

# Motor Fluctuations and Dyskinesias: Mitigation Strategies

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Parkinson Foundation of the National Capital Area  
Annual Symposium  
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*No Financial Disclosures*

***Important Reminder: Discuss your medical care with your neurologist.***

# Learning Case – Put on your thinking caps.

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A 73 year-old woman was diagnosed with Parkinson's disease six years ago. She is prescribed Carbidopa/Levodopa 25/100 two tablets four times daily and Rasagiline 1 mg daily. She has been enjoying life and feeling that her Parkinson's symptoms are well controlled.

At a routine follow-up appointment with her neurologist she mentions that she is sometimes getting some shaking in her leg.

*What could be the cause of her concerns?*

# Learning Objectives

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At the end of this session, you should be able to:

- Describe different types of motor fluctuations
- Identify three factors that influence motor fluctuations
- Discuss three ways to mitigate motor fluctuations

# Outline

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1. Movement Goals
2. Motor Terminology and Medication Management
3. Motor Fluctuations
4. Mitigating Motor Fluctuations
5. Summary and Application of Knowledge

# What are your movement goals? (Why do you want to move?)

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*Write down three goals.*

# What specific activities are important for you to accomplish?

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**Many movement activities vary from person to person:** typing on a computer, playing with grandchildren, painting a picture, playing pickleball, reading a book, riding a bicycle, going for a walk, preparing a meal, working out at the gym, dancing, etc.

**Other movements are common = activities of daily living (ADLs):** dressing, eating, bathing, grooming, ambulation

# **What are your doctor's goals for your movement, a.k.a., motor management?**

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1. For you to accomplish activities easily
2. For you to accomplish activities independently
3. For you to accomplish activities safely

# Motor Symptom Terminology

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## ***Cardinal* Motor Symptoms of Parkinson's Disease**

Shaking = ***Tremor*** = Rhythmic, Oscillatory Movement

Slowness = ***Bradykinesia***

Stiffness = ***Rigidity*** = Increased Muscle Tone / Tension

Gait Difficulty = ***Postural Instability***

## ***Another* Motor Symptom**

Twisting, Pulling = ***Dystonia*** = Non-rhythmic, relatively slow  
e.g., toe curling, ankle turning, neck turning



