A paved walkway in a park-like setting with trees and a large circular seal on the ground. The seal features a central emblem and the text 'THE OHIO STATE UNIVERSITY' and 'DISCIPLINA'.

# Principles of Symptom Management in Parkinson's Disease

**Pietro Mazzoni, MD PhD**



# Disclosures

- None



# Topics

- When to start carbidopa/levodopa
- Medication options for motor fluctuations
- Two reasons to refer for possible deep brain stimulation
- Medication options for behavioral symptoms



# **When to start carbidopa/levodopa**



# Case

- 78M with 18-month hx of feeling unsteady when walking. The unsteadiness has been gradually worsening, and he had a fall in the past year. He has been using a cane for about a month.
- Exam: moderate generalized parkinsonism that included hypomimia, slow gait, and a positive pull test



# Would you: (assume dx is PD)

- A. Suggest starting carbidopa/levodopa
- B. Start carbidopa/levodopa
- C. No need to start C/L at this time



# Answer

- ~~A. Suggest starting carbidopa/levodopa~~
- **B. Start carbidopa/levodopa**
  - Falls, subjective unsteadiness, positive pull test
  - Also start physical therapy
- ~~C. No need to start C/L at this time~~



# Case

- 64M with 3 yrs of reduced facial expressiveness, slowing of walking, softening of voice, reduction of right arm swing, reduction of handwriting size. He noticed that his right hand needed assistance from his left hand, “as if weak”.
- Arising from a couch and turning in bed is not difficult. He does not stumble. He does not feel unsteady and he has not fallen.
- Exam: moderate asymmetric parkinsonism that included hypomimia, hypokinesia, rigidity, and slow gait.



# Would you: (assume dx is PD)

- A. Suggest starting carbidopa/levodopa
- B. Start carbidopa/levodopa
- C. No need to start C/L at this time



# Answer

- ~~A. Suggest starting carbidopa/levodopa~~
- ~~B. Start carbidopa/levodopa~~
- **C. No need to start C/L at this time**
  - Symptoms are not bothersome or dangerous



# Reasons to start carbidopa/levodopa

- Bothersome symptoms
  - embarrassing tremor; reduced social life due to low energy; aching of joints
- Falls/Unsteadiness
  - Positive pull test (have a wall behind you)
  - Tandem gait may be intact



# Reasons NOT TO INSIST on carbidopa/levodopa

- Non-bothersome symptoms
  - Non-embarrassing tremor; slow gait
- But:
  - Patient may have become adjusted to symptoms
  - Suggest trying carbidopa/levodopa for 3 months and then decide



