



Levodopa/carbidopa intestinal gel therapy (Duodopa) for Parkinson Disease

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How do medications work in PD?


What is going on with treatment fluctuations?

How does DUODOPA work to get around these problems?

Who is the 'right patient' for this treatment?

What needs to happen for DUODOPA to be used?

What are some downsides to this treatment option?



Think of the brain's supply of dopamine like bread at a bakery

Spelt Sourdough \$6.50

Honey Spelt Bread \$6.00

5- Grain Pan Bread \$5.50

The baker plans to make enough bread for the customers expected that day

Simple Sourdough \$6.00

Ancient Multigrain Pan Bread \$6.00

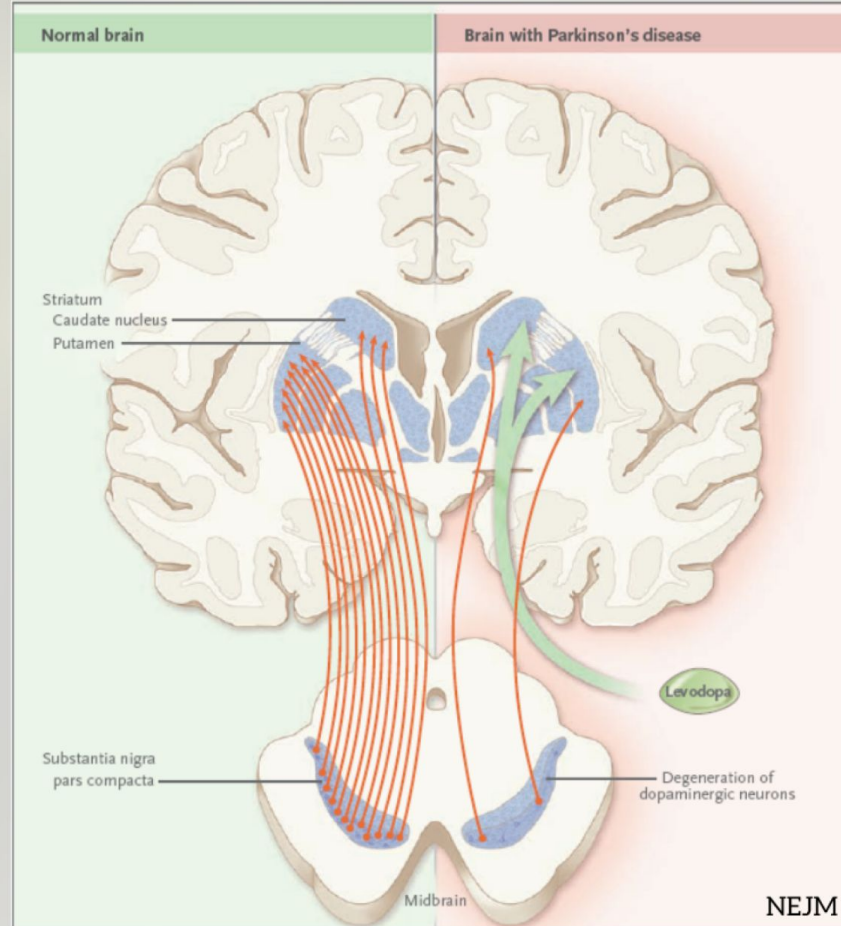
In PD, Loss of dopamine production is gradual

**The result, at some point, is that there is not enough product
and symptoms emerge**



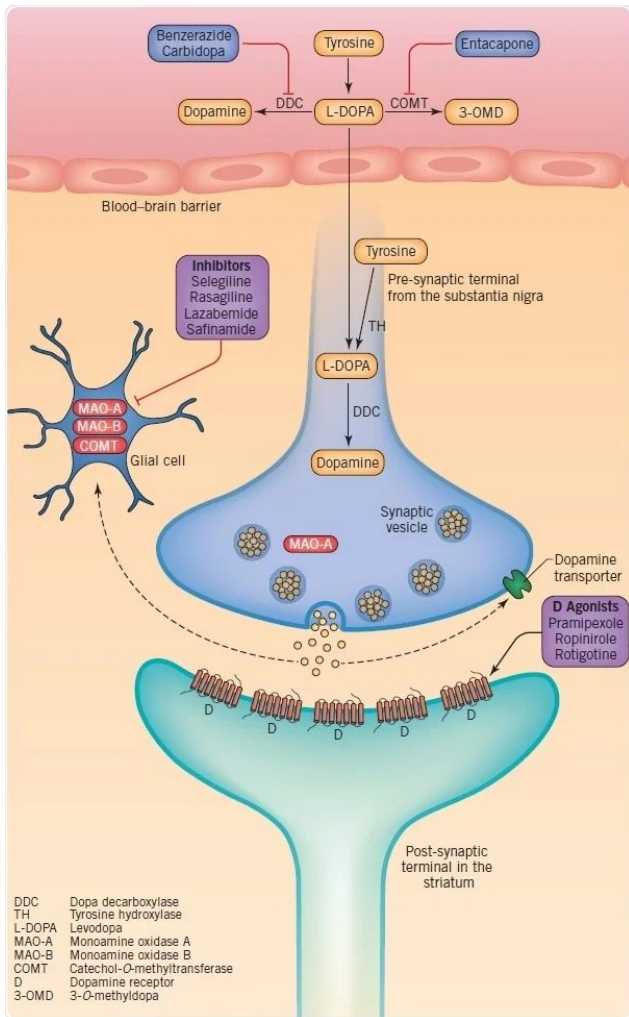
Dopamine deficiency is a SYMPTOM of the disease

In the healthy state, there are many dopamine cells making dopamine to use in normal daily activities



In PD there are some dopamine cells working, but can't make enough dopamine to meet the need

← Bakeries



Ingredients



Dough



Bread



Stocked /
packaged

Tyrosine



Levodopa



Dopamine



Stored for
use on
demand

How do PD treatments work?

Improve dopamine production
(more ingredients / dough)

Dopamine precursors like levodopa

LD



How do PD treatments work?

**Substitute the effect of dopamine production
(bypass the bakery, send donuts)
Dopamine agonists**

Dopamine
agonist



How do PD treatments work?