# Parkinsonian Tremor

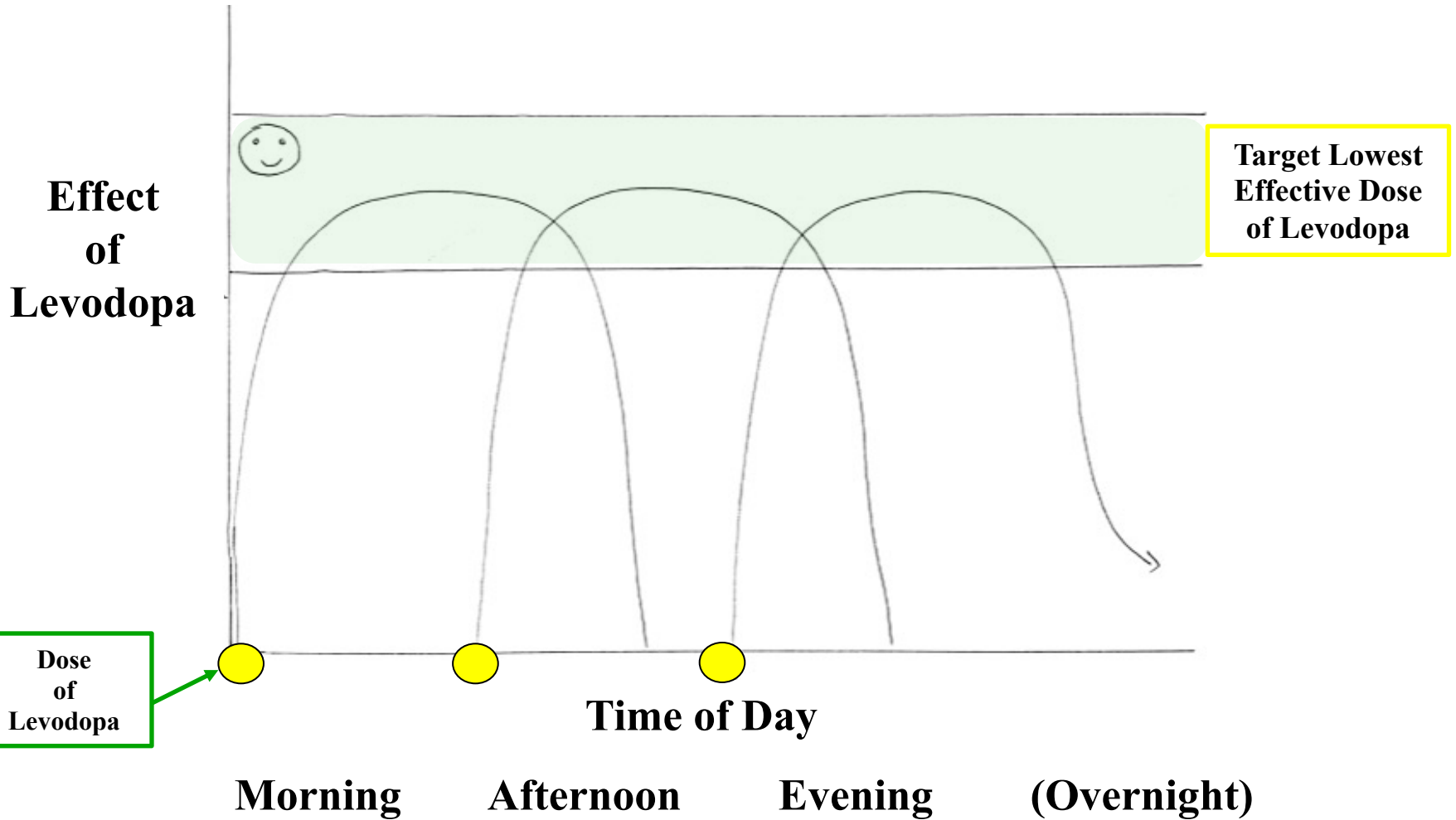


# PD Medications

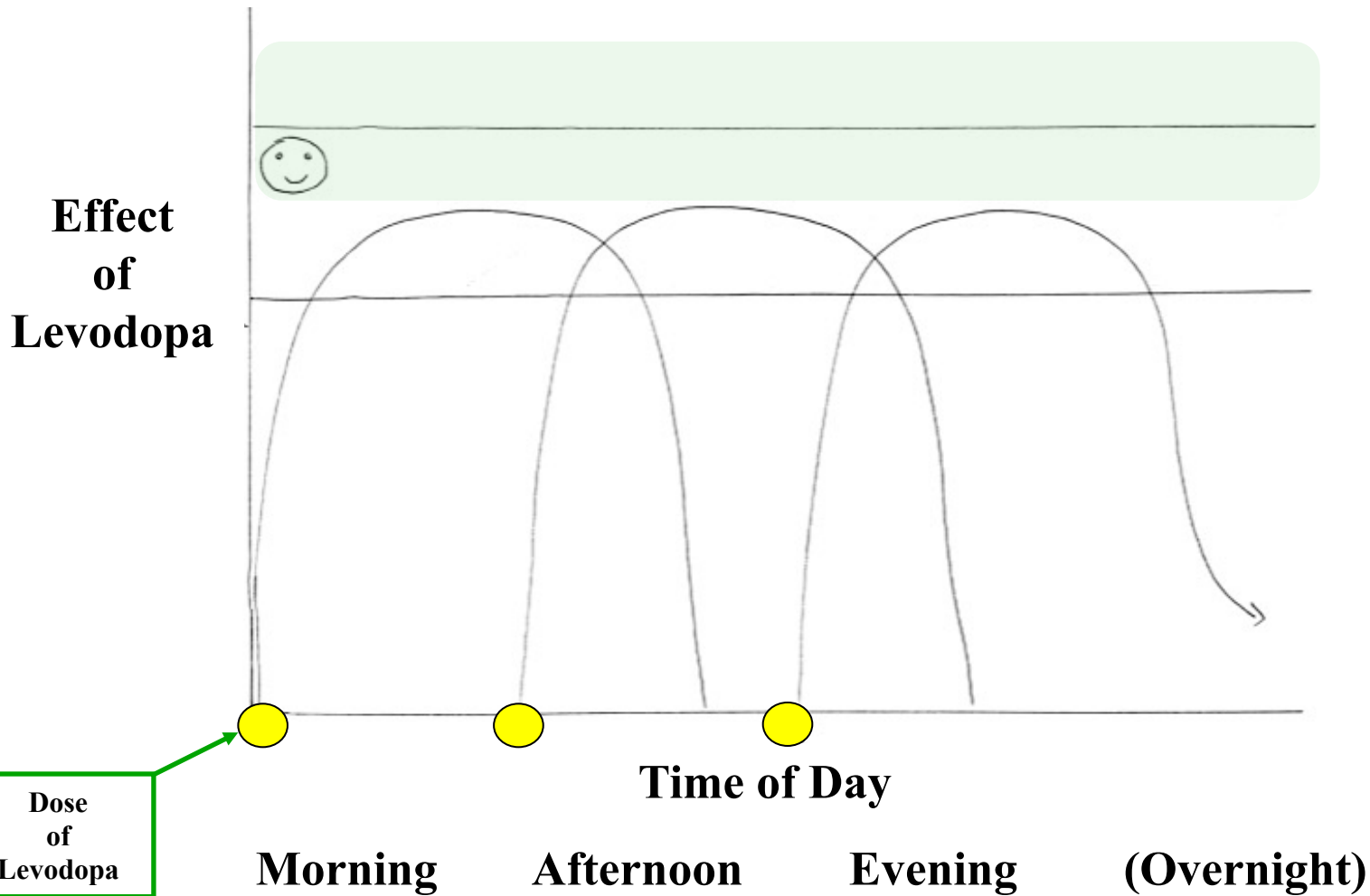
<u>Medication Class</u>	<u>Medication</u>	<u>Route of Administration</u>
L-dopa	Carbidopa/Levodopa (IR)	Oral, Sublingual, <u>Inhaled*</u>
	<b>Carbidopa/Levodopa CR</b>	Oral
	<b>Carbidopa/Levodopa ER</b>	Oral
	<i>Duopa</i> <sup>+</sup>	<i>Intestinal (external pump)</i>
<b>Dopamine Agonists</b>	Pramipexole IR/ER	Oral
	Ropinirole IR/ER	Oral
	Rotigitone	Transdermal (patch)
	Apomorphine*	<u>Injection*</u> , <u>Sublingual,*</u>
<b>MAO-B Inhibitors</b>	Selegiline	Oral
	Rasagiline	Oral
	Safinamide	Oral
COMT Inhibitors	<b>Entacapone</b>	Oral
	Tolcapone	Oral
	Opicapone	Oral
Other	<b>Amantadine IR/ER</b>	Oral
	<b>Istradefylline</b>	Oral
	Trihexyphenidyl HCl	Oral
	<b>Carbidopa</b>	Oral

IR, immediate release; CR, controlled release; ER, extended release; \* Rescue Medication, <sup>+</sup> *Advanced Therapy*

# Effect of Levodopa vs. Time of Day



# Effect of Levodopa vs. Time of Day Changes Over Years



# Motor Fluctuations

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**“ON”** = Absence of cardinal motor symptoms in the setting of medical management

