Navigating Hospitalization with Parkinson's Disease

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Parkinson's Foundation
CENTER OF EXCELLENCE

The Problem: Patients with PD are at high risk for complications when hospitalized

Solution: Bridging the care gap

Hospital Visits are Common for People with Parkinson's

- Up to **1 in 4** people with PD are admitted every year
- Hospitalized **1.5X** more frequently than others
- Hospitalized **2-14 days** longer than others

Gerlach OH, Winogrodzka A, Weber WE. Mov Disord 2011
Gerlach OH, Broen MP, van Domburg PH, Vermeij AJ, Weber WE. BMC Neurol 2012

Most Admissions of PWP are not for PD

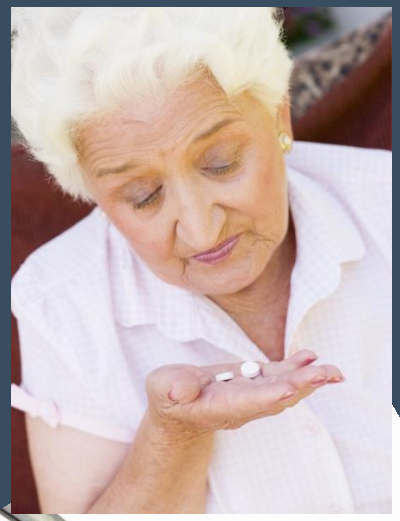
Only 15% of admissions are for managing PD

Most Common reasons for hospitalization:

- Falls with Fractures
- Pneumonia
- Encephalopathy
- Dementia
- Hypotension with Syncope

Temlett JA, Thompson PD. Internal medicine journal 2006
Klein C, Prokhorov T, Miniovitz A, Dobronevsky E, Rabey JM. Journal of neural transmission 2009
Low V, Ben-Shlomo Y, Coward E, Fletcher S, Walker R, Clarke CE. Parkinsonism & related disorders 2015

Multiple Classes of Drugs For Parkinson's Disease



- Levodopa Compounds
  - Carbidopa/levodopa (Sinemet)
  - Controlled Release Carbidopa/levodopa (Sinemet CR)
  - Carbidopa/levodopa/ entacapone (Stalevo)
  - Carbidopa/levodopa XR (Rytary)
  - Inhaled carbidopa/levodopa (Inbrija)
- Dopamine Agonists
  - Pramipexole (Mirapex)
  - Ropinerole (Requip)
  - Apomorpine SQ (Apokyn)
  - Apomorphine SL (Kynmobi)
  - Rotigitine Patch (Neupro)
- Anticholinergics
  - Trihexaphenedyl (Artane)
  - Benztropine (Cogentin)
  - Parsitan
  - Kemadrin
- NMDA Antagonists
  - Amantadine (Symmetrel)
  - Amantadine XR (Gocovri)
- MAOB Inhibitors
  - Selegeline (Eldepryl)
  - Zelopar (Eldepryl Zydis)
  - Rasagaline (Azilect)
  - Safinamide (Xadago)
- COMT Inhibitors
  - Entacapone (Comtan)
  - Tolcapone (Tasmar)
  - Opicapone (Ogentys)
- Adenosine Antagonists
  - Istradefylline (Nourianz)

Parkinson's Medication Regimens are complex

	8AM	12PM	4PM	8PM	HS
Carbidopa/levodopa 25/100 IR	1	1	1	1	
Carbidopa/levodopa 25/100 CR					1
entacapone 200 mg	1	1	1		
rasagiline 0.5 mg	1				

Potential problems when hospitalized…

1. Carbidopa/levodopa 25/100 Q4 but ….. How many doses?
2. Carbidopa/levodopa 25/100 4 times a day but not QID
3. Entacapone not TID---should be paired with particular Levodopa dose

Levodopa formulations are varied and complex

Multiple multidrug combinations:

- Carbidopa/levodopa: 10/100, 25/100, 25/250
  - half-life is ~ 90 minutes
- Carbidopa/levodopa/entacapone: 12.5/50/200 to 50/200/200
  - Same half-life but takes longer to absorb, and effects end later and is ~ 30% stronger

Different Pharmacokinetics by formulation:

- CR carbidopa/levodopa has bioavailability of ~ 70% of IR
- Rytary (carbidopa/levodopa extended release):
  - More stable plasma levels for 4-5 hours
  - Also has bioavailability of 70% IR
  - Total daily dose should be about 2X IR dose
  - C_{max} is 30% of IR. Thus individual dose may be 3X to get same plasma levels

PWPs often report complications and medication errors during hospitalization

Survey showed:

- **1/3** report complications
- **25%** report they did not receive medications correctly
- **21%** reported worsening motor function.