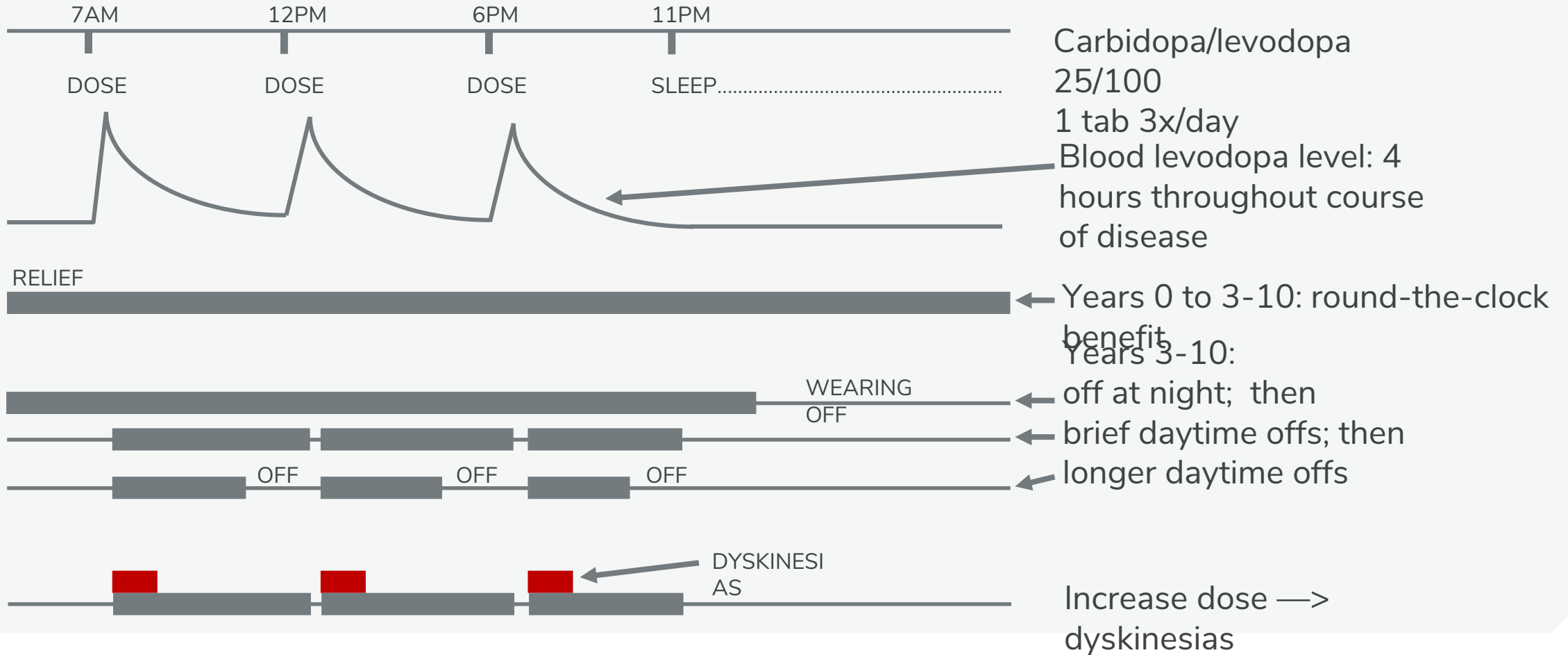
# How to start carbidopa/levodopa

- Carbidopa/levodopa 25/100 tabs
- Age <70
  - week 1, ½ tab 2x/day, morning & dinner; week 2, ½ tab 3x/day, morning-midday-dinner; week 3 & after, 1 tab 3x/day
- Age >70
  - week 1, ½ tab 2x/day, morning & dinner; week 2, ½ tab 3x/day, morning-midday-dinner; week 3, 1-0.5-0.5 tabs; week 4, 1-1-0.5 tabs; week 5 & after, 1 tab 3x/day
- Possible side effects
  - Nausea, vivid dreams, nightmares, visual hallucinations, paranoia, dizziness after standing up, fainting (with possible head injury)
- Update in 6 weeks

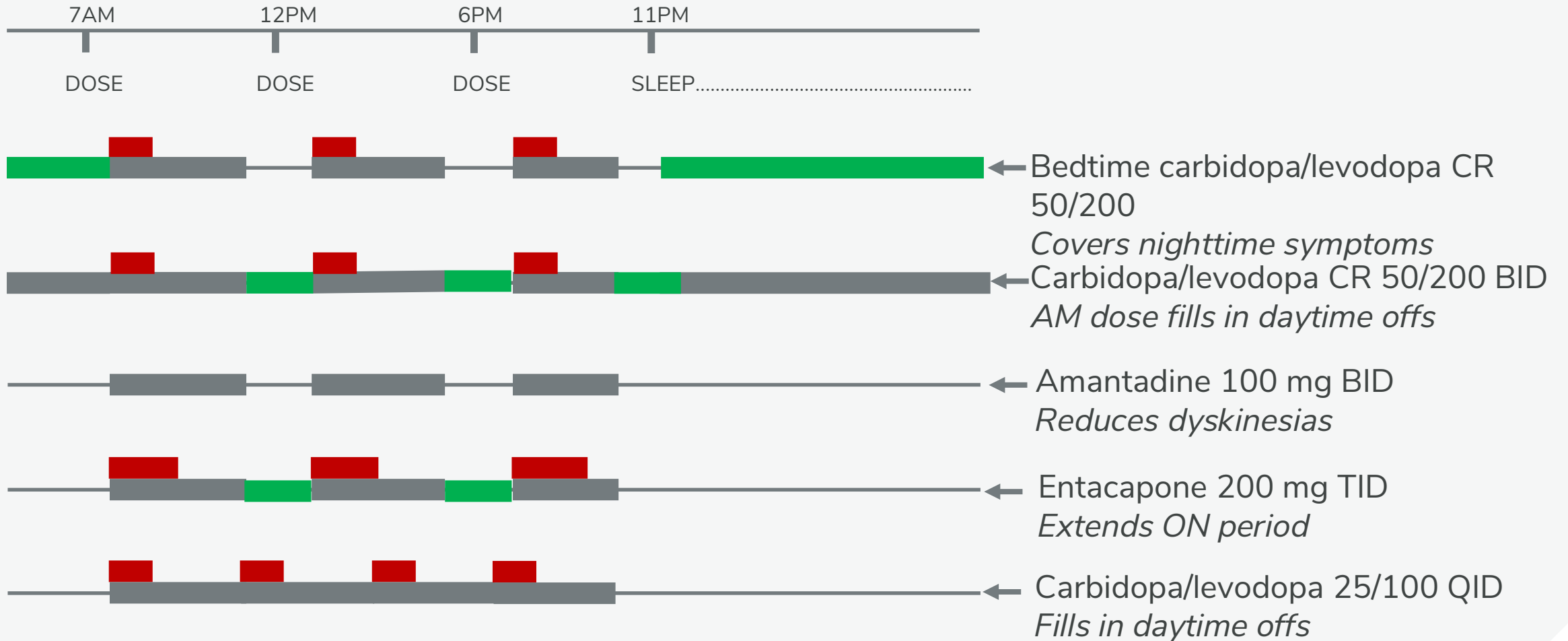
# Medication options for motor fluctuations



