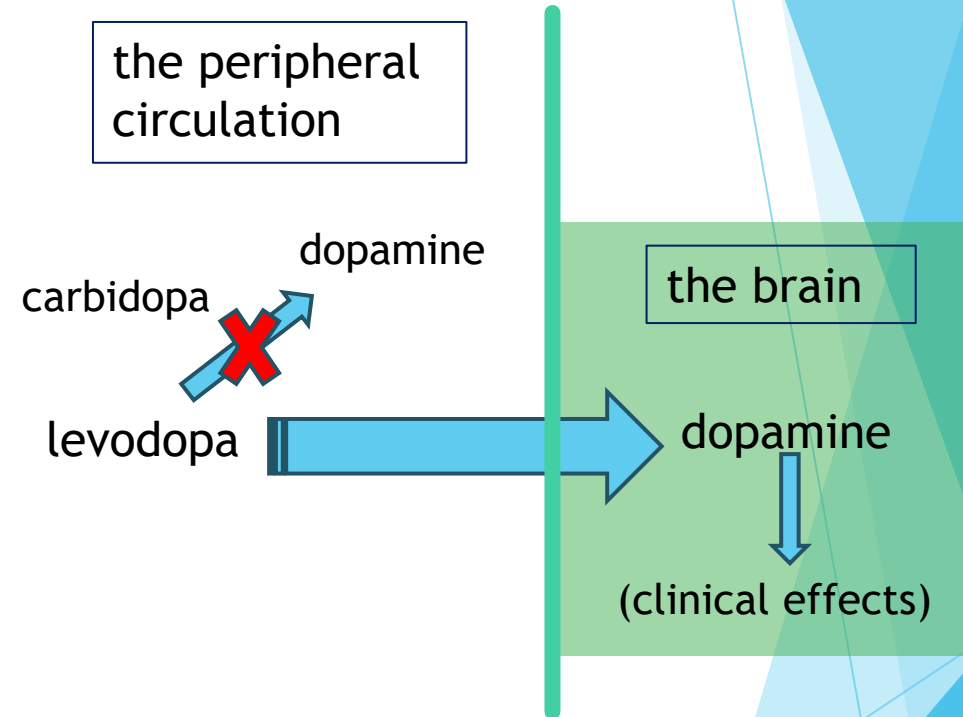
# Carbidopa/levodopa (CD/LD)

| Brand name                    | Formulation                  | Release properties/comment                    |
|-------------------------------|------------------------------|---|
| Carbidopa/levodopa (Sinemet®) | Tablet                       | Immediate release (IR)                        |
| Parcopa®                      | Orally disintegrating tablet | IR  |
| Sinemet CR (generic)          | Tablet                       | Controlled release (CR)                       |
| Rytary®                       | Capsule                      | Extended release (ER) (IR + ER)               |
| Dhivy® (approved 2/22)        | Scored tablet                | IR  |
| Duopa®                        | Enteral suspension           | Continuous over 16 hrs                        |
| CD/LD/entacapone (Stalevo®)   | Tablet                       | 3-drug combination pill with a COMT-inhibitor |

- ▶ Also available: carbidopa 25 mg (Lodosyn)

# Carbidopa/Levodopa: A combination medication


- ▶ How it works:
- ▶ **LEVODOPA** = can cross into the brain, where it is converted to dopamine
  - ▶ Levodopa is a precursor of dopamine
  - ▶ 2 enzymes found throughout the body (“peripheral circulation”) can break down levodopa and thus prevent it from reaching the brain.
  - ▶ To prevent the breakdown of levodopa in the body (before reaching the brain), it is combined with carbidopa
    - ▶ PLUS
- ▶ **CARBIDOPA** = Blocks (inhibits) the conversion of levodopa in the peripheral circulation, which allows more levodopa to cross into the brain. Carbidopa also serves to decrease side effects (like nausea) caused by levodopa