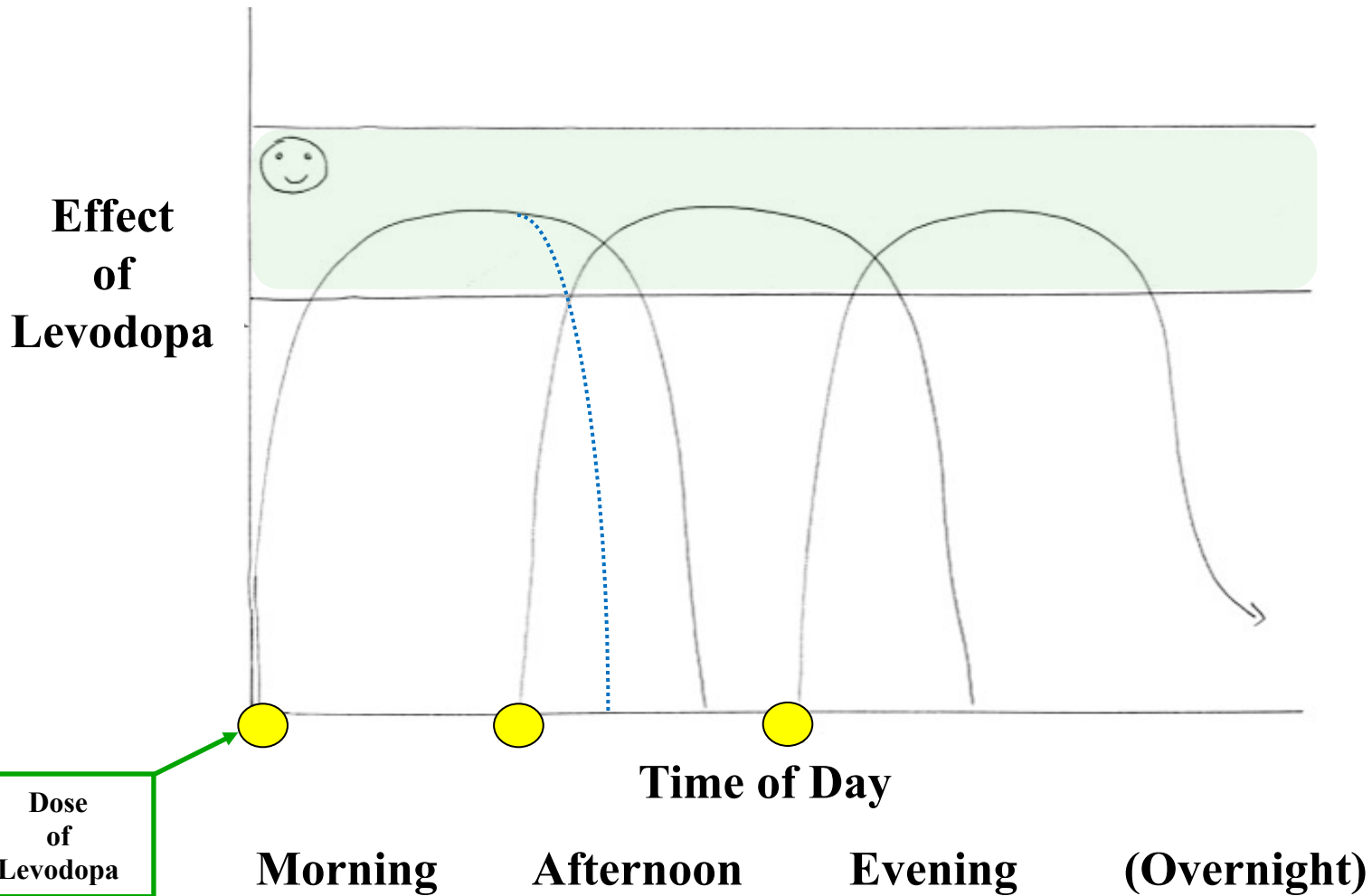
Optimal motor control → Good quality of life

**“OFF”** = Recurrence of motor symptoms when the beneficial effect of medications wanes/abates

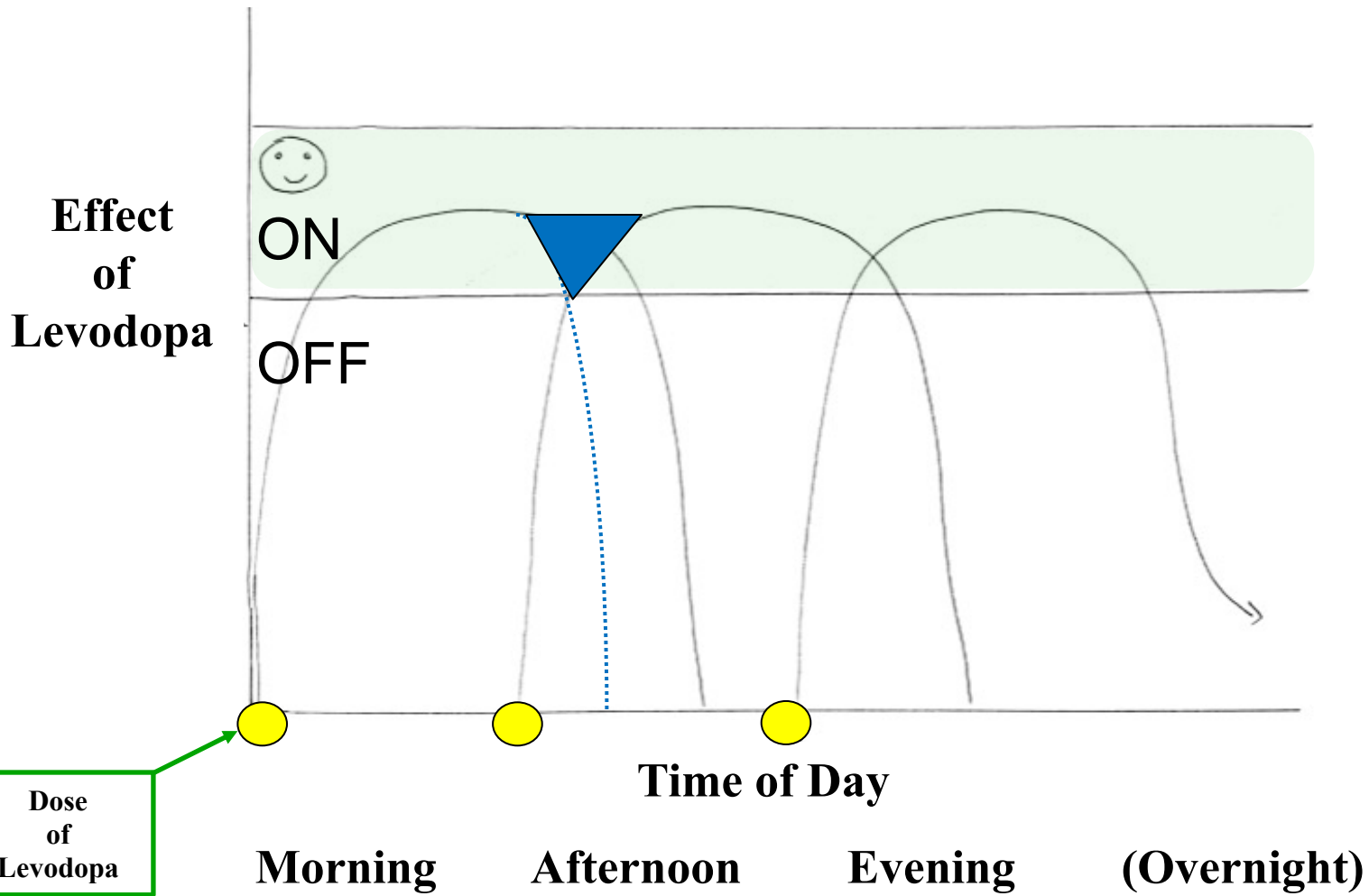
Suboptimal motor control → Disrupted quality of life