# Medication effect changes over the years



# Medication Adjustment Options



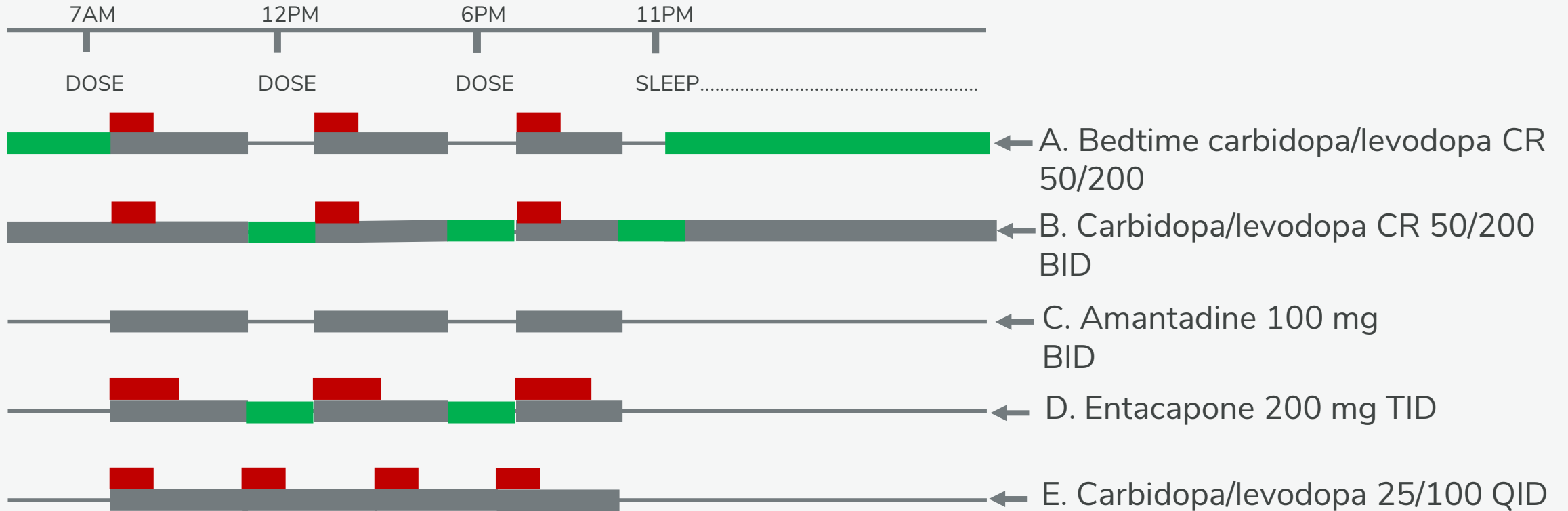


# Case

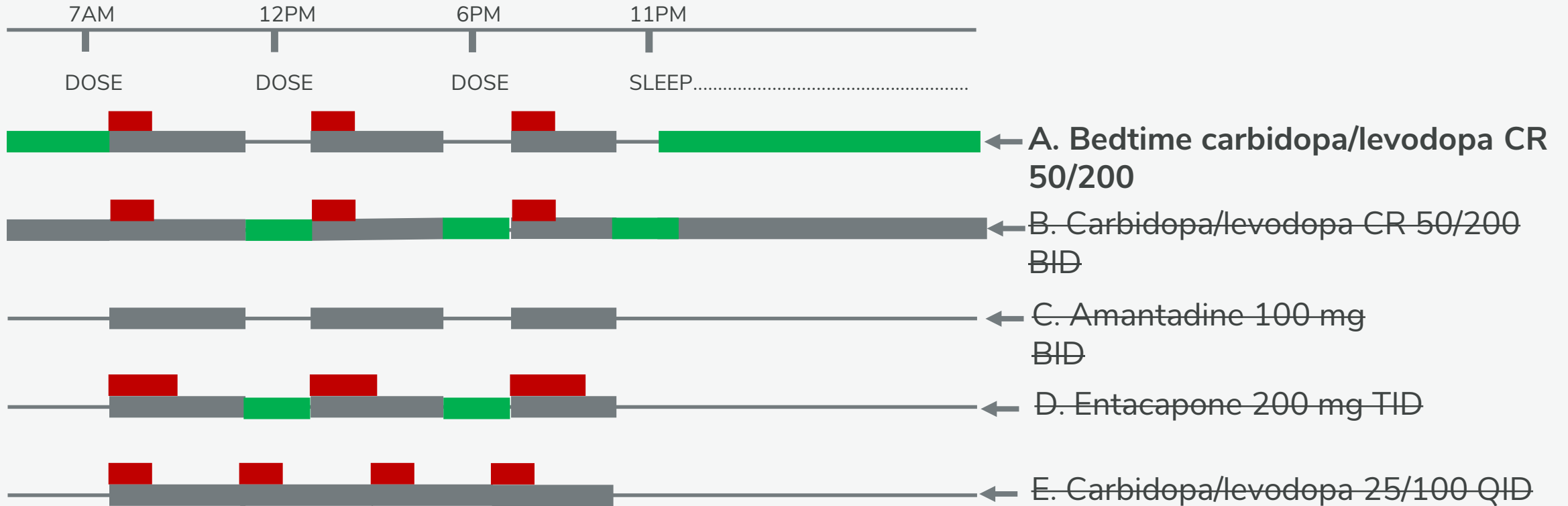
- 67F with PD for 7 years that began with L arm dystonia and later rigidity. Good response to levodopa.
- Meds: carbidopa/levodopa 25/100, 1 tab TID
- She wakes up early and is up for several hours. During that time she finds it difficult to find a comfortable position. She does not find herself ruminating