# Carbidopa/levodopa

- ▶ Place in therapy:
  - ▶ CD/LD is the “gold standard” treatment
- ▶ Side effects
  - ▶ Nausea, fatigue, dizziness, headache; orthostatic hypotension, dyskinesia, confusion, hallucinations
- ▶ Drug interactions: iron products (including vitamins with iron); separate by 2 hours
- ▶ Administration: ideally take on an empty stomach for best absorption.
  - ▶ Due to nausea, often need to take with food
  - ▶ Dietary protein can hinder the absorption of levodopa (LD)

# Dopamine Agonists (DA)

|            |   |            |   |
|------------|---|------------|---|
| DA agonist | Pramipexole   | Mirapex    | Nausea, dizziness, orthostatic hypotension, swelling of ankles, dyskinesia, hallucinations, confusion, somnolence, sleep attacks, impulse control disorders<br><br>Neupro can lead to a skin reaction at the patch site |
|            | Pramipexole (extended release)  | Mirapex ER |   |
|            | Ropinirole  | Requip     |   |
|            | Ropinirole (extended release)   | Requip XL  |   |
|            | Apomorphine (injection)   | Apokyn     |   |
|            | Apomorphine (sublingual film)   | Kynmobi    |   |
|            | Rotigotine (transdermal patch)  | Neupro     |   |
|            | <div data-bbox="147 772 575 848" data-label="Text"> <p>“On-demand” use</p> </div>  |            |   |

## Place in therapy

- Alternative to levodopa for initial therapy; but not quite as potent
- Lower risk of dyskinesia

# Dopamine Agonists

- ▶ How this drug class works:
- ▶ Directly stimulate dopamine receptors (mimics dopamine) in the brain
  - ▶ Dopamine agonists can cross into the brain



# MAO-B inhibitors

| Mechanism of action                             | Generic name                       | Trade name® | Potential side effects*  |
|---|------------------------------------|-------------|--|
| MAO-B inhibitor, inhibits breakdown of dopamine | Selegiline                         |             | Selegiline can cause insomnia  |
|   | Selegiline (orally disintegrating) | Zelapar     | Dizziness, nausea, gastrointestinal upset, dyskinesia, hallucinations, confusion, headache   |
|   | Rasagiline                         | Azilect     |  |
|   | Safinamide                         | Xadago      | Note possible drug interactions between MAO-B inhibitors and other medications<br><br>Safinamide exerts its effects through other mechanisms of action as well |

|                         |   |
|-------------------------|---|
| <b>Place in therapy</b> | <ul style="list-style-type: none"> <li>• Modest effect on motor symptoms</li> <li>• Selegiline &amp; rasagiline can be used alone for mild symptoms or in combination with a dopamine agonist or carbidopa/levodopa (CD/LD)</li> <li>• Safinamide is approved only as add-on therapy for patients taking CD/LD</li> </ul> |
|-------------------------|---|

# Interactions with MAO-B inhibitors--drugs to avoid

| Medication Type   | Medication Name                               | Trade Name®   |
|---|---|---|
| Narcotics/Analgesics  | Meperidine                                    |   |
|   | Tramadol                                      | Ultram  |
|   | Methadone                                     | Dolophine   |
| Antidepressants   | St. John's Wort                               | Several Brands  |
| Muscle Relaxants  | Cyclobenzaprine                               | Flexeril  |
| Cough Suppressants  | Dextromethorphan                              | Robitussin products, other brands—<br>found as an ingredient in various<br>cough and cold medications |
| Decongestants/Stimulants                                      | Pseudoephedrine<br>Phenylephrine<br>Ephedrine | Sudafed products, other brands—<br>found as an ingredient in various cold<br>and allergy medications  |
| Medications that inhibit Monoamine<br>oxidase non-selectively | Linezolid (antibiotic)                        | Zyvox   |
|   | Phenelzine                                    | Nardil  |
|   | Tranlycypromine                               | Parnate   |
|   | Isocarboxazid                                 | Marplan   |

Risk of severe high blood pressure (hypertensive crisis) with some of the above interactions; others can cause anxiety, confusion, hallucinations