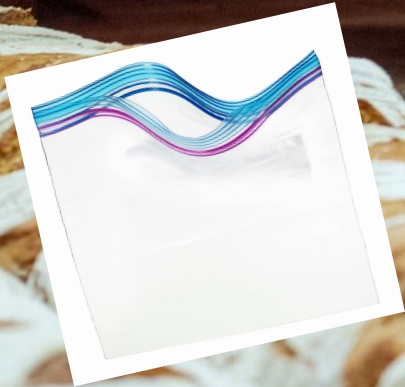
Make dopamine last longer
(Preserve the dough / bread)

Selegiline, rasagiline, safinamide

Entacapone

entacapone

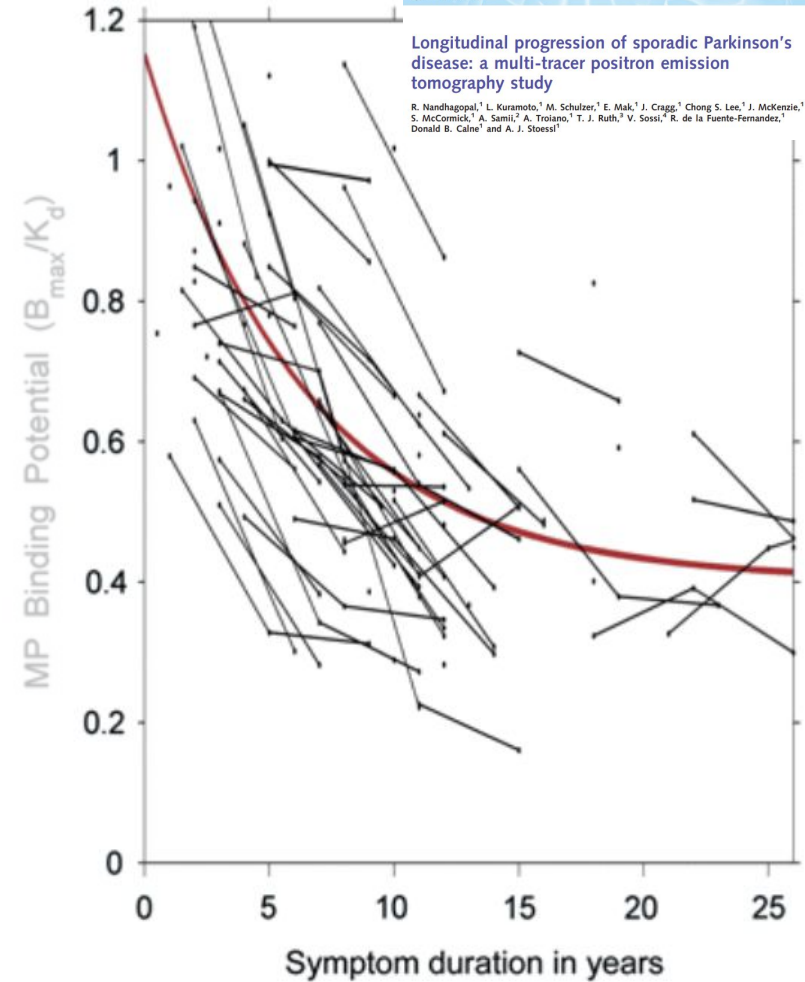
MAOI



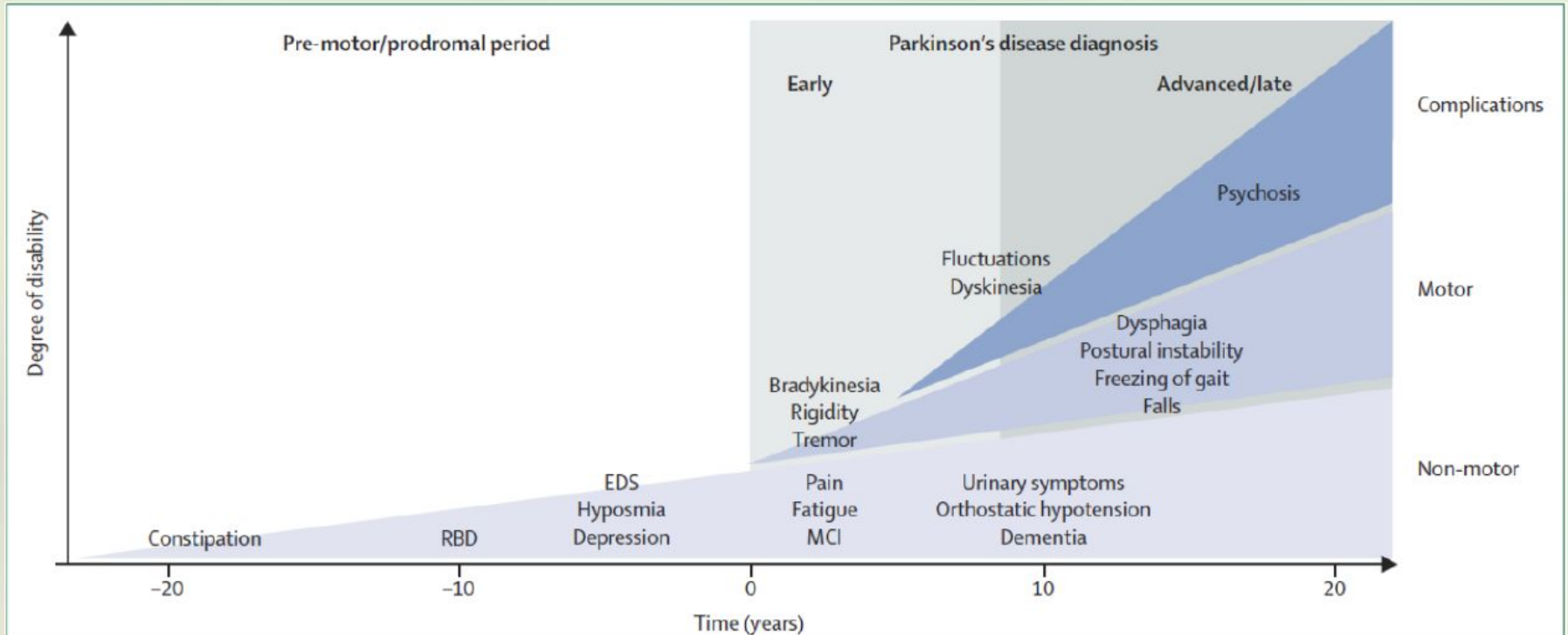
Over time, the
number of bakeries is
still changing



Providing the same
amount of ingredients
has a different effect

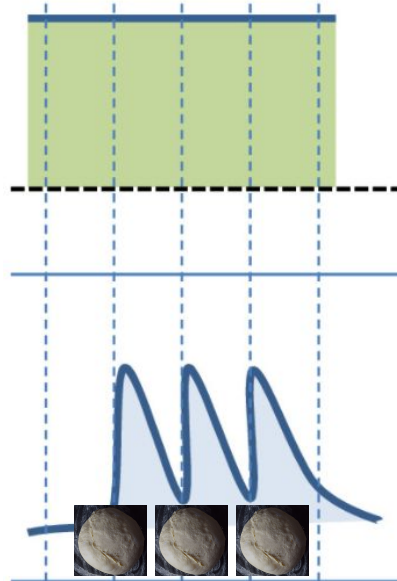


What will happen over time?