# Medication Adjustment Options



# Medication Adjustment Options

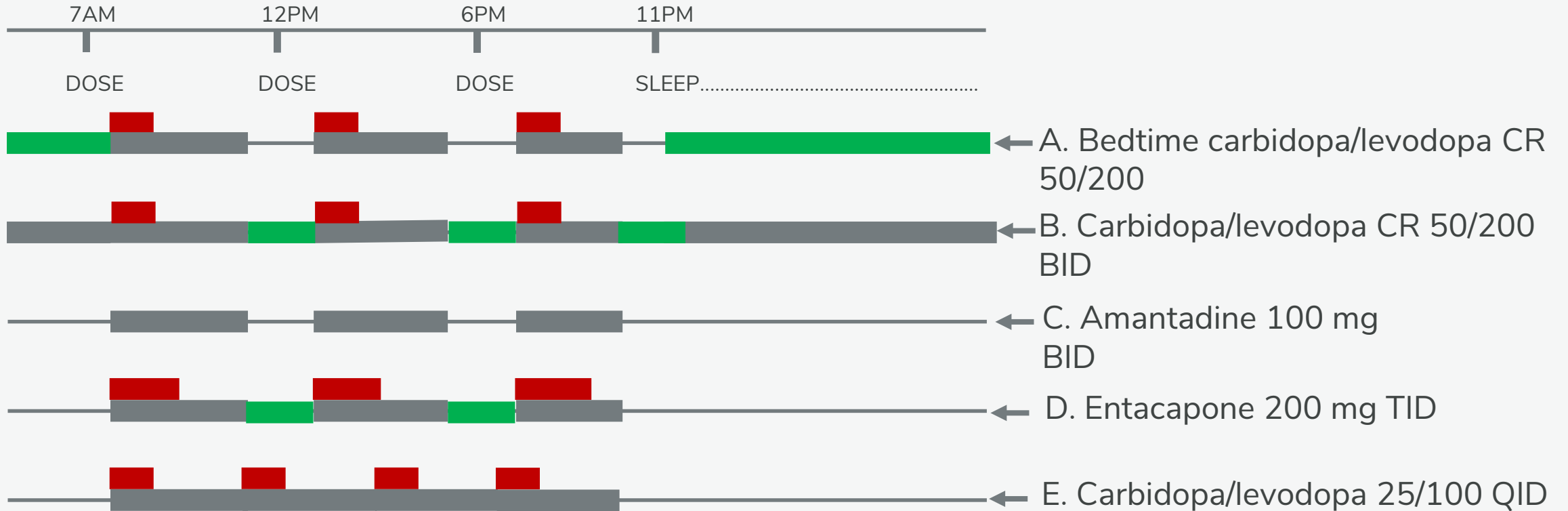


# Case

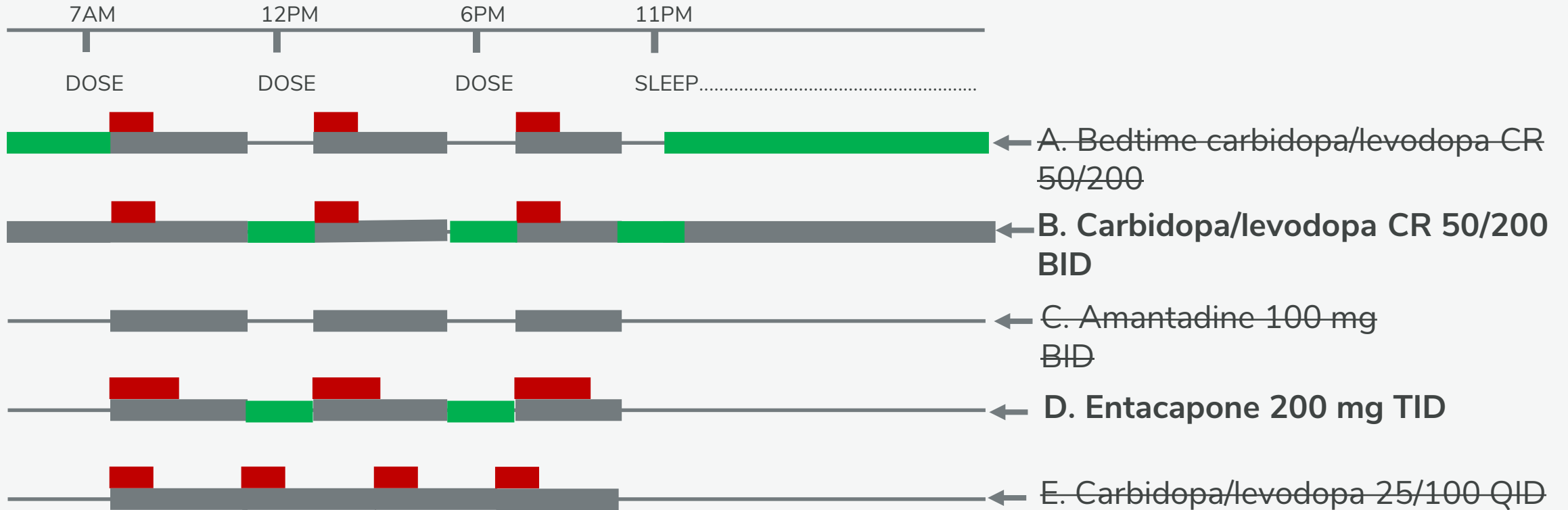
- 77F with PD for 7 yrs that began with reduced energy, slowing of gait, micrographia. Had a good response to carbidopa/levodopa 25/100.
- Wearing off 2 yrs ago: aching pain in R shoulder for 30 minutes before doses 2 and 3
- Increased carbidopa/levodopa but dyskinesias appeared