Another study showed 28% (~5 pt.) worsening of UPDRS motor rating scores from beginning to end of hospitalization.

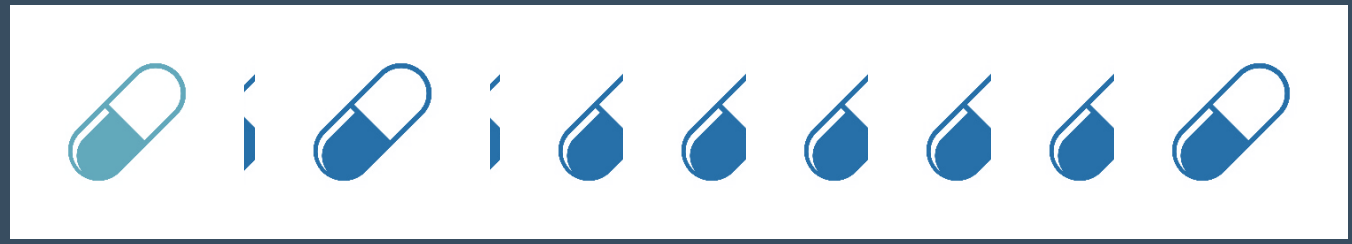
Gerlach OH, Broen MP, van Domburg PH, Vermeij AJ, Weber WE. BMC Neurol 2012
Gerlach OH, Broen MP, Weber WE. Parkinsonism & related disorders 2013

Hospitalization with Parkinson’s Disease

CHALLENGES

High Rate of medication error in PWP when hospitalized

18% Of All Medication Events



90% Of All PD Patient Admissions

½ of these were missing doses
1 in 5 received contraindicated medications

Hou JG, Wu LJ, Moore S, et al. Parkinsonism Relat Disord. 2012

Medication is Critical for Function in Parkinson's Disease

Off Medication

On Medication

Timing is Critical for Administering PD Medications

Medications wearing off may produce significant change including:

- Freezing of gait
- Complete immobility
- Falls
- Dysphagia
- Tremors
- Dystonia (may be very painful)
- Shortness of breath
- Anxiety

Dosing too early may cause significant complications including:

- Dyskinesia
- Psychosis
- Orthostasis
- Syncope
- Falls

Aminoff MJ, Christine CW, Friedman JH, et al.. Parkinsonism & related disorders 2011
Nance MA, Boettcher L, Edinger G, et al. Journal of Parkinson's disease 2020.

Contraindicated Medications Often Worsen Parkinson's Disease

These medications significantly block dopamine function:

Antiemetics:

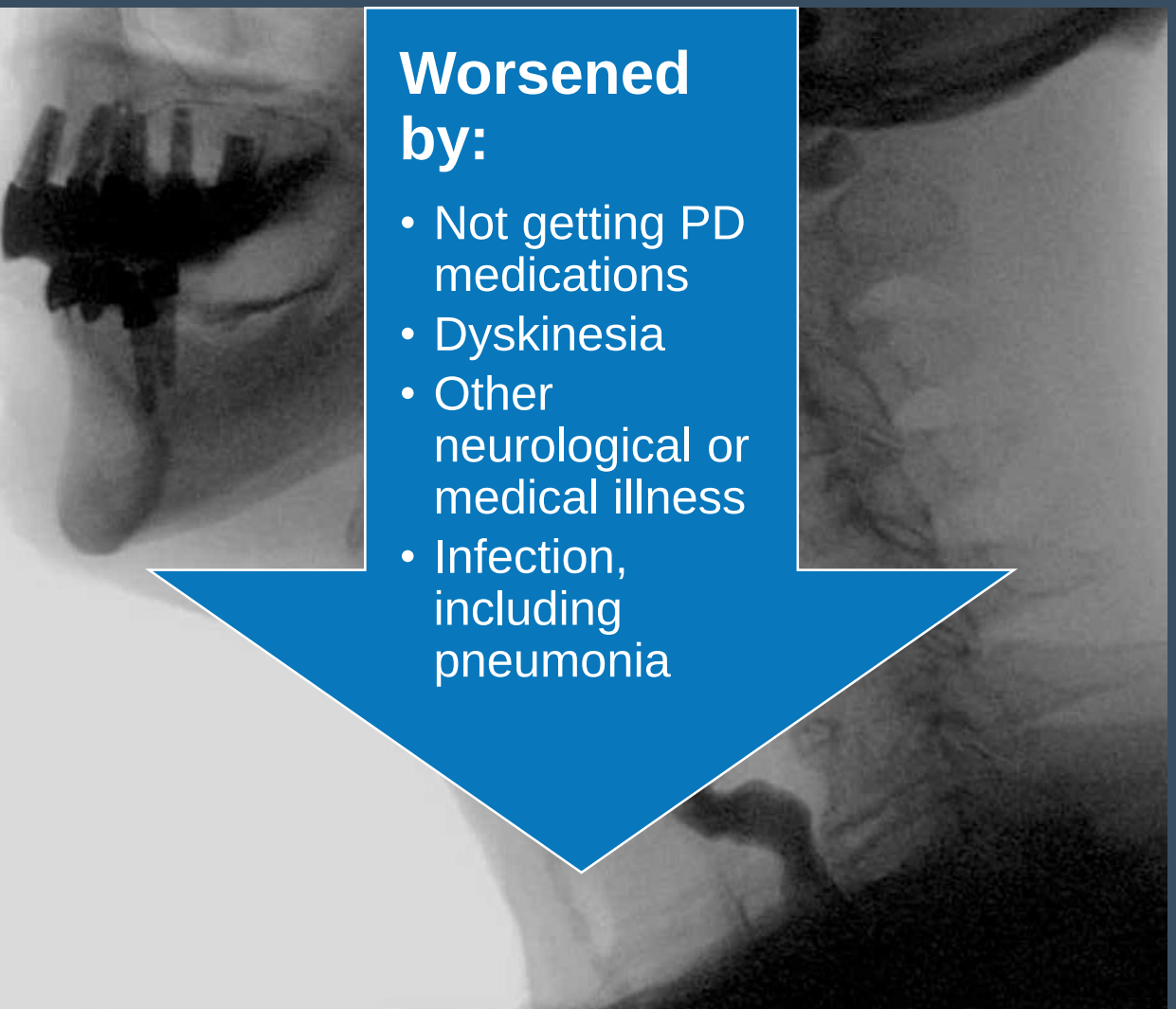
- Promethazine (Phenergan)
- Prochlorperazine (Compazine)
- Metoclopramide (Reglan)

All antipsychotics except:

- Pimavanserin (Nuplazid)
- Quetiapine (Seroquel)
- Clozapine (Clozaril)

www.parkinson.org

Specific Challenges: Dysphagia



Worsened by:

- Not getting PD medications
- Dyskinesia
- Other neurological or medical illness
- Infection, including pneumonia

Approach:

- Speech therapy, maintain PD medications as best possible
- Treat underlying conditions
- In some cases can use dispersible levodopa, rotigotine patch*, apomorphine*

* if drug/class appropriate for patient

Avoid prolonged period of NPO without PD medications

Specific Challenges: Psychosis

Brought on or worsened by:

- Infection, medical illness, metabolic derangements
- Increased dopaminergic dose
- Anticholinergic medications
- Narcotics

Appropriate Management:

- Maintain a home regimen that worked well prior to admission
- Use quetiapine, clozapine, pimavanserin to treat
- Correct underlying problems

May lead to mismanagement that worsens PD:

- Providers may give contraindicated antipsychotics or stop PD medication

Specific Challenges: Dyskinesia

Significant increase may be clue to error in medication regimen:

- Wrong dose
- Wrong formulation
- Dosed too early
- Inappropriate substitution

May lead to:

- falls
- patient discomfort
- swallowing problems
- inability to participate in therapy

Specific Challenges: Orthostasis

>50% of people with PD have NOH

Aggravated by:

- increase in dopaminergic medications
- aggressive management of HTN in patient with NOH
- Dehydration
- Discontinuation of NOH treatment due to supine hypertension

Negative Implications:

- Increased falls
- Inability to mobilize and participate In PT

Approach:

- Make sure PD medications are correct
- Hydrate
- Midodrine, fludrocortisone, droxidopa
- Na in diet, elevate head of bed
- Exercise

Specific Challenges: Prognosis and Goals of Care

- PD slowly gets worse over many years
- It doesn't suddenly get worse, but…
- Symptoms temporarily are much more severe when ill

Impact:

Makes it hard for provider just meeting patient to determine where they are in disease timeline

Impact of medication errors is significant in PWP

Up to 61% of patients with errors have significant sequelae including:

- Increased complications
- Reduced ability to participate in rehabilitation
- Increased length of stay
- Increased mortality rates by **2X**
- Contraindicated anti-dopaminergics increases falls by **5X**

Lertxundi U, Isla A, Solinis MA, et al. Parkinsonism & related disorders 2017
Martinez-Ramirez D, Giugni JC, Little CS, et al. PLoS One 2015
Magdalinou KN, Martin A, Kessel B. Parkinsonism & related disorders 2007
Tanaka M, Suemaru K, Ikegawa Y, Tabuchi N, Araki H. Yakugaku Zasshi 2008.

Symptoms of PD worsen with concomitant illness

PD Symptoms may be worsened transiently by:

- Anesthesia
- Infection/Inflammation (Particularly UTI, Pneumonia)
- Metabolic Changes
- Endocrine Changes (hypothyroidism, etc.)
- New medications for other medical problems

Most reasons for admission put PWP at risk

Falls/Injury

- →Narcotics → Psychosis
- →Surgery → antiemetics (often on post-op order sets)→worsens motor symptoms

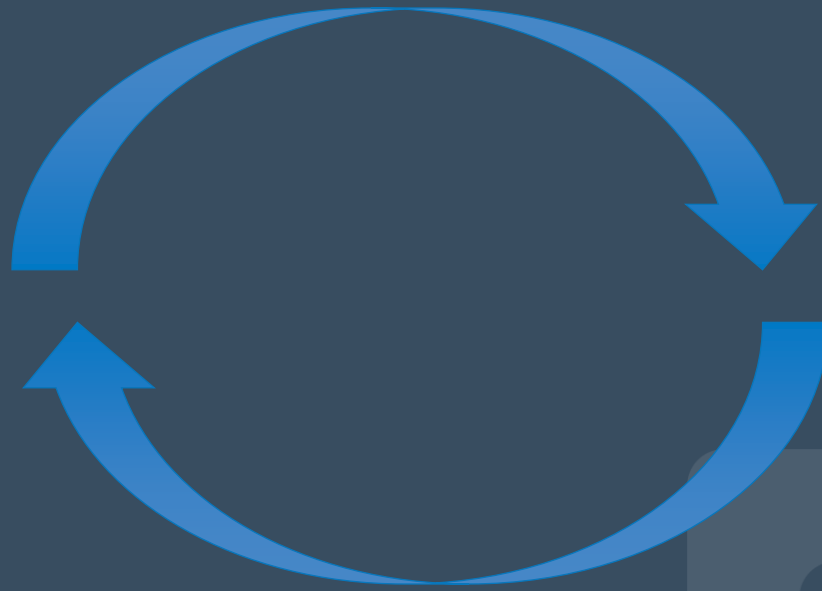
Infections

- →worsens PD motor symptoms→ may lead providers to increase PD medications→ increased confusion, hallucinations, dyskinesia
- →increases confusion/psychosis→ may lead providers to give contraindicated antipsychotics

Elective Surgery

- →Narcotics…
- →Antiemetics…
- →May be NPO for prolonged time → May not get PD medications → worsening motor function and swallowing …

"Vicious Cycle"



Most common complications during hospitalization

1. Confusion (20-34%)
2. Aspiration Pneumonia (3-10%)
3. UTI (8-15%)
4. Falls (1-25%)
5. Pressure Sores (up to 25%)

Skelly R, Brown L, Fakis A, et al. Parkinsonism & related disorders 2014
Gerlach OH, Broen MP, van Domburg PH, Vermeij AJ, Weber WE.. BMC Neurol 2012
Chou KL, Zamudio J, Schmidt P, et al. Parkinsonism Relat Disord 2011

Guidance and Best Practices

SOLUTIONS

Hospitalization with Parkinson’s Disease

SOLUTIONS: EDUCATION

Empowering Healthcare Providers

1. Best practice is keeping patients on their stable home regimen and timing while hospitalized
2. Have patients bring branded medications from home if not on formulary.
    - May write for nurse to dispense from home supply (will need bottle with prescribing information and not just pill organizer)
    - Patient/caregiver may take on own (if medically able)

3. Write medications with custom precise administration times. (Do not use hospital schedules i.e. b.i.d, t.i.d., q.i.d. etc.)