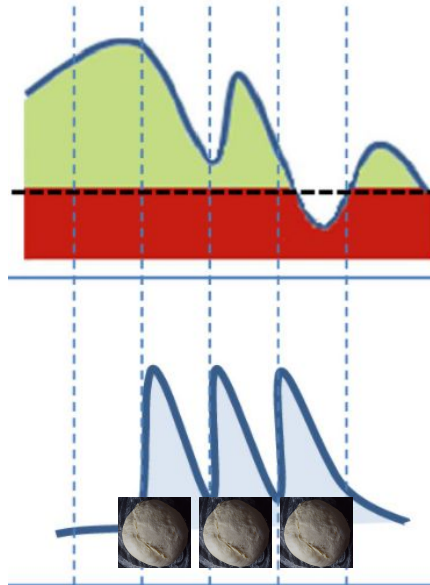
Effect



Medication dose

Early in the course of PD, a prolonged and consistent response to levodopa is common

Fluctuating response

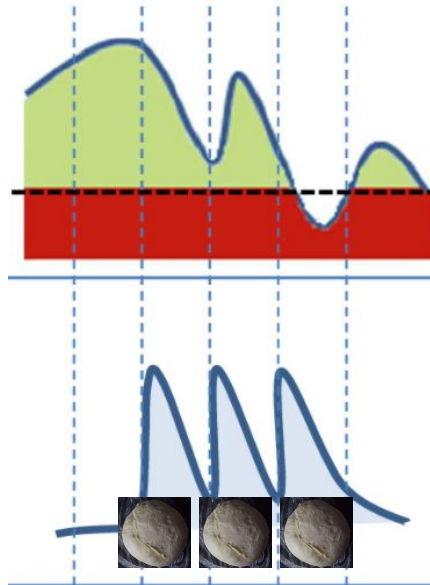


Over time, the response to each dose is less consistent and usually shorter duration



Partly this is because there
are less bakeries working
well over time

Fluctuating response

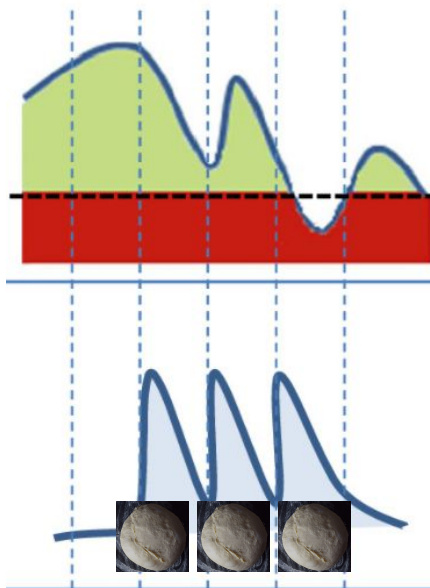


Over time, the response to
each dose is less consistent
and usually shorter duration

PwPD also may have poor
absorption of levodopa
(i.e. “baking fail”)



Fluctuating response



Over time, the response to
each dose is less consistent
and usually shorter duration

Reasons for poor dose responses (“Baking fails”)