# Medication Adjustment Options



# Medication Adjustment Options

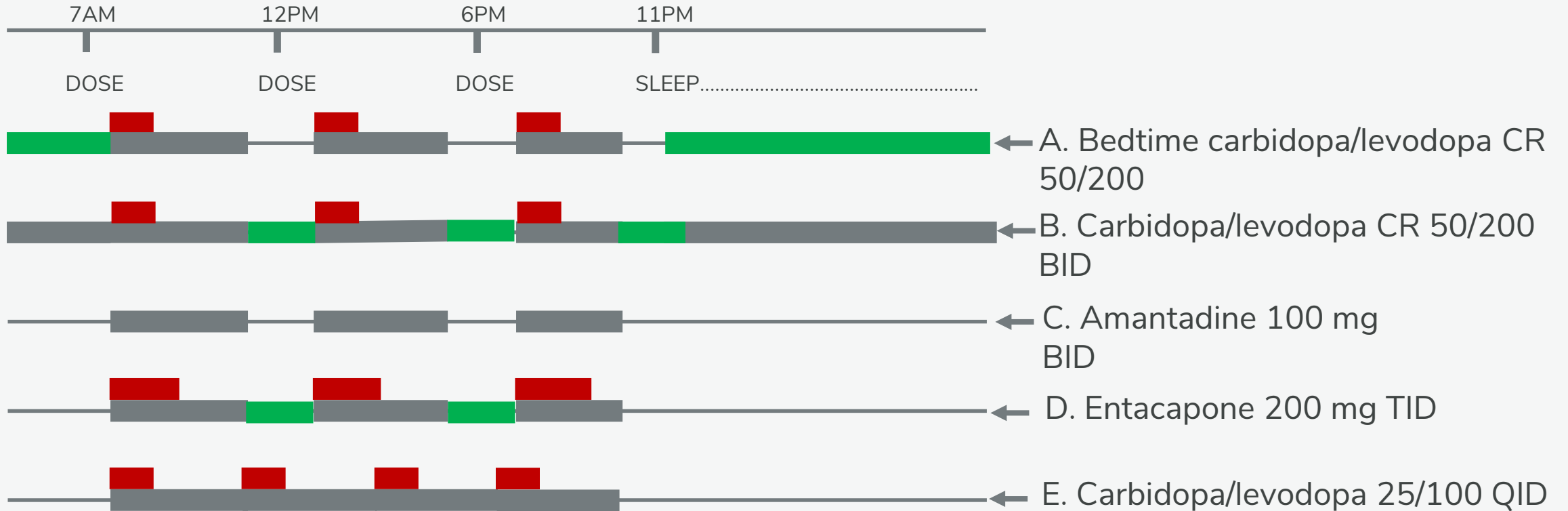


# Case

- 67F with PD for 8 years that began with L shoulder pain and reduced arm swing, walking with "stiff" appearance.
- Good response to carbidopa/levodopa, now 25/100 1 tab TID
- Mild offs (neck stiffness) 1 hr before 2<sup>nd</sup> & 3<sup>rd</sup> doses
- New: bothersome L shoulder dyskinesias for 1 hr after each dose