4. Specify that PD medications should be given on time (+/- 15-30 min. maximum) and discuss with nursing team

Empowering Healthcare Providers

5. Avoid contraindicated antiemetics and antipsychotics. May put in plan to avoid anti-dopaminergics or add to allergies as “intolerance/contraindication due to medical condition”

6. Avoid new anticholinergic medications, or anticholinergic medication in cognitively impaired patients. Avoid or minimize use of narcotics.

7. Plan NPO time carefully and try to re-introduce PD medication ASAP and consider alternatives if must be NPO longer than 12-24 hrs.

8. Discuss challenges with patients neurologist, a movement disorders specialist or consulting neurologist. *This may not always be possible. Having your PF action plan is key at this point.*

Empowering Nurses

1. When documenting home medications be precise on the times that the patient takes them
2. Check PD medications that are written on a hospital schedule and not by the hour or time
3. Prioritizing timing of PD medications particularly levodopa and dopamine agonists. Should be on time, all the time +/- 15-30 minutes
4. Be cautious with PRNs, check with pharmacy for cautions and contraindicated medications
5. Encourage PWP to stay mobile and active when able to do safely and make sure they have assistance when needed to avoid falls

Empowering Rehabilitative Therapy

1. Coordinate times for therapy around typical medication on times.
2. Encourage nurses to give medications on time prior to therapy so the patient is ready for you when you arrive.
3. Be mindful and look for orthostatic hypotension

4. For speech therapy, be patient with patients who have been NPO when evaluating for dysphagia and be prepared to re-assess

Advantages to Education Based Approaches

- Essential for awareness
- Inexpensive
- Easy / Quick to implement

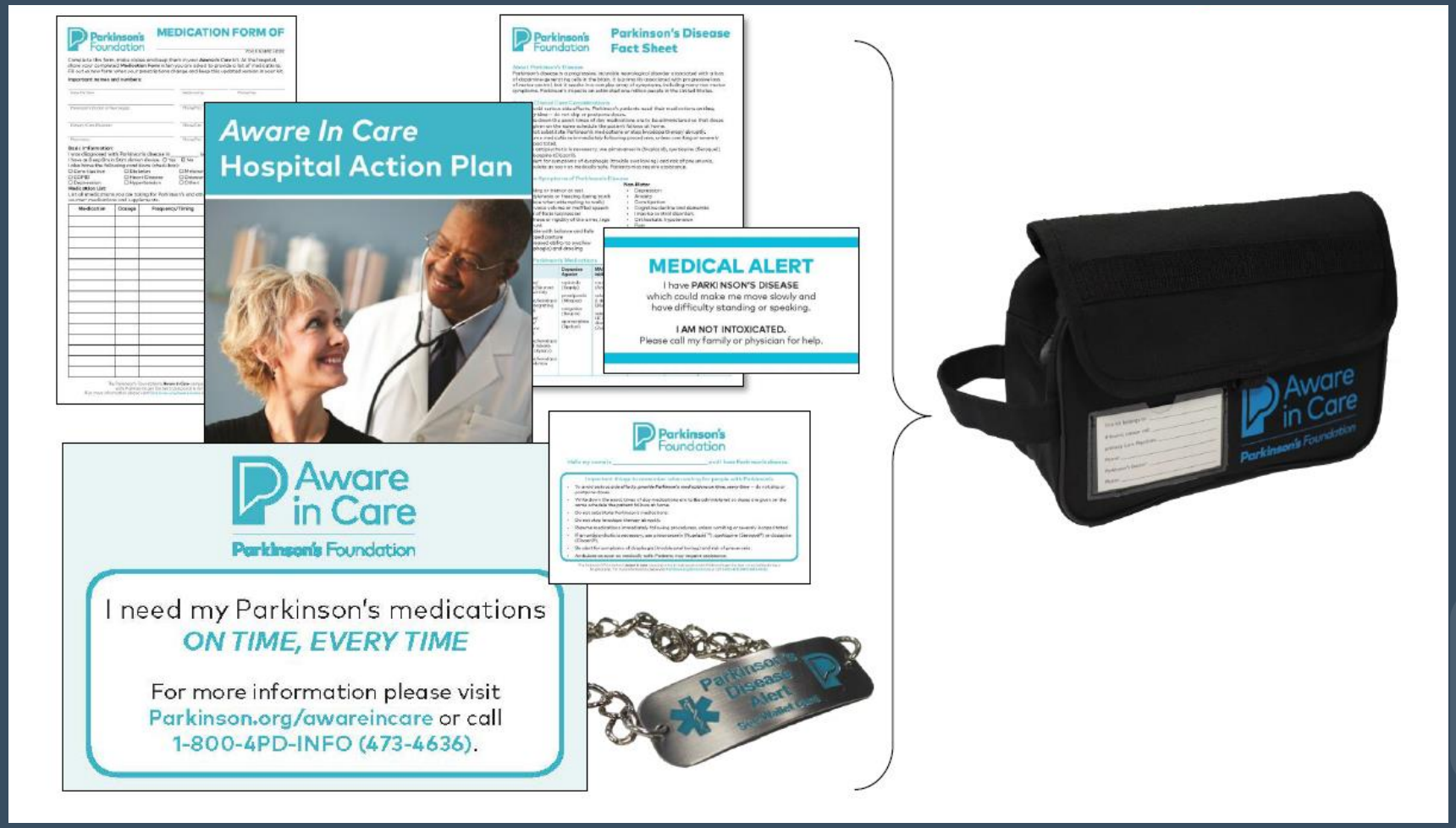
Education Alone Can Significantly Reduce Errors