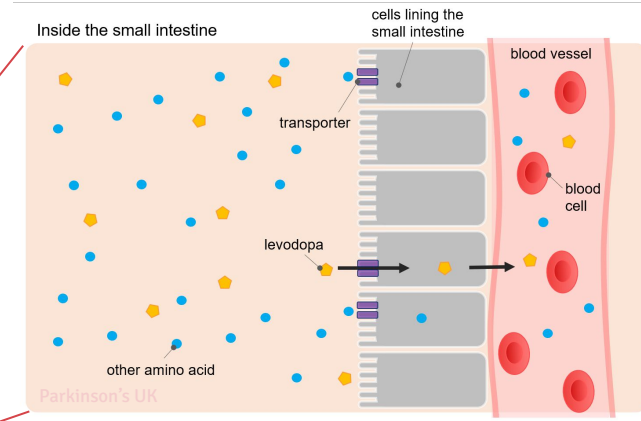


There, it is
turned into
dopamine by
the dopamine
cells

Once in the
bloodstream,
levodopa is taken
to the brain

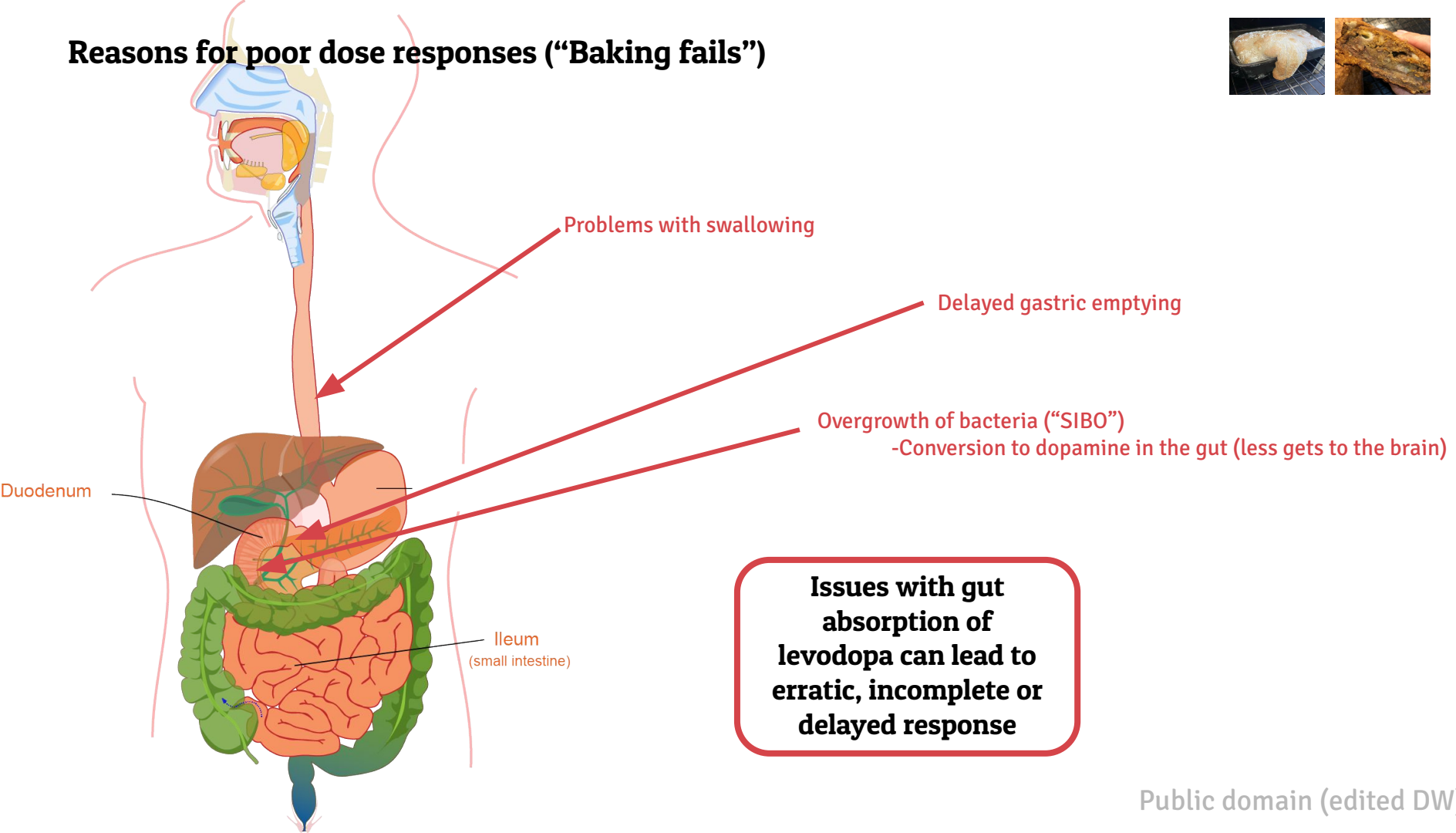
Duodenum

Ileum
(small intestine)



**Absorption of levodopa
in the small intestine
competes with other
amino acids**

Reasons for poor dose responses (“Baking fails”)



Tools to figure out how well treatment is working for a person with PD:



**Good old fashioned history
and physical**

Parkinson's Disease Symptom Diary

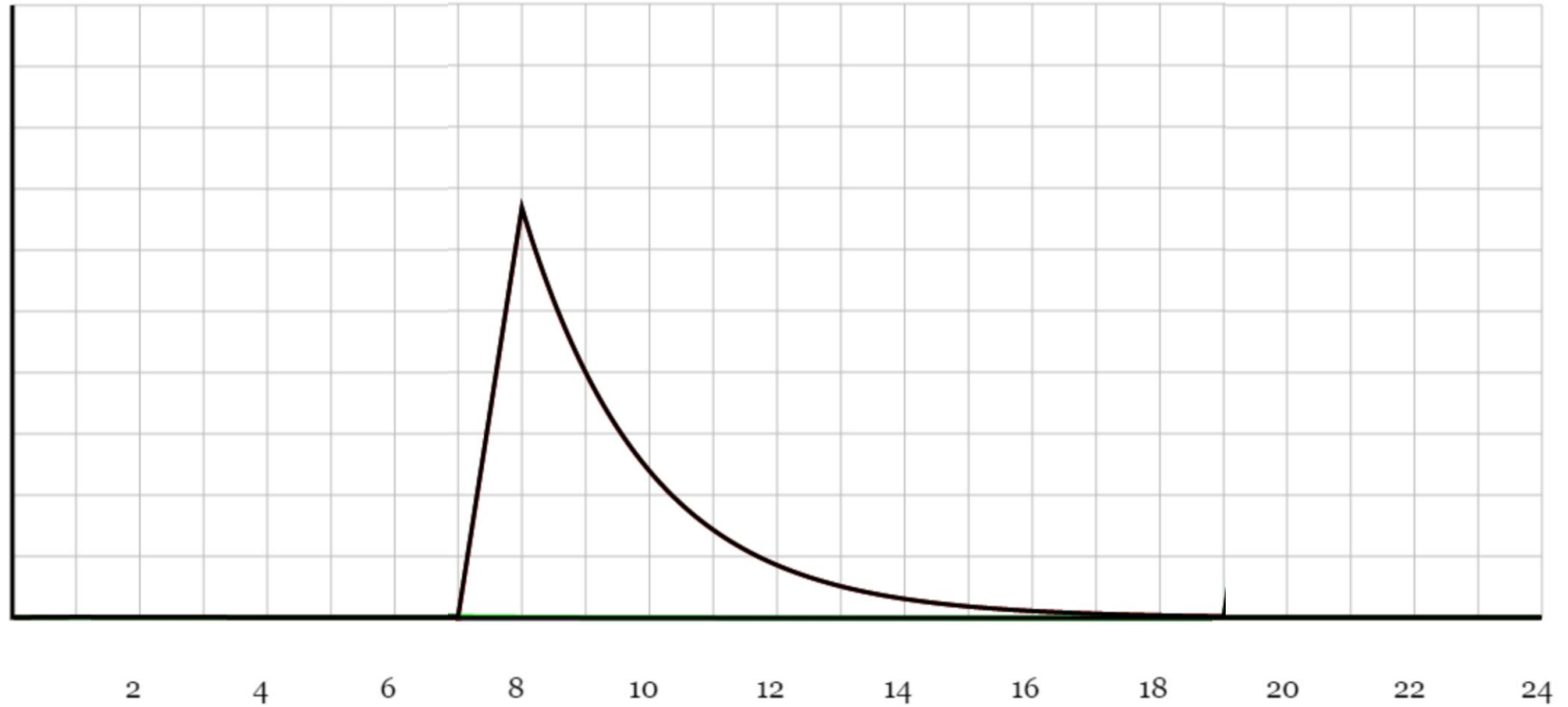
| Parkinson's Symptoms | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 1 | 2 | 3 | 4 |
|----------------------|---|---|---|---|---|---|---|---|---|----|----|----|---|---|---|---|---|---|---|---|---|----|----|----|---|---|---|---|
| mobility | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| +3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| +2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| +1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| -1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| -2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| -3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tremor | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 No tremor | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 Mild | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 Mod-Severe | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dystonia | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 No dystonia | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 Mild | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 Mod-Severe | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Medication taken | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