~ 50% people will develop fluctuations at 5 years.

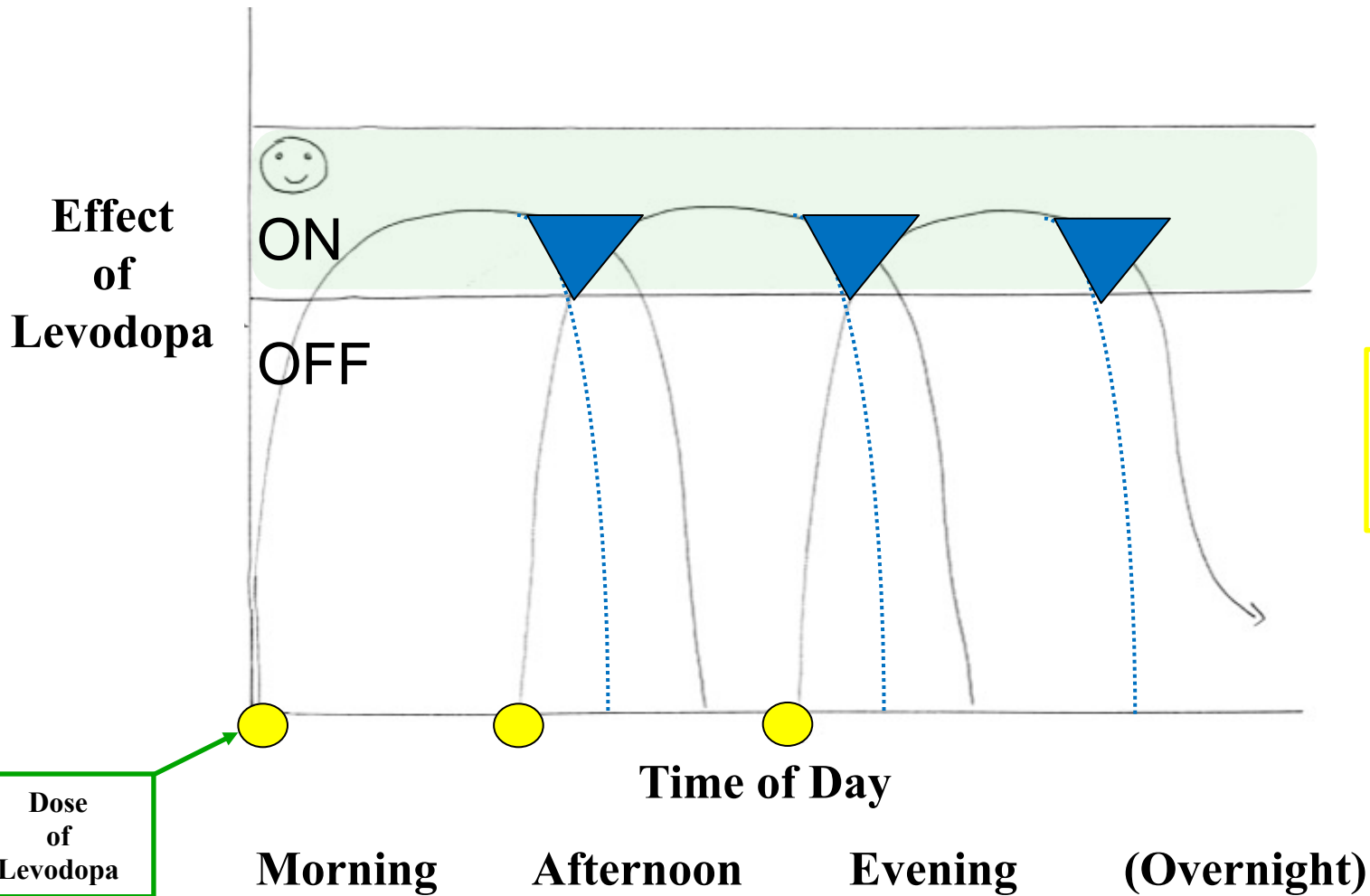
# Effect of Levodopa vs. Time of Day Changes Over Years