Lance et al. showed that **in-service education** and pharmacist review had significant impact after 3 months:

- Reduced medication error from 22.5% → 9.3%
- Reduced Complications from 45%→38%
- Eliminated medication error related deaths
- Length of stay: 13 days → 8 days

Lance S, Travers J, Bourke D. Internal medicine journal 2021

Tools for Education by the PWP or Care-partner



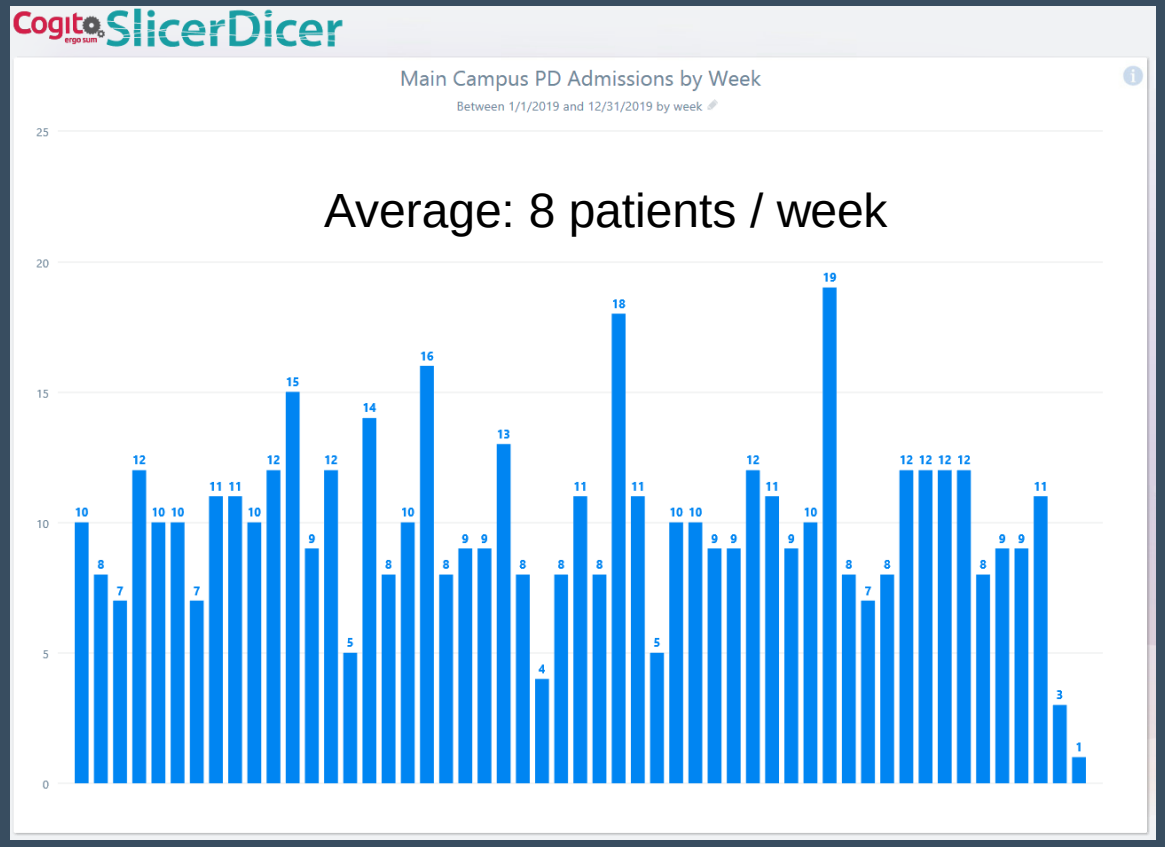
Hospitalization with Parkinson’s Disease