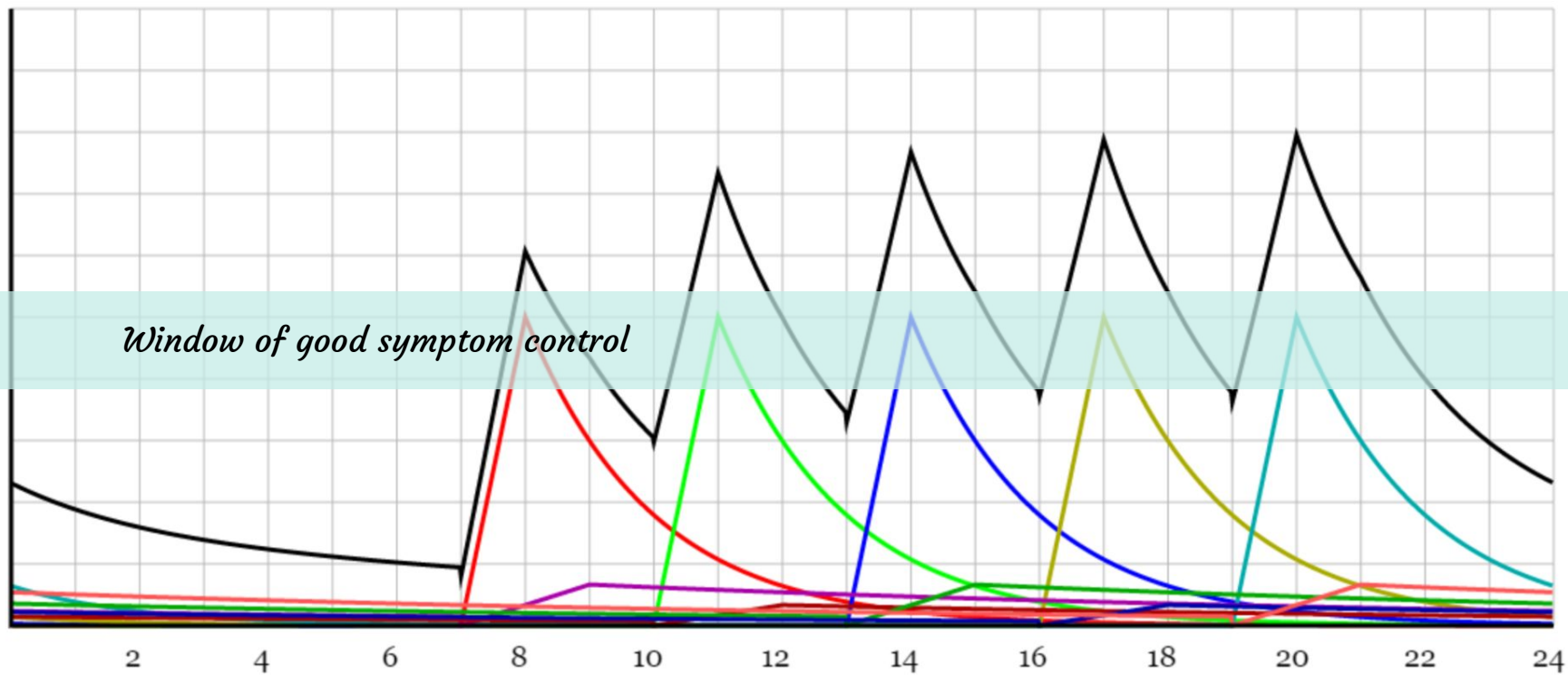
Symptom diaries



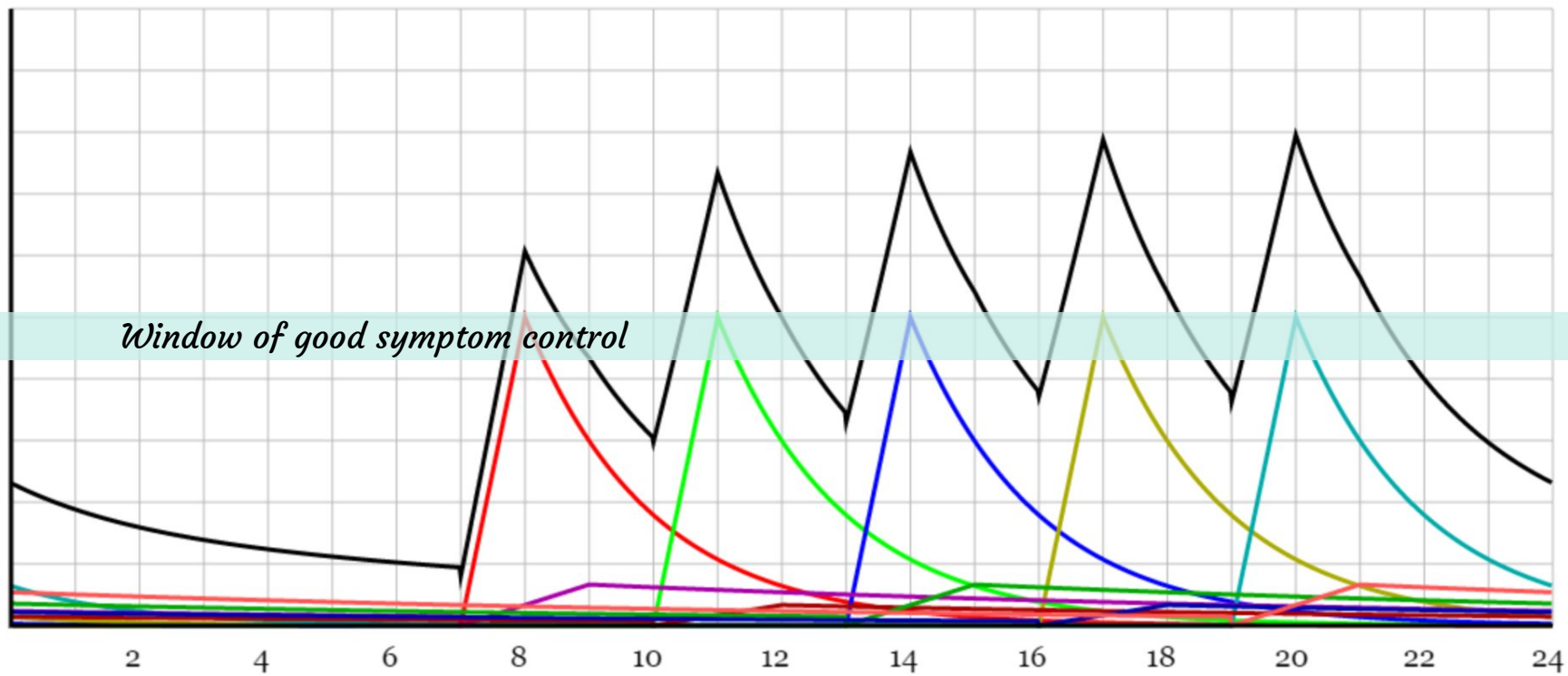
Motion trackers

Estimating how medication works - if absorption and delivery to the brain is 'perfect'