# Effect of Levodopa vs. Time of Day



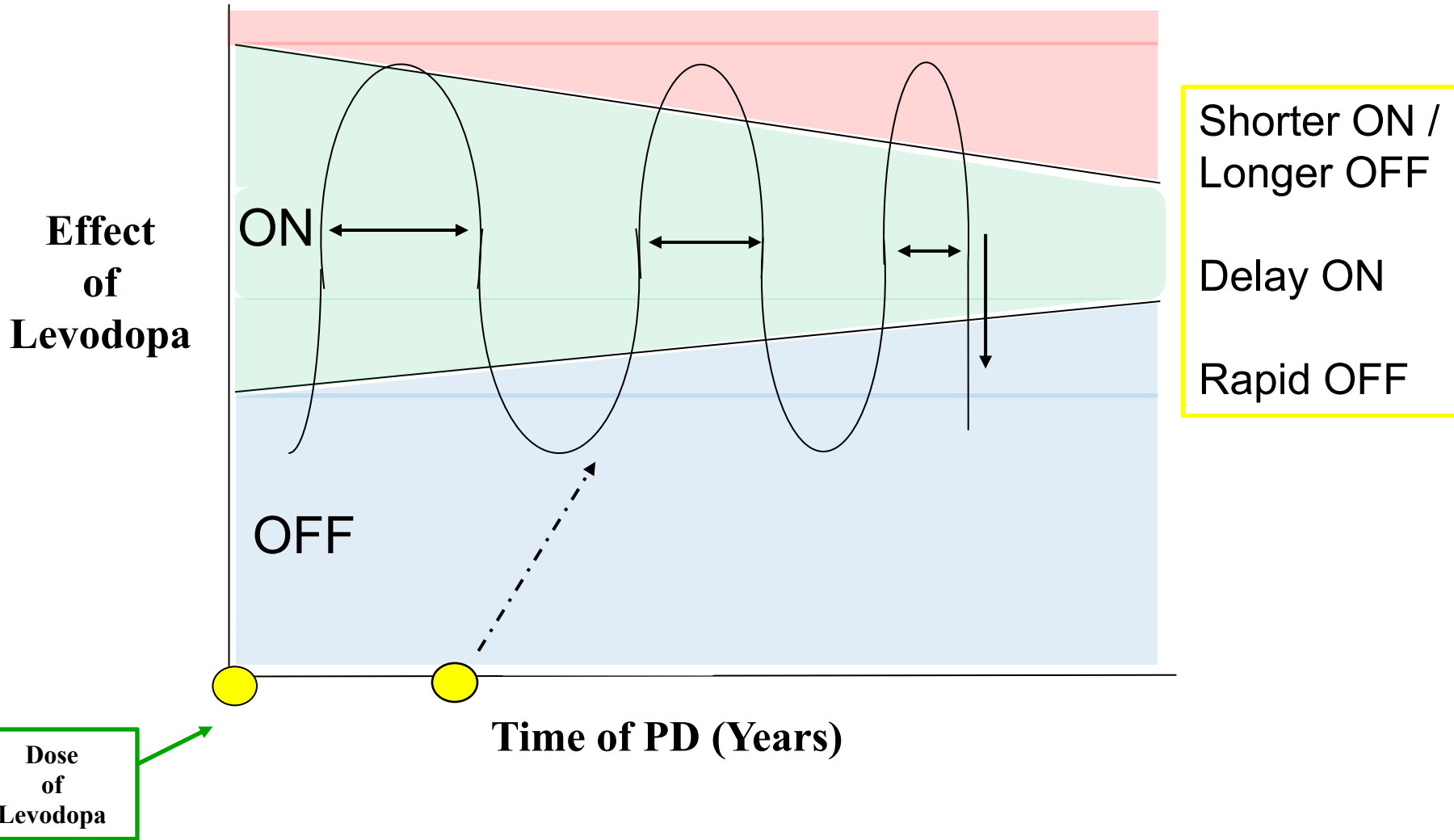
# Effect of Levodopa vs. Time of Day



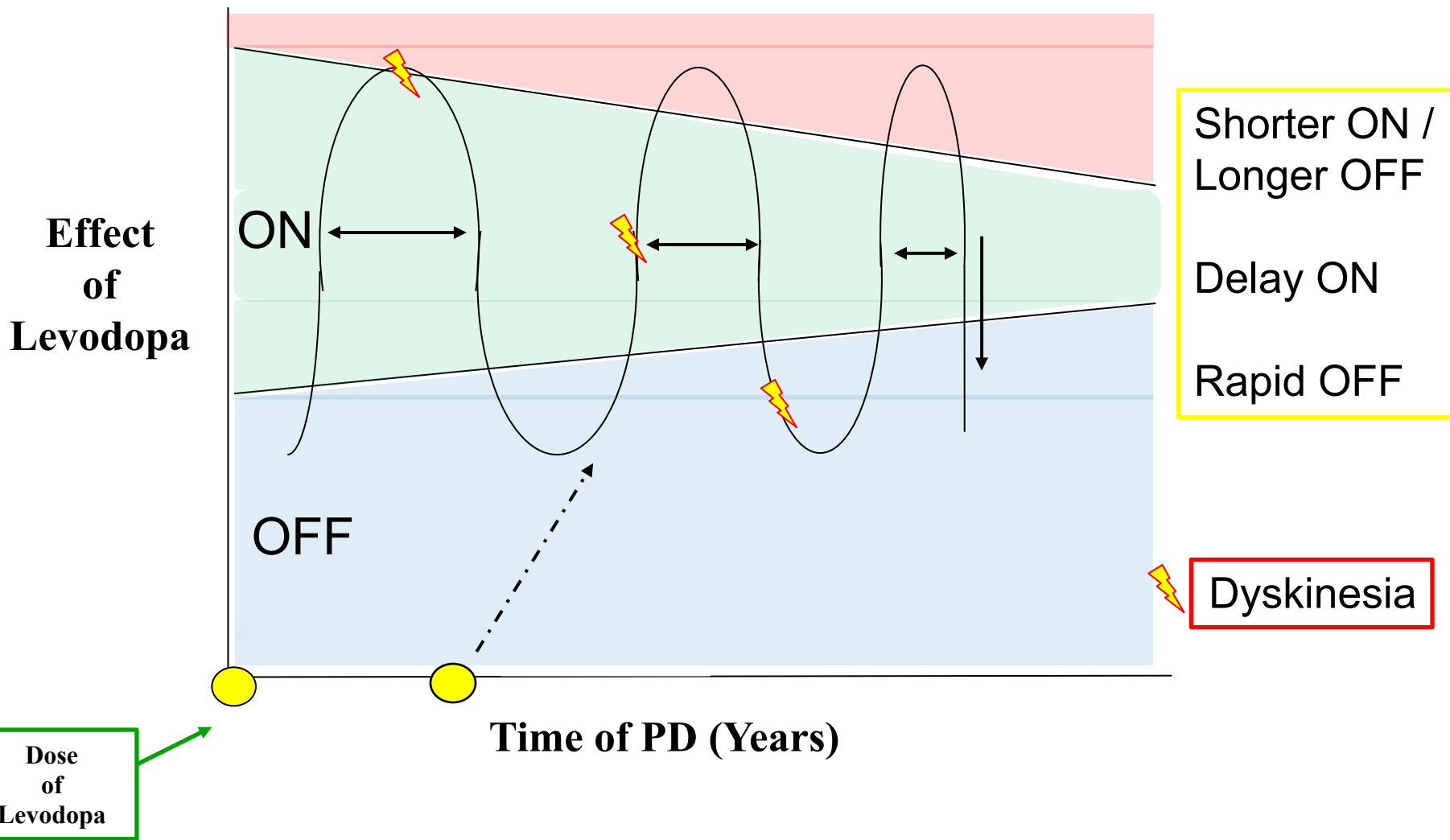
If needed,  
keep a log of  
symptoms  
and times