# Amantadine

|   |                                  |            |  |
|---|----------------------------------|------------|--|
| Mixed mechanisms,<br>including NMDA<br>antagonism | Amantadine                       |            | Hallucinations, leg<br>swelling, dizziness, mottled<br>skin (livedo reticularis),<br>confusion, dry mouth and<br>eyes, constipation,<br>dizziness, orthostatic<br>hypotension, somnolence<br><br>Dose needs to be adjusted<br>for kidney dysfunction |
|   | Amantadine<br>(extended release) | Gocovri    |  |
|   | Amantadine<br>(extended release) | Osmolex ER |  |

- |                     |   |
|---------------------|---|
| Place in<br>therapy | <ul style="list-style-type: none"><li>• Modest effect on motor symptoms</li><li>• Younger patients, mild disease</li><li>• Gocovri® approved for treating dyskinesia and “OFF” episodes</li></ul> |
|---------------------|---|

# Amantadine

- ▶ How this drug works:
- ▶ Increases availability of dopamine in the brain;
- ▶ Blocks “NMDA” receptors
- ▶ Mechanism of action is less specific (not fully known)

# Anticholinergic Medications

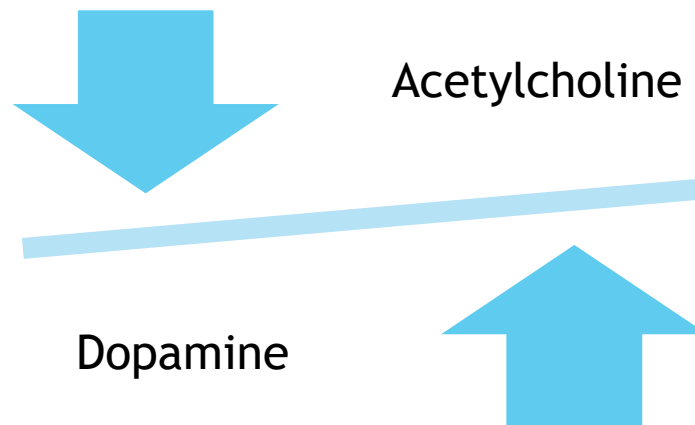
|                 |                 |          |   |
|-----------------|-----------------|----------|---|
| Anticholinergic | Trihexyphenidyl |          | Dry mouth and eyes, constipation, urinary retention, memory impairment, confusion, depression, hallucinations |
|                 | Benztropine     | Cogentin |   |

|                         |  |
|-------------------------|--|
| <b>Place in therapy</b> | Early treatment; younger than 65 years old<br>When tremor is main symptom<br>Caution in older adults (can contribute to memory issues & confusion) |
|-------------------------|--|

# Anticholinergic Medications

- ▶ How this drug class works:
- ▶ Blocks the action of acetylcholine in the brain, which thereby corrects the imbalance between dopamine and acetylcholine
  - ▶ Acetylcholine is a messenger molecule in the nervous system

In the brain:  
Depletion of dopamine  
leads to a relative  
excess of acetylcholine



# Medications for motor symptoms that can be added to carbidopa/levodopa therapy

COMT\*  
inhibitors



Block (inhibit) the  
breakdown of  
levodopa in the  
peripheral circulation  
(mostly)

Istradefylline  
(adenosine 2A  
antagonist)



Increases **dopamine  
activity** in brain by  
blocking adenosine  
activity

\*Catechol-O-methyl transferase

# COMT inhibitors

|  |            |          |   |
|--|------------|----------|---|
| COMT inhibitor, inhibits breakdown of levodopa | Entacapone | Comtan   | Same as carbidopa/levodopa. In addition: diarrhea, discoloration of body fluids<br><br>Tasmar can cause liver failure and requires monitoring of liver function |
|  | Tolcapone  | Tasmar   |   |
|  | Opicapone  | Ongentys |   |