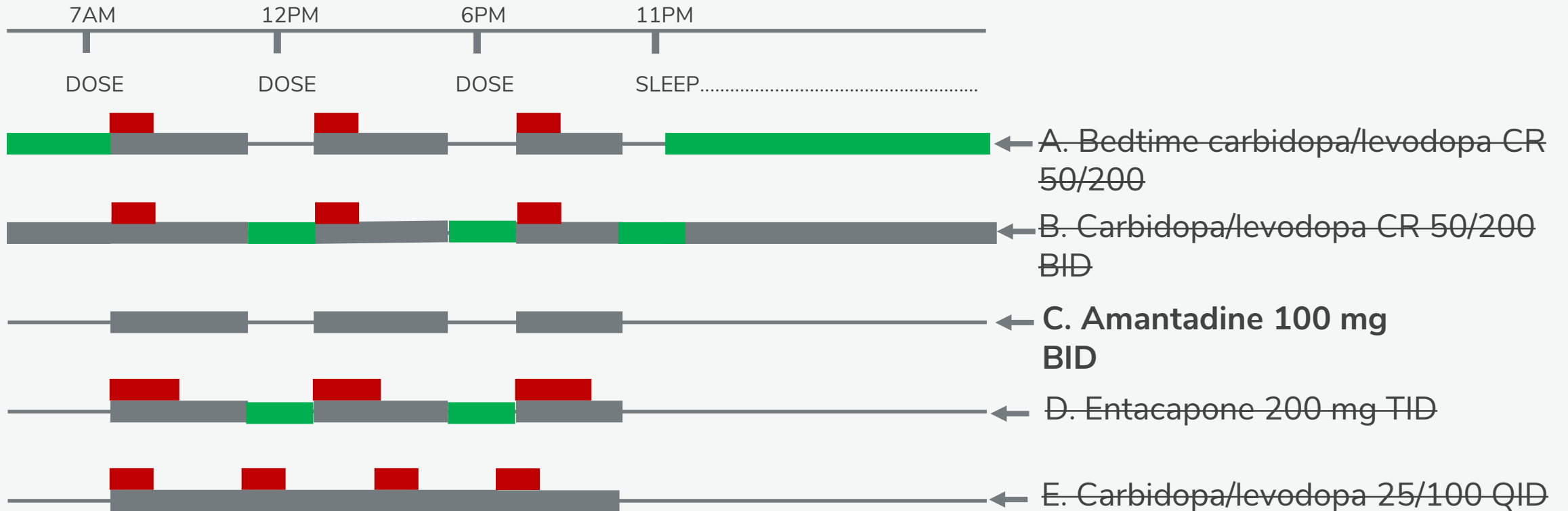


# Medication Adjustment Options





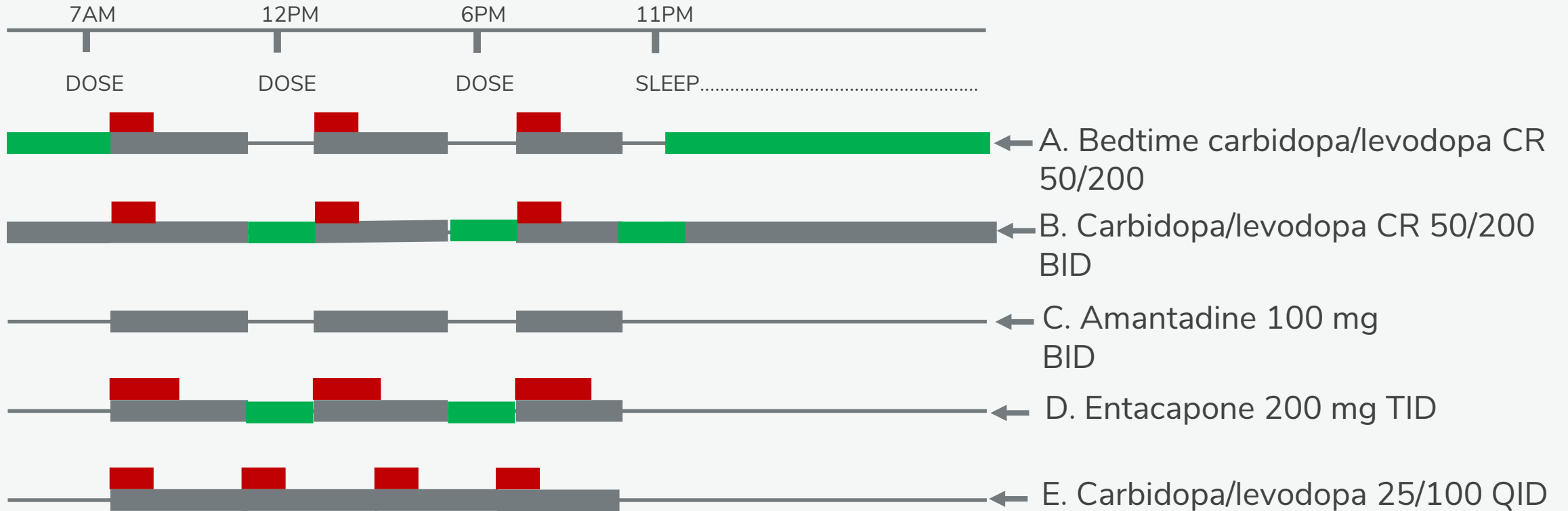
# Medication Adjustment Options



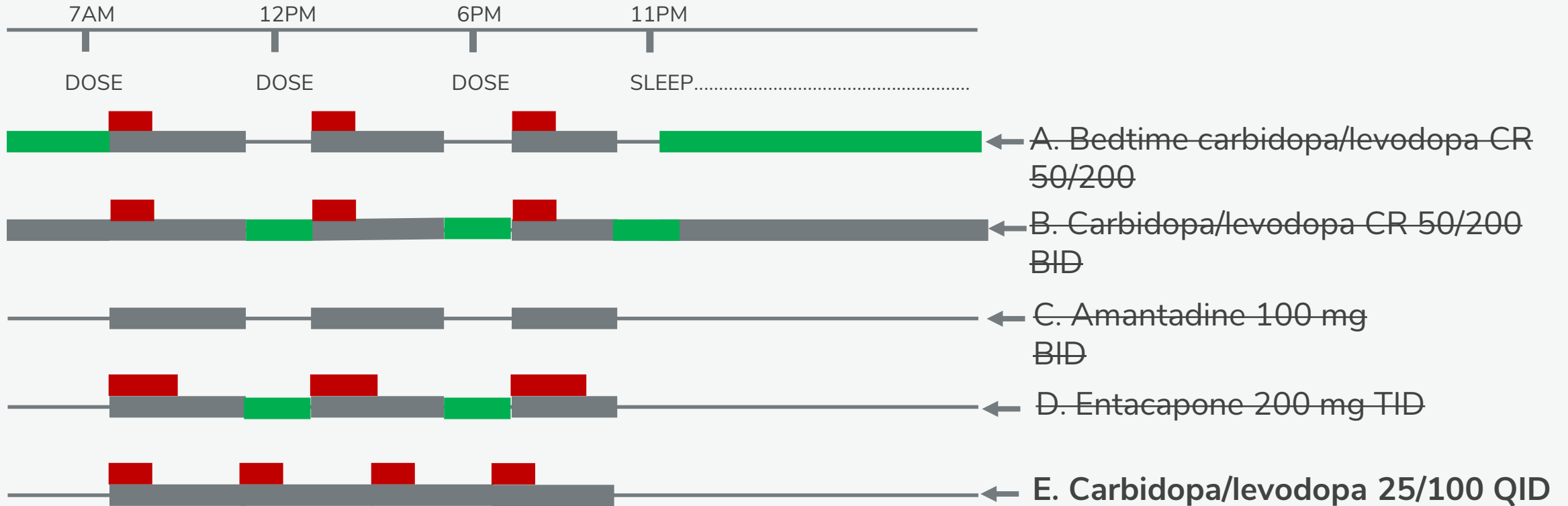
# Case

- 58M with PD for 10 years that began with L hand rest tremor
- Now on carbidopa/levodopa 25/100, 3 tabs every 4 hours 4x/day
- Also on carbidopa/levodopa CR 50/200 BID, entacapone, amantadine
- Symptom course during the day
  - Mild dyskinesias start 30 minutes after each dose and last 20 minutes
  - Bothersome offs 30 minutes before & 30 minutes after doses 2, 3, 4
  - Off symptoms include large-amplitude rest tremor of the L arm; painful cramping of the toes in the left foot; feeling rigid and stiff; difficulty moving

# Medication Adjustment Options



# Medication Adjustment Options



# Adjustments for Motor Fluctuations

- Increase doses of carbidopa/levodopa TID for wearing off
- Add amantadine for dyskinesias
  - 100 mg TID (BID, morning & noon, if age >70)
- Add entacapone for wearing off
  - 200 mg tabs, 1 tab with each dose of carbidopa/levodopa
- Increase frequency of carbidopa/levodopa
- Extra carbidopa/levodopa doses (crushed, in fizzy drink)
  - Any time there is unexpected or deep off



# For side effects

- Nausea
  - add carbidopa (Lodosyn) 25 mg tabs, 1 tab to each carbidopa/levodopa dose
  - replace carbidopa/levodopa 25/100 TID with carbi/levo CR 50/200 BID
- Nightmares/Hallucinations/Paranoia
  - quetiapine 25 mg tabs, 1 tab at bedtime
- Orthostatic hypotension
  - salty snacks
  - midodrine 5 mg tabs, 1 tab TID
  - fludrocortisone 0.1 mg tabs, 1 tab qAM