# Effect of Levodopa vs. Duration of PD: Motor Fluctuations

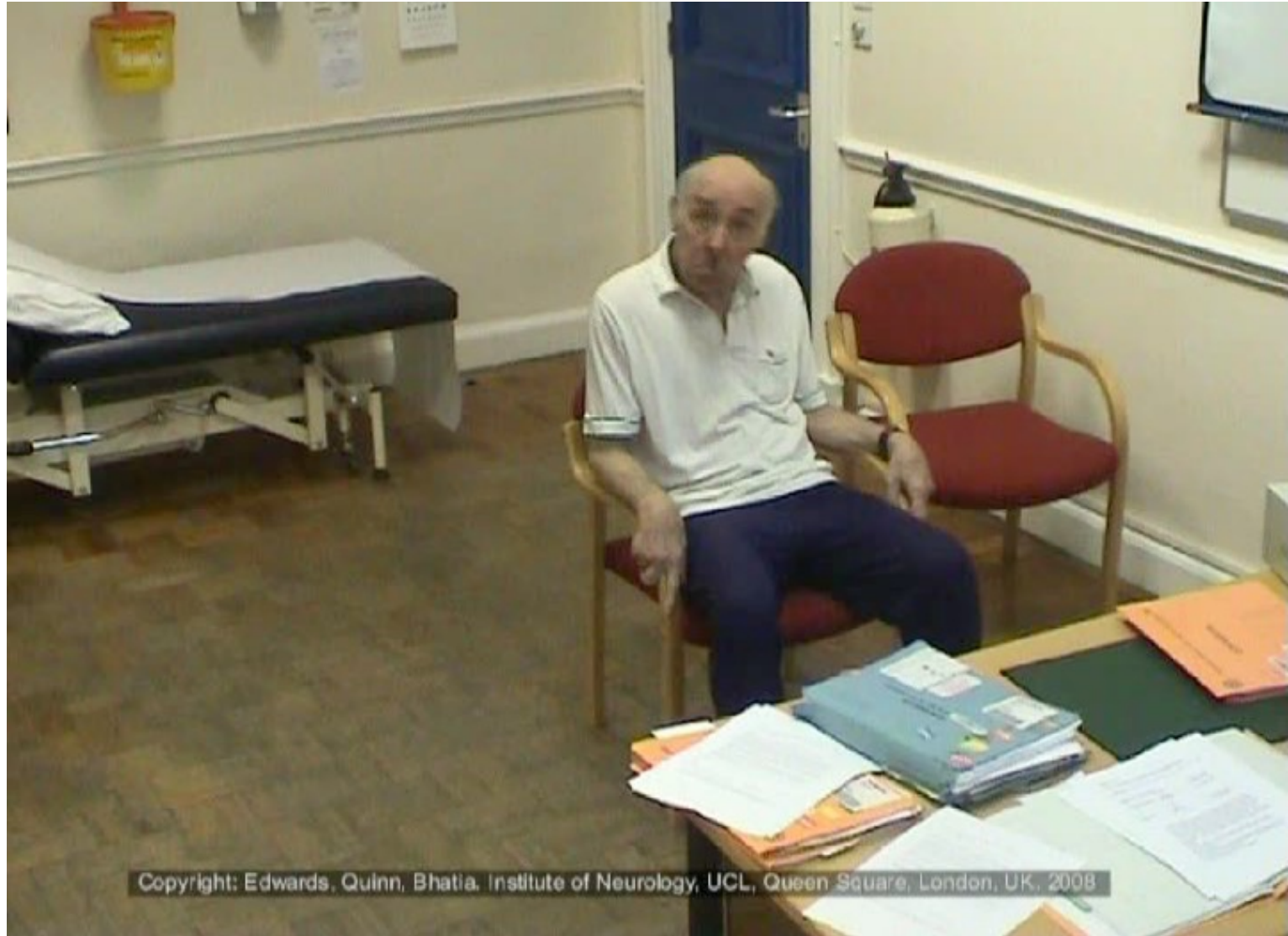


# Effect of Levodopa vs. Duration of PD: Motor Fluctuations



# *Dyskinesia*: dance-like, wiggling, non-rhythmic movements

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# Risk Factors for Dyskinesias

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- Years of PD
- Young Age at Onset of PD
- Higher Cumulative Levodopa Dose
- Low Body Weight
- Female
- Entacapone

# Mitigating Motor Fluctuations: Three-pronged Approach

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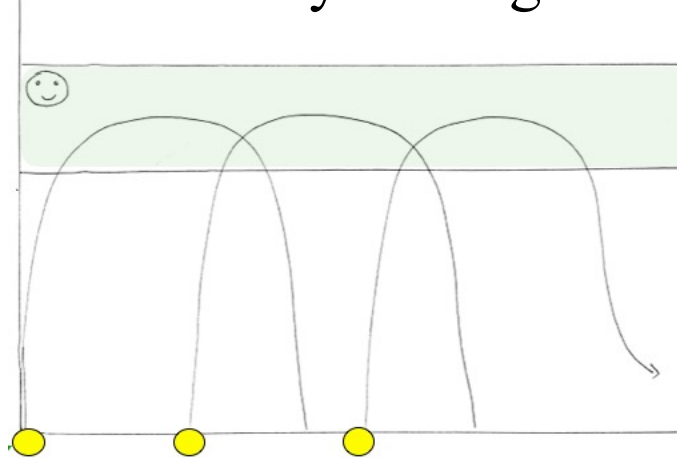
**1. Lifestyle**