COMT inhibitors allow more levodopa to cross into the brain (where it is then metabolized to dopamine)

|  |                               |         |   |
|--|-------------------------------|---------|---|
| DOPA decarboxylase inhibitor/DA precursor/COMT Inhibitor | Carbidopa/Levodopa/Entacapone | Stalevo | Same as carbidopa/levodopa and COMT inhibitor |
|--|-------------------------------|---------|---|

|                  |  |
|------------------|--|
| Place in therapy | <ul style="list-style-type: none"> <li>• <u>Add-on</u> therapy to LD/CD for end-of-dose wearing off, OFF episodes</li> <li>• Never used alone (it must be added on to levodopa therapy)</li> </ul> |
|------------------|--|



# Selective adenosine A2A receptor antagonist

|                        |                |          |   |
|------------------------|----------------|----------|---|
| Adenosine 2A inhibitor | Istradefylline | Nourianz | Dyskinesias, dizziness, constipation, nausea, hallucinations and insomnia |
|------------------------|----------------|----------|---|

Of note, istradefylline improves motor symptoms without increasing dopamine activity; this can be important for some patients (for whom dyskinesia is a concern)

|                  |  |
|------------------|--|
| Place in therapy | <ul style="list-style-type: none"><li>• <u>Added to CD/LD</u> therapy for OFF episodes</li><li>• Not to be used on its own</li></ul> |
|------------------|--|

# Drug therapy options for managing motor symptoms

Carbidopa/levodopa

Dopamine agonists

COMT inhibitors

MAO-B inhibitors

Amantadine

Anticholinergic agents

Istradefylline  
(adenosine 2A antagonist)

# Rescue or “on demand” therapy for OFF episodes

| Drug name    | Brand name | Route of administration | Drug class, comments  |
|--------------|------------|-------------------------|---|
| Apomorphine* | Apokyne®   | Subcutaneous injection  | Dopamine agonist  |
| Apomorphine* | Kynmobi®   | Sublingual film         | Dopamine agonist  |
| Levodopa     | Inbrija®   | Oral inhalation         | Levodopa product; only can be used if patient <u>already taking LD/CD</u> |

\*Note: serious drug interaction with most anti-nausea medications, including ondansetron

# Medications to avoid or use with caution

- ▶ If you are taking an MAO-B inhibitor: Drugs that **interact with MAO-B inhibitors** need to be avoided or used with caution
- ▶ For all individuals with Parkinson's: Drugs that **can worsen Parkinson motor symptoms** (APDA handout) need to be avoided or used with caution
  - ▶ Medications that block dopamine activity
  - ▶ Medications that are used to treat nausea
    - ▶ Metoclopramide (Reglan®), Compazine, Phenergan (for example)
  - ▶ Antipsychotic agents such as haloperidol, olanzapine, risperidone
    - ▶ Exceptions = clozapine, quetiapine (Seroquel), pimavanserin (Nuplazid)
  - ▶ Rarely: lithium, diltiazem

**\*\*Not all healthcare professionals will know these interactions\*\***

# Management of NONmotor symptoms:

- ▶ Constipation
- ▶ Orthostatic hypotension
- ▶ Drooling (sialorrhea)
- ▶ Dysphagia
- ▶ Overactive bladder
  - ▶ Urgency, frequency
- ▶ Sexual disorders
  - ▶ Erectile dysfunction
- ▶ Decreased sense of smell
- ▶ Pain (related to muscle rigidity)
- ▶ REM sleep behavior disorder
- ▶ Restless leg syndrome
- ▶ Daytime drowsiness
- ▶ Depression, anxiety
- ▶ Psychosis
  - ▶ hallucinations, delusions
- ▶ Cognitive impairment
  - ▶ Parkinson's Disease dementia