  - if cardiac disease present: involve cardiologist



# **Two reasons to refer for possible deep brain stimulation**



# Case

- 63M with rest and posture tremor in the right arm for 5 years, which spread to the R foot. No other (subjective) symptoms. He tried propranolol, selegiline, ropinirole, carbidopa/levodopa, amantadine, all without benefit. The tremor now interfered with his work as an stage actor.
- He had, on the initial visit, prominent rest tremor and mild asymmetric rigidity, hypokinesia, and reduced R arm swing. I prescribed levodopa in gradually increasing dose. No improvement of tremor with levodopa 900 mg.



# Would you:

- A. Refer for DBS
- B. Increase carbidopa/levodopa
- C. Add another medication



# Answers:

- A. Refer for DBS
- B. Increase carbidopa/levodopa
- ~~C. Add another medication~~



# Case

- 68F with PD for 9 years. Motor fluctuations for past 2 years.
- Meds:
  - Carbidopa/levodopa 25/100 tabs, 1-2-2-2-2-1.5 tabs at 5am-7am-10am-1pm-4pm-7pm
  - Entacapone 200 mg tabs, 1 tab at 5am-7am-10am-1pm-4pm-7pm
  - Carbidopa/levodopa ER 50/200 at 12midnight
  - Amantadine 100 mg caps, 1 cap TID at 7am-1pm-7pm
  - Botox in both feet for dystonic foot cramps, every 3 months
- ...and yet: dyskinesias x 2 hours, offs x 2 hours
  - Dose → Dysk x30min → ON for 1hr → OFF for 30 min
  - This cycle is repeated every 2 hours

# Would you:

- A. Refer for DBS
- B. Increase carbidopa/levodopa
- C. Add another medication



# Answer:

- A. Refer for DBS
- ~~B. Increase carbidopa/levodopa~~
- ~~C. Add another medication~~