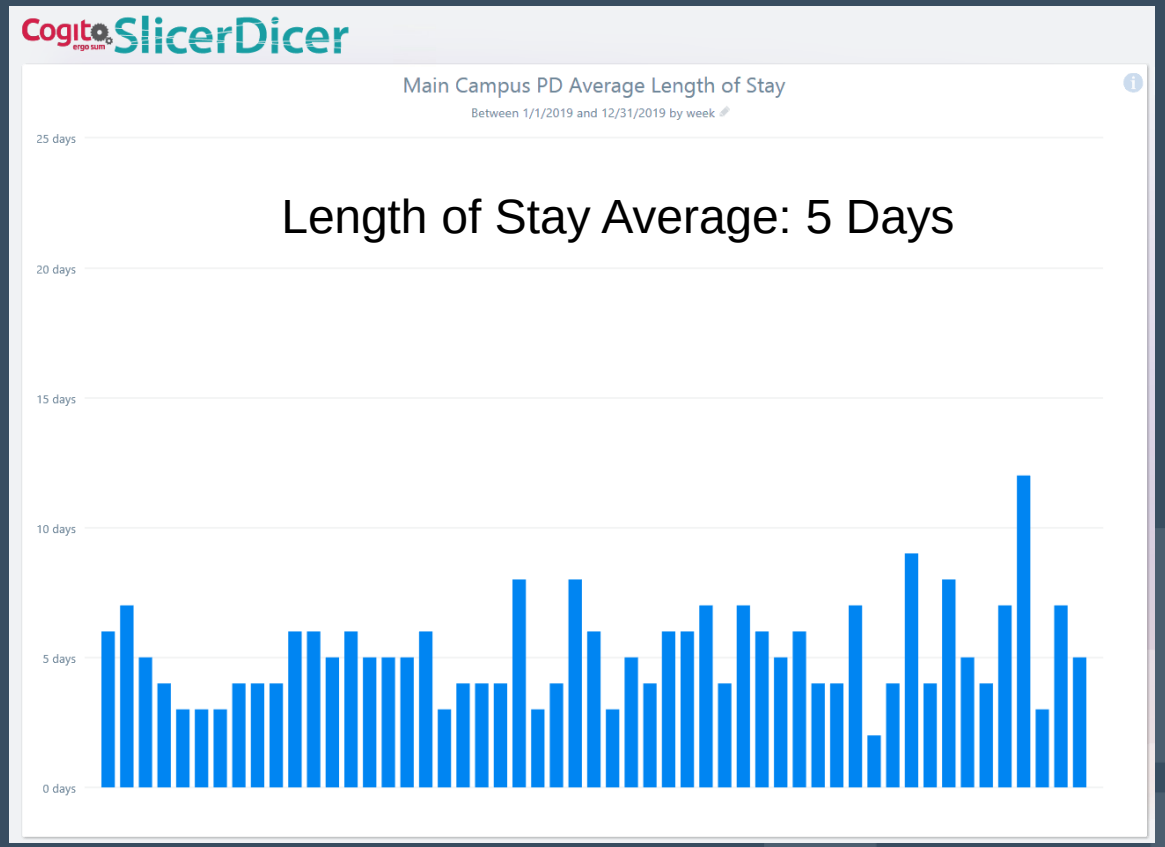
SOLUTIONS: ACTIVE INTERVENTION

Parkinson’s NP Consultation Services

- Brings disease specific expertise to where the patients have problems
- Screen for:
  - **Medication errors**
    - Formulation/dose
    - Timing
    - Contraindicated
  - **Disease related complications/exacerbation**