# Medications approved to treat specific nonmotor symptoms

| Symptom treated                    | Mechanism of action            | Generic name | Trade name® | Potential side effects*  |
|------------------------------------|--------------------------------|--------------|-------------|--|
| Parkinson's disease psychosis      | Inverse serotonin agonist      | Pimavanserin | Nuplazid    | Swelling of legs or arms, nausea, confusion, constipation<br><br>QT interval prolongation (abnormal heart rhythm), increased risk of death in elderly patients with dementia-related psychosis |
| Neurogenic orthostatic hypotension | Norepinephrine precursor       | Droxidopa    | Northera    | Headache, dizziness, nausea, high blood pressure (especially when lying down)  |
| Parkinson's disease dementia       | Acetylcholinesterase inhibitor | Rivastigmine | Exelon      | Stomach upset, nausea, loss of appetite  |

# Dietary Supplements, regulation

- ▶ Dietary supplements are regulated in a different manner compared to prescription medications

| Prescription and OTC products   | Dietary supplements  |
|---|--|
| Regulated as drugs  | Regulated as foods   |
| Products cannot be marketed without FDA approval                                    | Products do not need FDA approval to be marketed   |
| Manufacturer must prove that drug is safe AND effective before seeking FDA approval | FDA can seek removal if supplement found unsafe (burden of proof on the FDA), and <u>only after marketed</u> |
| Manufacturers must meet purity and quality standards set by the FDA                 | Manufacturers encouraged to follow “good manufacturing practices”  |

# Dietary Supplements, safety & effectiveness

- ▶ “Buyer Beware” regarding product safety and effectiveness
- ▶ Most supplements lack sufficient research to know safety and effectiveness
  - ▶ Small studies, short duration
- ▶ Lack of research means we don’t have information about interactions and adverse effects, for example



# Dietary Supplements in Parkinson's Disease (PD)

| Selected supplements                 | Comments   |
|--------------------------------------|--|
| B-complex vitamins (B12, B6, folate) | Might improve effectiveness CD/LD, decrease side effects           |
| Calcium (through diet is best)       | Helpful for bone health and to decrease risk osteoporosis          |
| Coenzyme Q10                         | No clear evidence to support benefit; however, still being studied |
| Creatine                             | No benefit   |
| Ginger                               | Can be helpful for nausea  |
| Glutathione                          | Research ongoing; best absorbed via diet                           |
| Vitamins C, E                        | Conflicting data but possible benefit; vitamin E bleeding risk     |
| Vitamin D                            | Helpful if vitamin D levels are low                                |

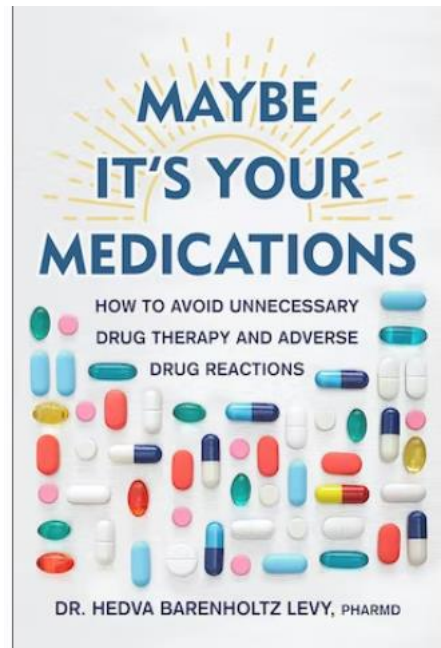
# Treatment - Nondrug (nonpharmacologic)

- ▶ Exercise
  - ▶ Tai Chi, balance training
- ▶ Dietary
  - ▶ calcium/vitamin D (for bone health)
  - ▶ drink plenty of fluids (helps with constipation and low blood pressure)
- ▶ Physical therapy
- ▶ Occupational therapy
- ▶ Speech therapy