# Reasons to refer for DBS evaluation

- Bothersome tremor, not responsive to carbidopa/levodopa
  - Up-titrate dose to ~900 mg/day (3 tabs TID of C/L 25/100)
- Motor fluctuations not manageable with a reasonable medication regimen
  - Fluctuations: dyskinesias; wearing off episodes
  - Trade-off between dyskinesias and offs (narrow therapeutic window)



# Medication options for behavioral symptoms

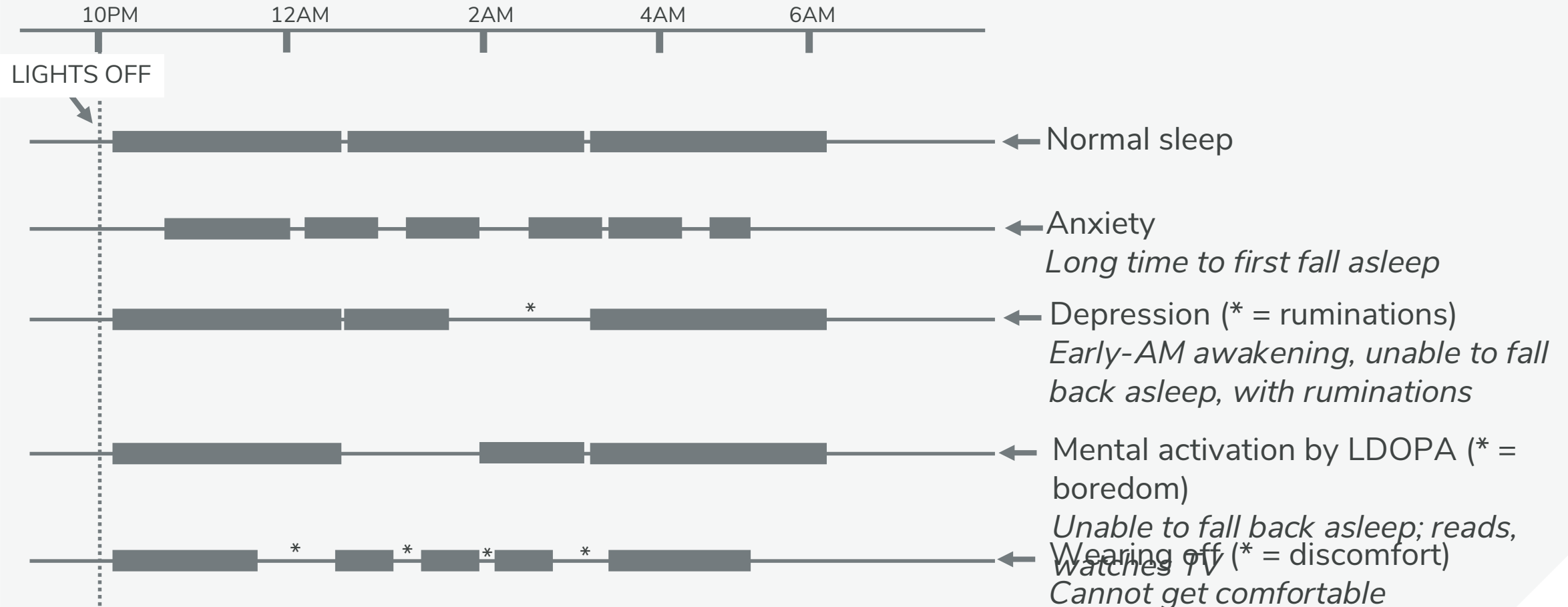


# Why treat behavioral-plus symptoms?

- They amplify motor symptoms; disrupt a brittle medication schedule
  - Can mimic PD progression, but fast
- Anxiety/Depression
  - Increase in motor symptoms
- Levodopa-induced psychosis
  - Mild: sleep disruption, nightmares; Severe: hallucinations, paranoia
- Constipation/Dehydration
  - Increase in motor symptoms
- Orthostatic hypotension
  - Poor concentration, confusion while sitting



# Sleep disruption pattern points to its cause



# First-line treatment

- Anxiety/Depression
  - SSRI (fluoxetine 20 mg qAM) + cognitive behavioral therapy
- Levodopa-induced psychosis
  - Quetiapine 25 mg tabs, 1 tab at bedtime
- Constipation
  - Gentle laxative daily, always (polyethylene glycol qAM; docusate TID)
  - True laxative when constipated (bisacodyl supp, mag citrate, lactulose)
- Dehydration
  - Summer outings; air travel; late fall (home heat comes on). Eat fruit & vegetables
- Orthostatic hypotension (usually due to PD)
  - “He just sits on the couch all day”. Salty snacks, midodrine, fludrocortisone



# Topics

- When to start carbidopa/levodopa
  - ...it's never too early
- Medication options for motor fluctuations
  - ...raise dose; add CR, entacapone, amantadine; shorten dose interval
- Two reasons to refer for possible deep brain stimulation
  - ...levodopa-resistant tremor; motor fluctuations
- Medication options for behavioral symptoms
  - ...SSRI (anxiety, depression); quetiapine (mental activation/hallucinations)