**2. Medications**

**3. Advanced Therapies**

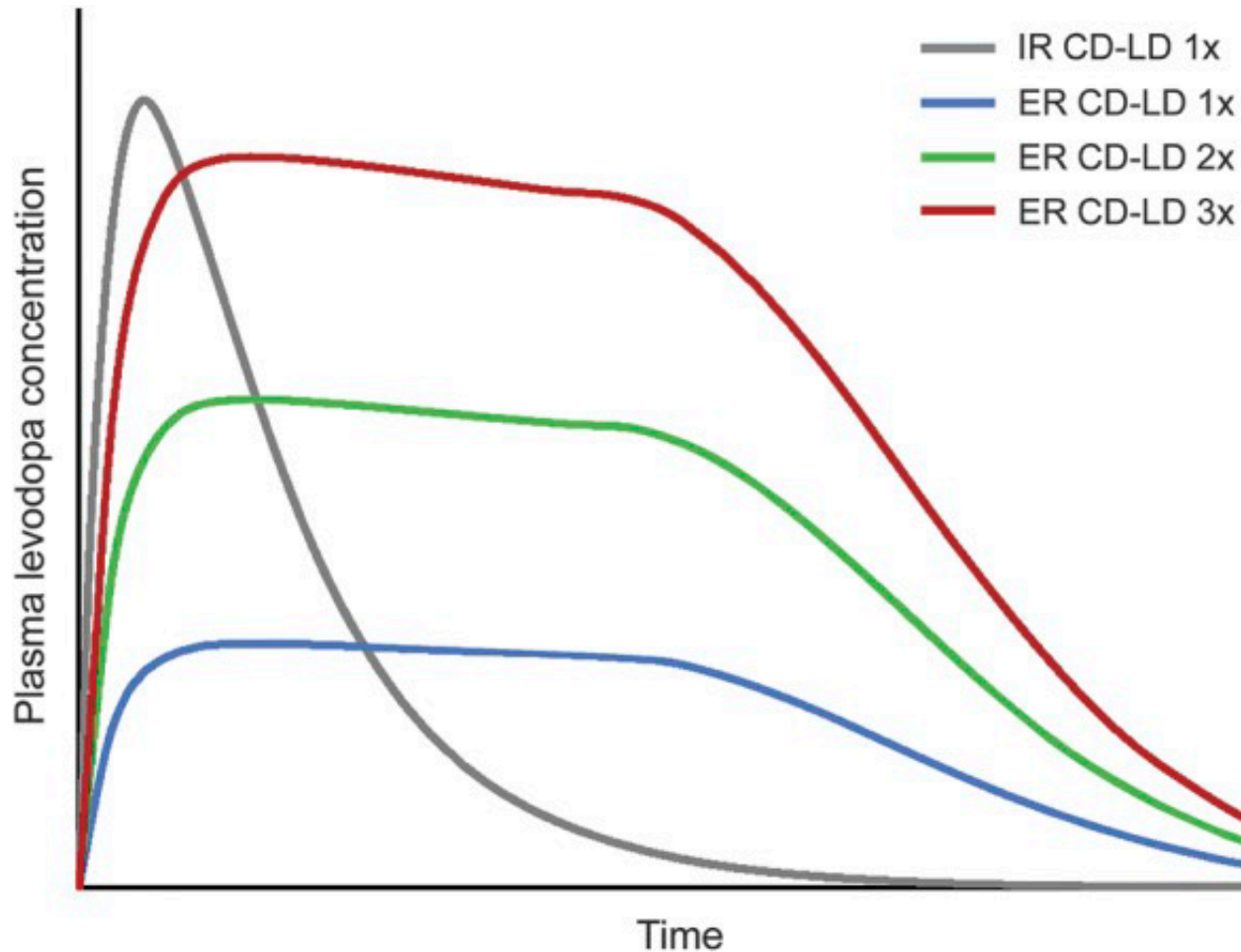
# Lifestyle Variables

- 1. Medication Adherence** – Working with your neurologist, determine necessary doses for your optimal quality of life. Stay within 30 min of your target dose times. Set alarms.



- 2. Exercise Regimen** – Exercise regularly. Discuss possible supplemental treatment before extensive exercise.
- 3. Dietary Regimen** – If fluctuations occur and above factors are optimized, then separate Carbidopa/Levodopa from meals/proteins.

# Medication Adjustments



Example: Switching Carbidopa/Levodopa from IR to “ER” (IR+CR) increases ON / decreases OFF times.

# PD Oral Medication Comparisons in Brief

<u>Medication Class</u>	<u>Relative Advantages</u>	<u>Relative Disadvantages</u>
L-dopa	<b>Robust Motor Benefit</b> Modest Side Effect Profile	3x or More Daily Dosing More Fluctuation Highest Risk Dyskinesia
Dopamine Agonists	Strong Motor Benefit <b>Once Daily Dosing</b> Can be used alone or w/L-dopa	<b>Mental Status Side Effect Risk</b>
MAO-B Inhibitors	Modest Motor Benefit Modest Side Effect Profile <b>Once Daily Dosing</b> Can be used alone or w/L-dopa	
COMT Inhibitors	Modest Motor Benefit Extends / Used w/L-dopa Dose	<b>Increase Risk Dyskinesia</b>
Amantadine IR/ER	Modest Motor Control <b>Decreases Dyskinesia</b> Can be used alone, usu. w/L-dopa	<b>Mental Status Side Effect Risk</b>
Istradefylline	Modest Motor Control	
Carbidopa	Higher dose may be helpful for fluctuations.	



# PD Medications

<u>Medication Class</u>	<u>Medication</u>	<u>Route of Administration</u>
L-dopa	Carbidopa/Levodopa (IR)	Oral, Sublingual, <u>Inhaled*</u>
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# Advanced Therapies in Brief

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## **Levodopa-Carbidopa Intestinal Gel Infusion**

A tube is surgically implanted through the abdomen into the stomach. Daily LD-CD gel is infused through the tube into the gut through an external pump.