# Managing Parkinson's Disease, Additional Considerations

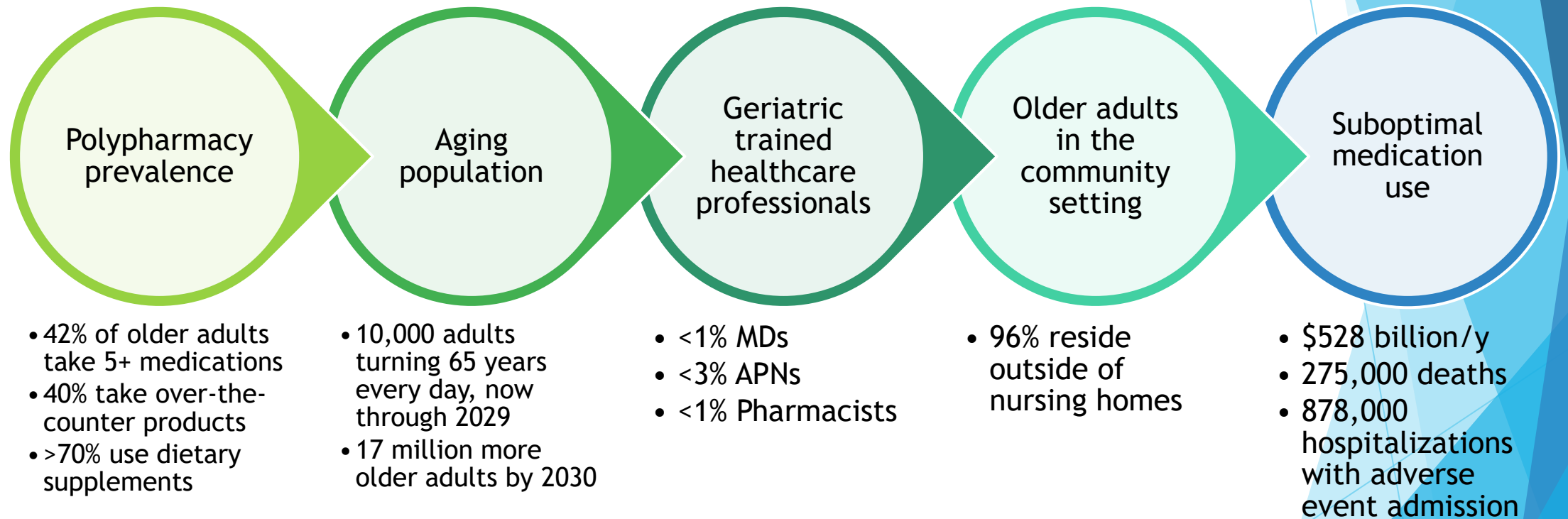
- ▶ Timing of medications
  - ▶ Educate caregivers!
- ▶ Keep a movement diary to help with medication adjustment
- ▶ Drug interactions
  - ▶ Be informed; always ask
- ▶ Communicate with healthcare team about symptoms
  - ▶ Reach out if anxiety, depression
- ▶ Stay mentally and socially active