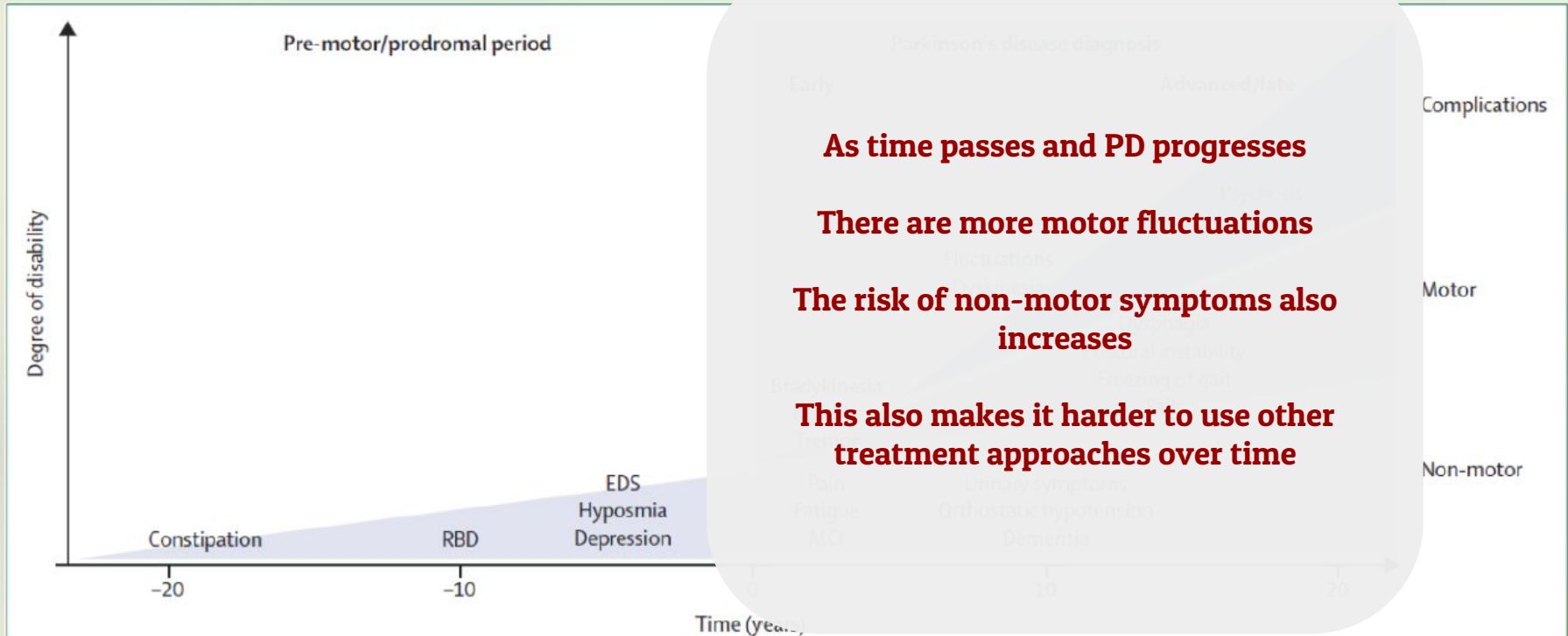


Window of good symptom control



Window of good symptom control

What will happen over time?





How do medications work in PD?

What is going on with treatment fluctuations?

How does DUODOPA work to get around these problems?

Who is the 'right patient' for this treatment?

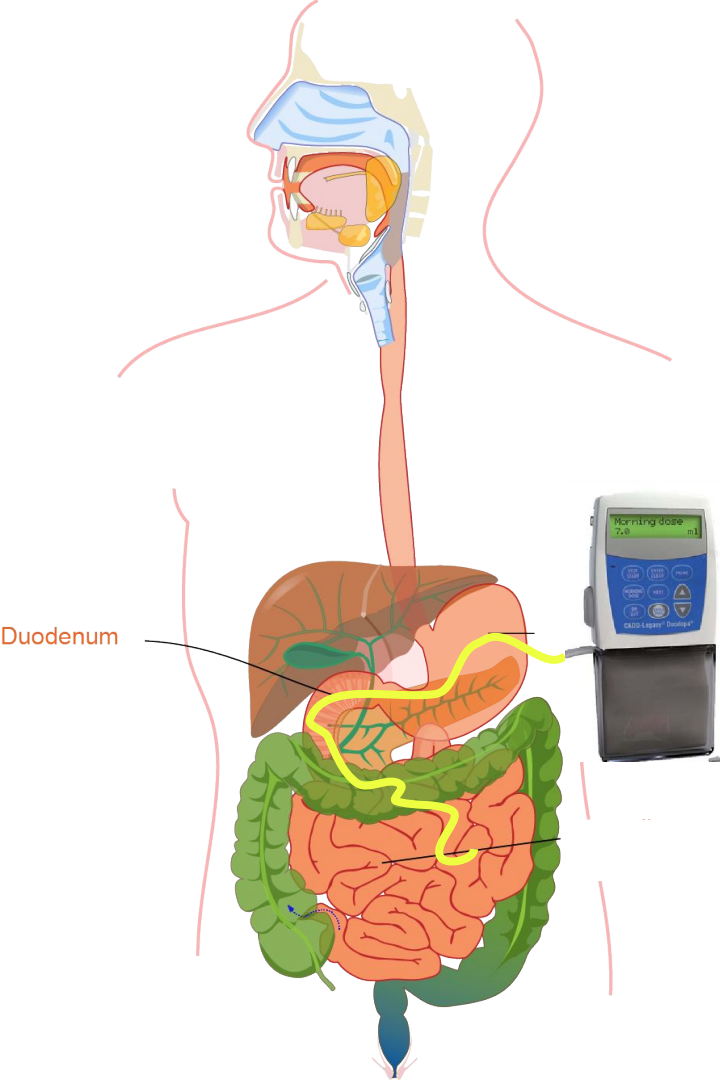
What needs to happen for DUODOPA to be used?

What are some downsides to this treatment option?