Indication: Treat Motor Fluctuations

Optimal Oral Management, Dopamine Benefit

*Considerations:* Pump/GI Complications / Rx Side Effects, incl. Dyskinesia

## **Deep Brain Stimulation (DBS)**

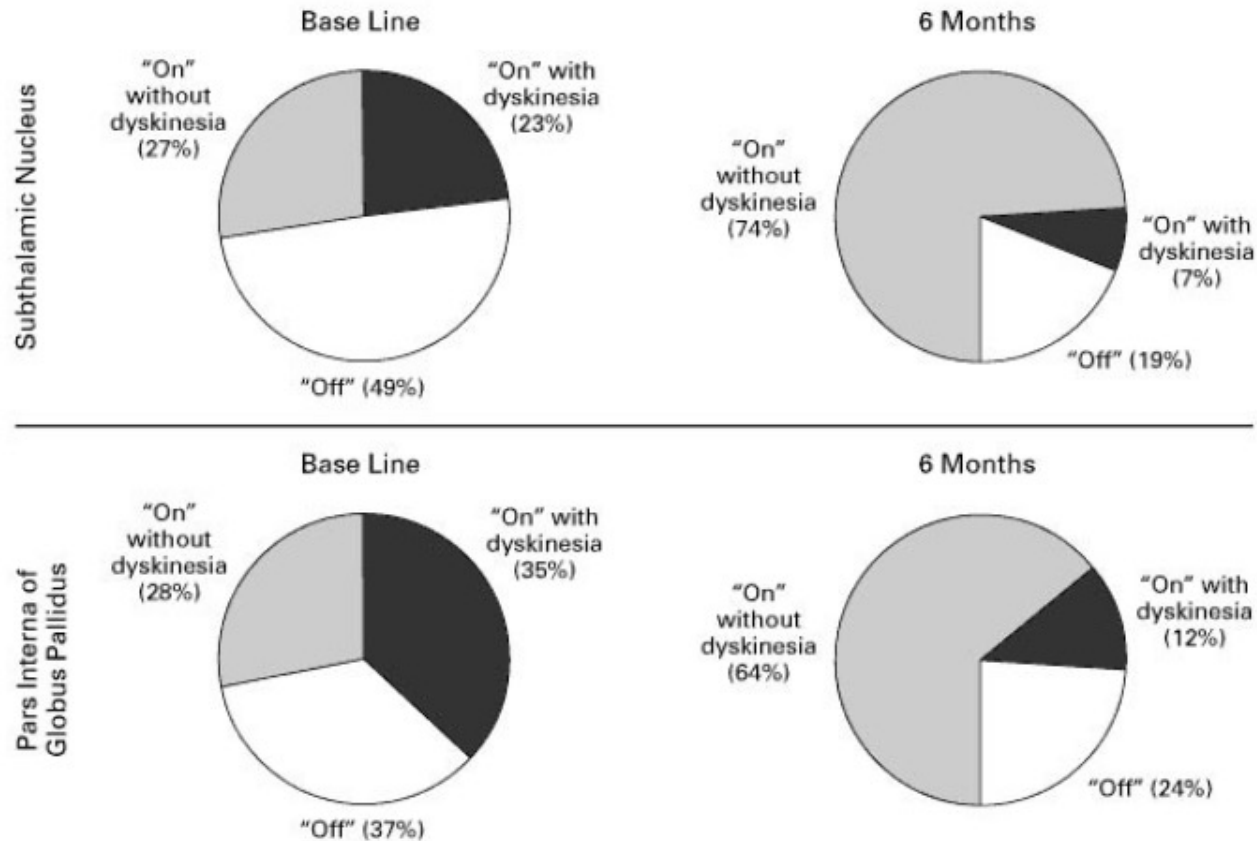
Electrodes are implanted in the brain and programmed remotely to provide motor symptom benefit and reduce the dose of dopamine medications.

Indications: Motor Fluctuations, Dyskinesia; (Others)

Optimal Oral Management, Dopamine Benefit

Considerations: Brain Surgery, Low Complications; Cognitive Health

# DBS Improves ON Time and Reduces Dyskinesia



Clinical benefit is sustained for at least 10 years.

# Summary

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If you experience motor fluctuations or dyskinesias, you and your neurologist should discuss:

- A. Your Movement Goals
- B. Medication Options / Benefit vs. Side Effect Profile
- C. Adherence to Your Medication Schedule
- D. Additional Lifestyle Variables: Exercise, Diet
- E. Device-aided Therapies / Educate Early

Thank you for your attention.

Are you ready for a quiz?

# Quiz Question 1

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What should you do first if you notice that on some days that your Parkinson's disease symptoms are not as well-controlled as you would like them to be?

- A. Take some extra medication now and again to help your symptoms.
- B. Separate your medication from your meals.
- C. Start taking vitamins to help your brain work better.
- D. Attentively adhere to the medication doses and timing you have planned with your neurologist.

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# Quiz Question 2

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Which of the following medications is most likely to be associated with motor fluctuations?

- A. Melatonin
- B. Carbidopa/Levodopa IR
- C. Once daily dopamine agonist
- D. Amantadine
- E. All of the above

# Quiz Question 2

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Which of the following medications is most likely to be associated with motor fluctuations?

A. Melatonin

B. Carbidopa/Levodopa IR

C. Once daily dopamine agonist

D. Amantadine

E. All of the above

# Quiz Question 3

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Which of the following factors may be associated with the development of motor fluctuations?

- A. Advanced Parkinson's Disease
- B. Overuse of Carbidopa/Levodopa
- C. Inconsistent Medication Timing
- D. Routine Exercise
- E. Adherence to a well-timed regimen of lowest effective doses of PD medications

# Quiz Question 3

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C. Inconsistent Medication Timing

D. Routine Exercise

E. Adherence to a well-timed regimen of lowest effective doses of PD medications

# Quiz Question 4

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If you suffer from dyskinesias, you can conclude that your Carbidopa/Levodopa is no longer effective for treating your motor symptoms.

A. True

B. False

# Quiz Question 4

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A. True

B. False

# Learning Case – Put on your thinking caps.

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At a routine follow-up appointment with her neurologist she mentions that she is sometimes getting some shaking in her leg.

*What could be the cause of her concerns?*

*What is your first question for her?*

*Good health!*