# Maybe It's Your Medications: How To Avoid Unnecessary Drug Therapy and Adverse Drug Reactions



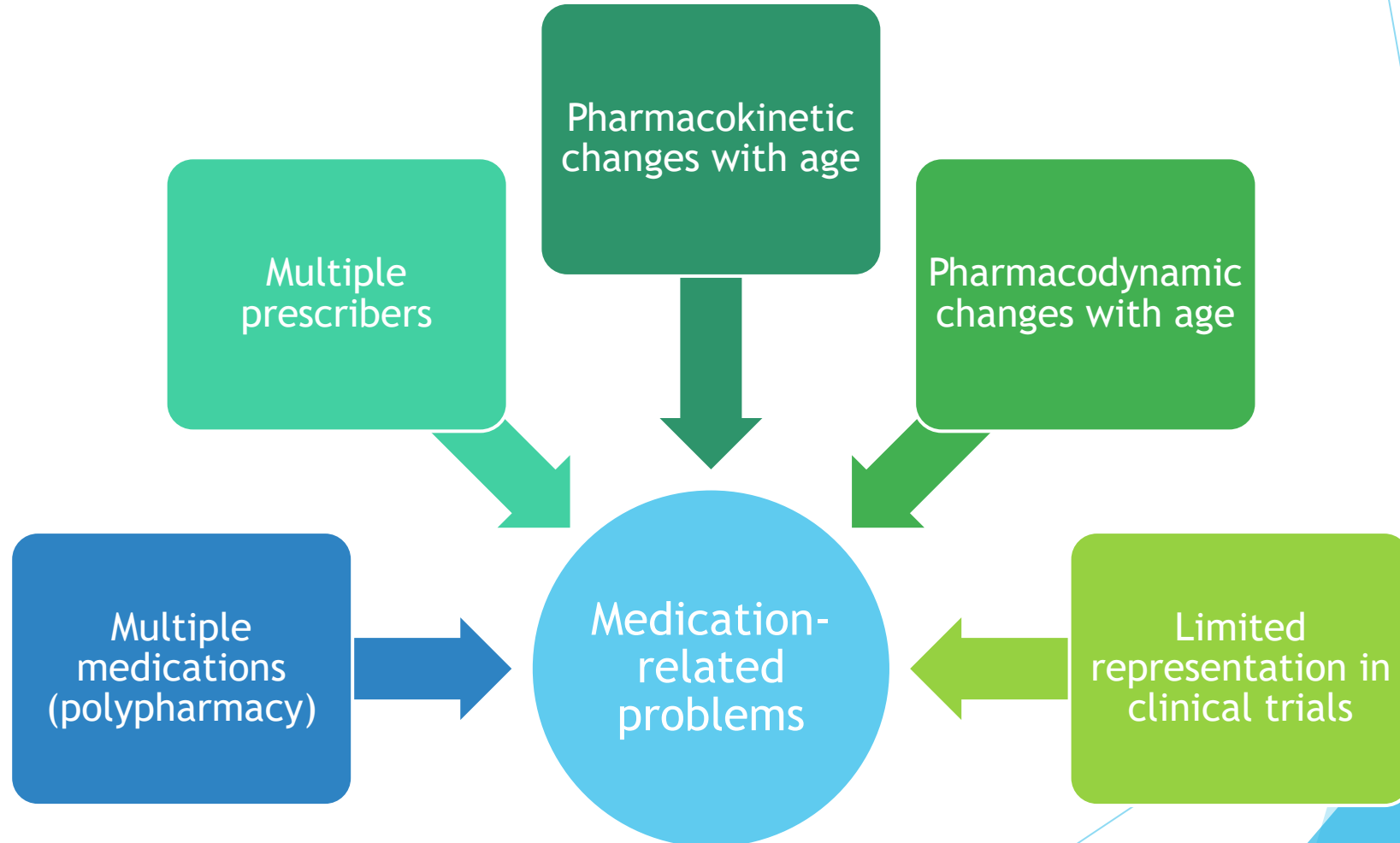
- ▶ Why is this book needed, and why now?
- ▶ Patient engagement in medication use is necessary to achieve safe and appropriate medication use
- ▶ Quality of life
- ▶ Healthcare costs
- ▶ But individuals typically do not know what to ask or where to begin