As the need for 'ingredients' becomes more frequent

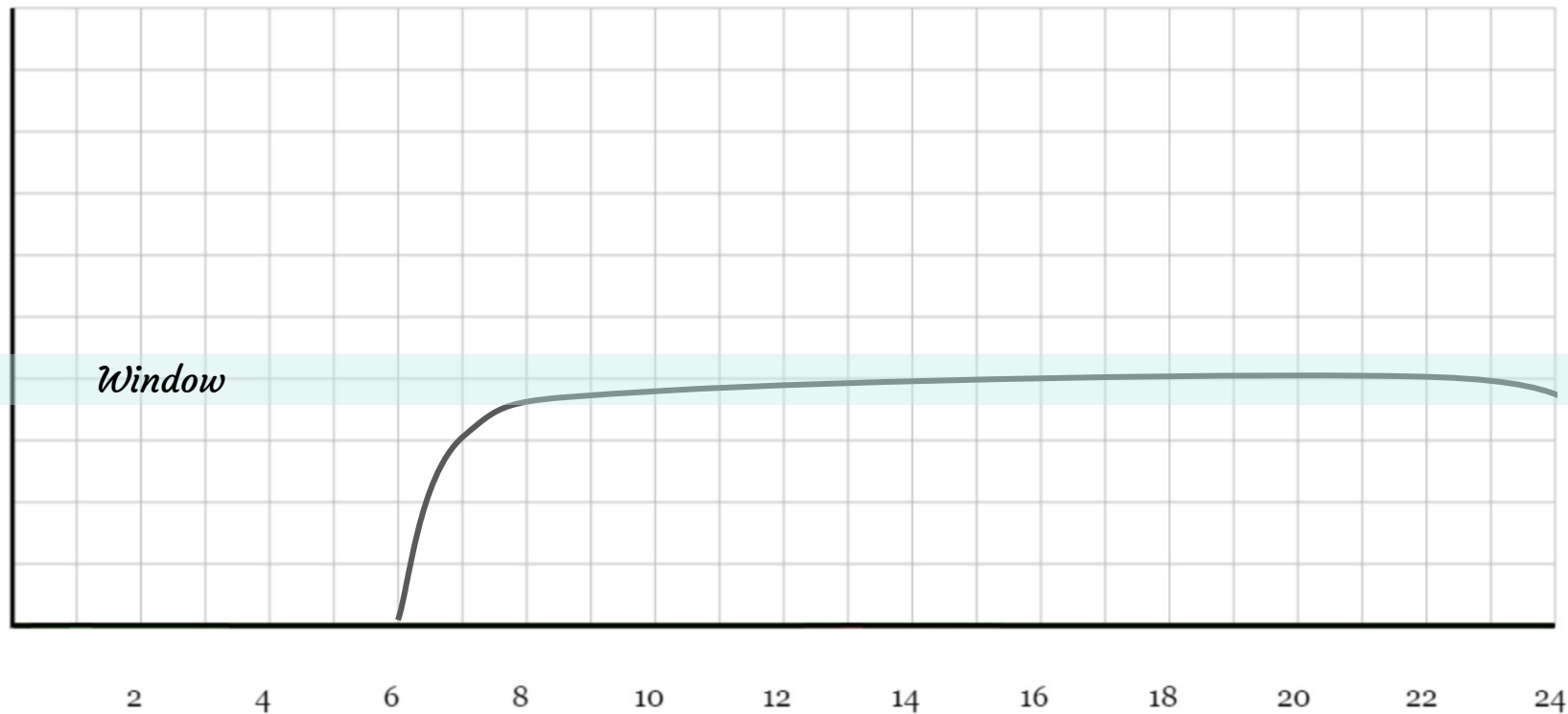
Continuous gradual delivery of levodopa ('dough') can target a consistent effect



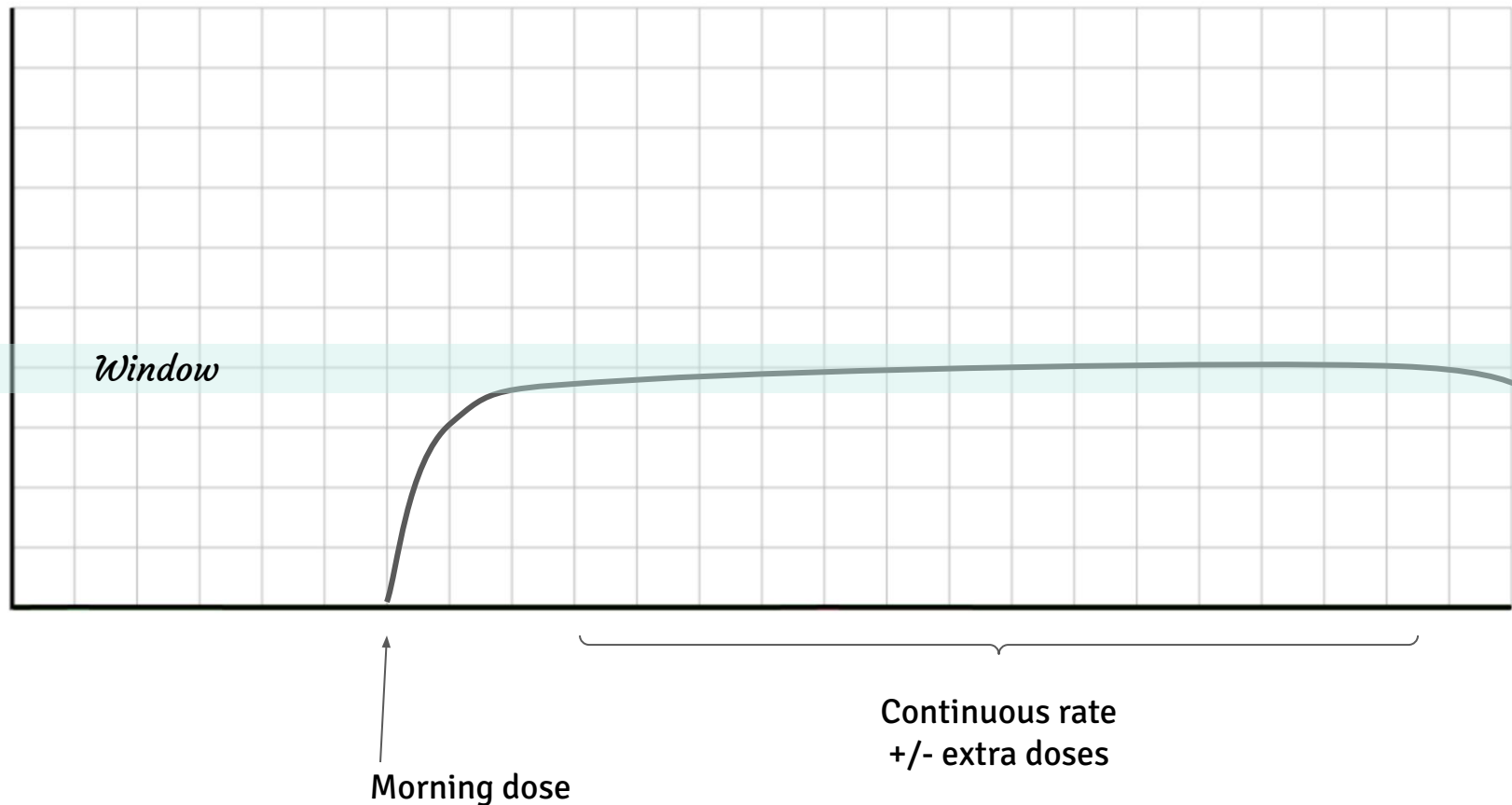
Duodopa delivers a continuous supply of levodopa carbidopa gel to the small intestine

This allows a more consistent absorption of 'ingredients' into the bloodstream, and more steady delivery to the brain dopamine cells

The goal of DUODOPA therapy is to establish a steady treatment effect in the “window” of good symptom control



The goal of DUODOPA therapy is to establish a steady treatment effect in the “window” of good symptom control



Who is the right patient for DUODOPA?

**Levodopa responsive
Parkinson Disease**

**Motor fluctuations
Dyskinesia**

These are disabling

**Despite adequate
effort to treat with oral
medications**

**The benefits are
expected to outweigh
the risk of**

**Tube insertion
Prolonged tube use**

**Adequate support for management of the system
(Care partner)**

What needs to happen to start DUODOPA treatment?

**Review with
movement
disorder
specialist to
consider
medication
options**

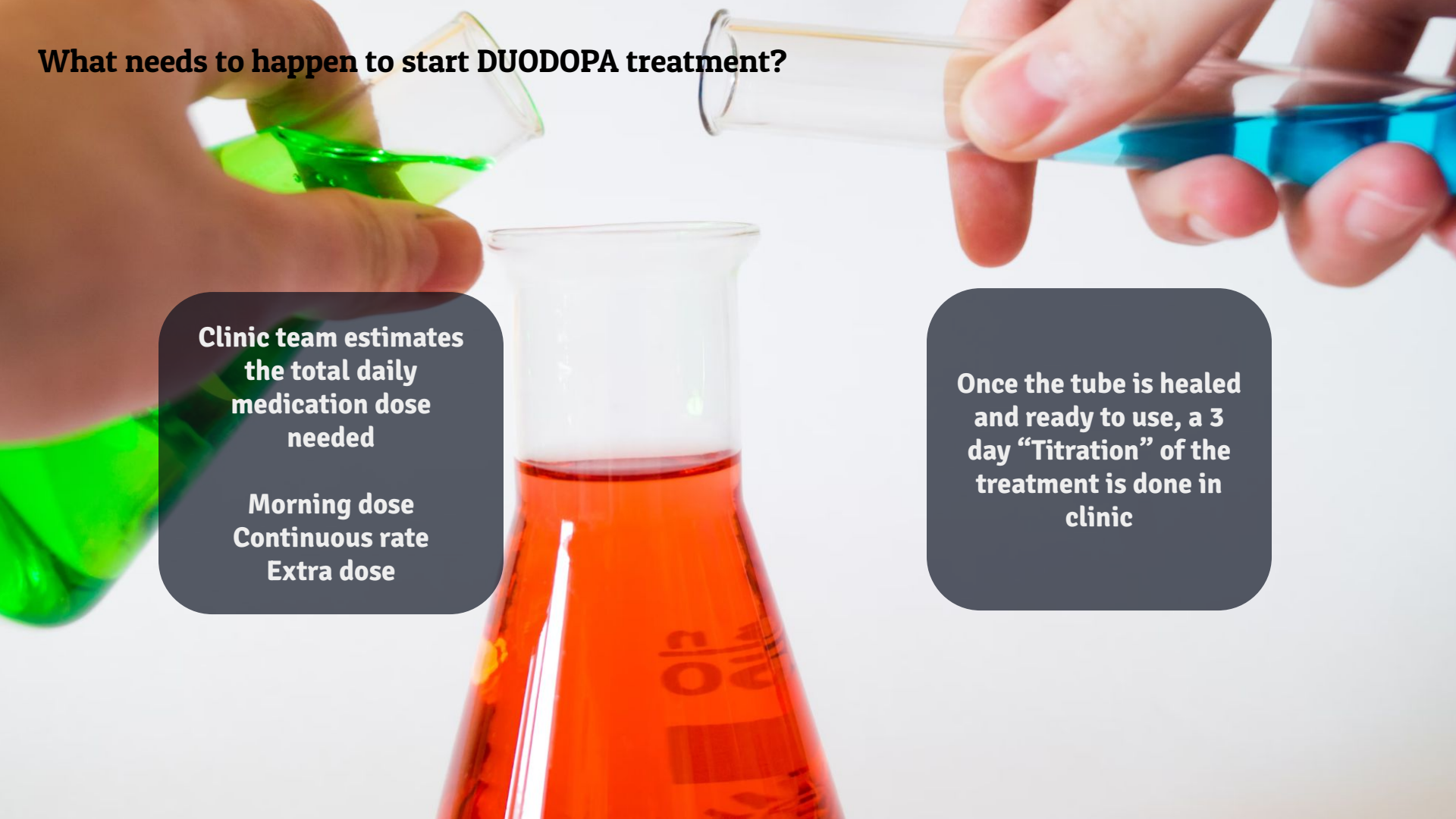
**Teaching about
the procedure
and the pump
system

(patient and
caregiver)**

**Apply for
coverage of the
medication by
Pharmacare or
insurance**

**Referral to
gastroenterologist
for PEG-J tube
placement**

What needs to happen to start DUODOPA treatment?

A laboratory setting with a hand pouring green liquid from a test tube into a flask containing orange liquid, and another hand holding a test tube with blue liquid.

**Clinic team estimates
the total daily
medication dose
needed**

**Morning dose
Continuous rate
Extra dose**

**Once the tube is healed
and ready to use, a 3
day “Titration” of the
treatment is done in
clinic**

Risks

Tube complications

**Blockage
Removal
Migration
Breakage**



Wound (stoma) complications

**Scar tissue
Infection
Leaking**



Other

**Weight loss
Vitamin deficiencies
Pump issues**

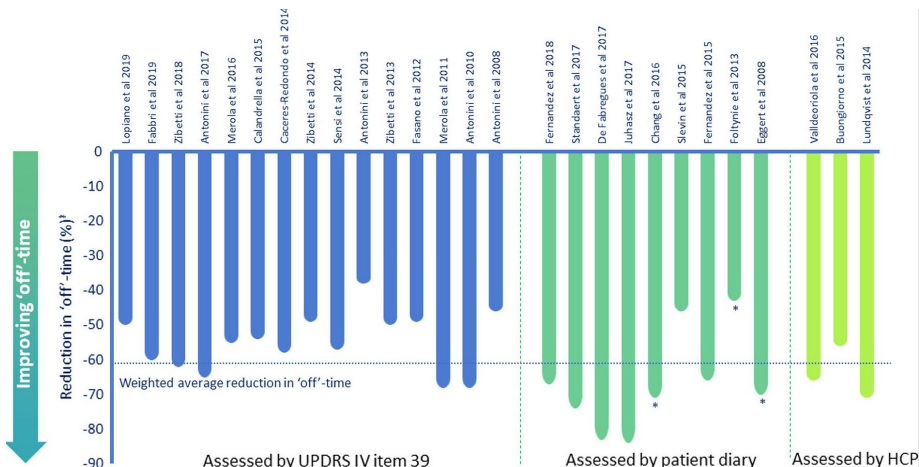




REVIEW

The Long-Term Impact of Levodopa/Carbidopa Intestinal Gel on ‘Off’-time in Patients with Advanced Parkinson’s Disease: A Systematic Review

Angelo Antonini · Per Odin · Rajesh Pahuja · Jason Aldred ·
 Ali Alobaidi · Yash J. Jalundhwala · Pavnit Kukreja · Lars Bergmann ·
 Sushmitha Inguva · Yanjun Bao · K. Ray Chaudhuri



This therapy has been in use for >15 years in some European centers

There is evidence to support long term effectiveness of treatment and persistent improvement in “OFF” time

PwPD should weigh benefits and risks of oral medication options with the benefits and risks of this approach

THANKS!