# The Perfect Storm in Health Care



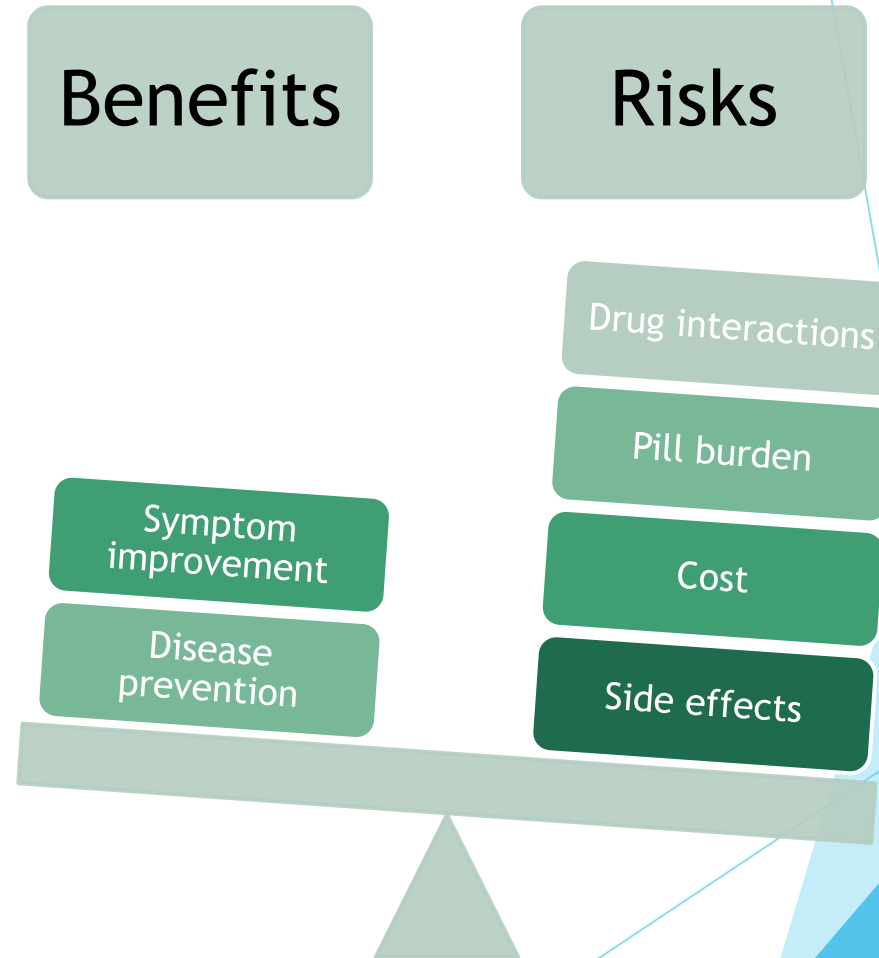
Qato 2016, Rowe 2021, Woodall 2022, Zippia 2023

# Older adults more vulnerable to impact of suboptimal medication use



# Medication use: risks and benefits

- ▶ FDA approves medications based on clinical evaluation of harm vs benefit
  - ▶ A drug will not benefit every person
  - ▶ Harms will vary for each person
- ▶ Consumers need to advocate for safe medication use



# Safe Medication Use Strategies

What steps can you take  
*today?*



# 1. Have a complete, accurate, & current medication list

Carry it with you and share with health-care professional at each encounter

- Include ALL medicines you take:
  - Prescription, OTC, and Supplements

**INCLUDE** for each medicine:

- Reason for taking the medicine
- Prescriber name & when started

## 2. Avoid Unnecessary or Harmful Medications

Only use drug therapy that is benefiting you

- Benefits should outweigh possible harms
- This includes nonprescription medications, too!

Recognize that medications are not intended “forever”

- Medications should be “re-prescribed” on regular basis
- Medication list should be “right-sized” on regular basis

Deprescribing = the systematic approach to reduce doses or stop medications that no longer are needed or are causing harm

- Patients & caregivers need to initiate deprescribing conversations with their doctors

### 3. Recognize your role on the health-care team

Be an active participant - be engaged!

- You know you best!

Be involved in drug therapy choices and decisions

- Person-centered care: what matters most to you?
- Shared decision making: be informed and part of the conversation

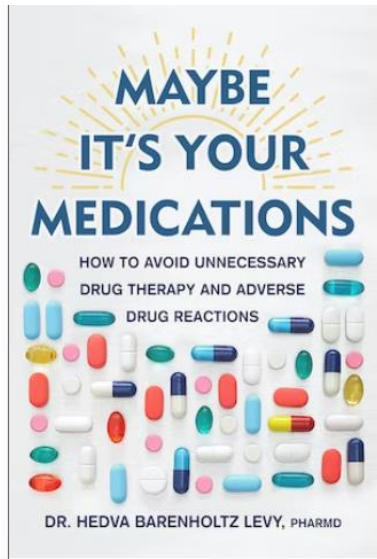
Communicate & advocate

- Ask questions about your drug therapy
- Speak up about concerns

Thank  
you!



Time for  
Your  
Questions  
? ? ?



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