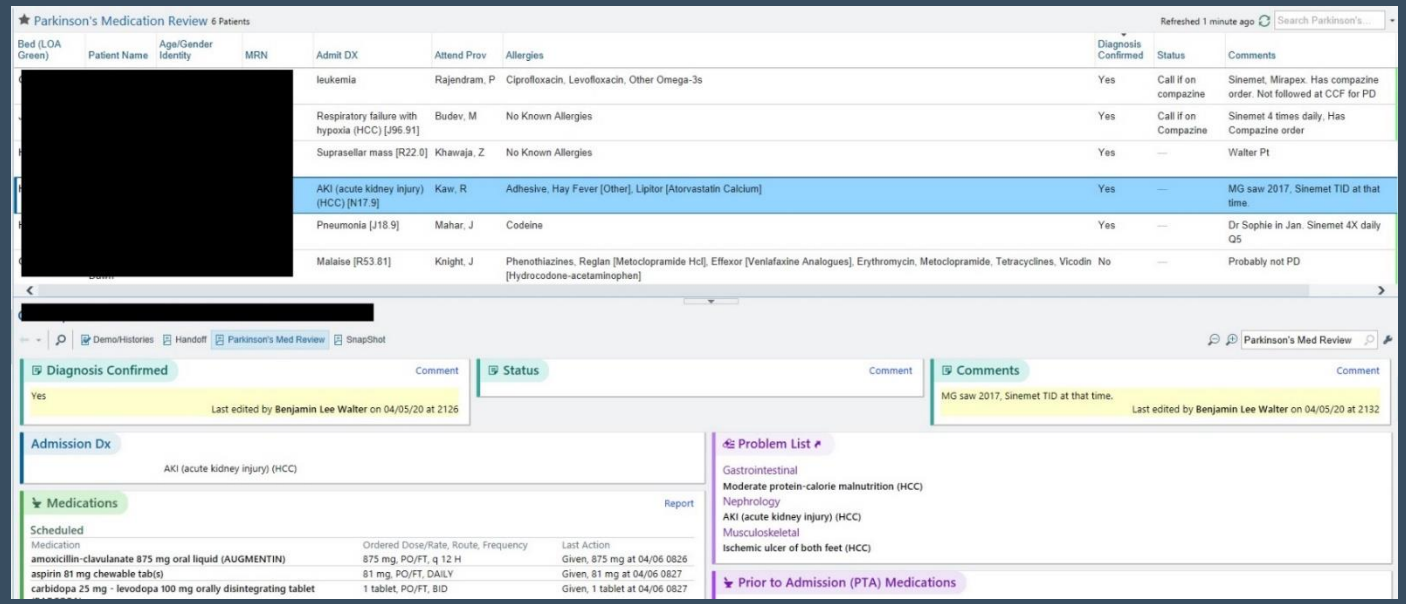
Weekly Admission Data





Proactive PD Patient Screening Lists

- Filters out Patients who have diagnosis of PD and are admitted
- Quick view and compare current medications to reported prior to admission
- Sharable and viewable to all team members
- Updatable columns for sorting, comments, and action items



Advantages to this approach

- **Proactive, not reactive**
- Errors occur starting with admission and translation of home medication to hospital medications and treatment plan
- Effect of errors compound over time
- **Brings PD expertise to where the patient is getting care**

Justifying inpatient PD services

Effective inpatient PD interventions may:

- Reduce length of stay, cost of care
- May reduce complications, morbidity and mortality
- May improve quality of life and patient experience

Parkinson's Inpatient Quality and Safety Initiative

Parkinson's Foundation $332,900 Grant

2-year study:

1-year prospective, adaptive intervention compared to a historical control across 2 different settings

- tertiary care center
- regional hospital (Fairview)

We will first determine the rate of medication errors from the home regimen and deviations in administration in our historical reference year in both care settings (**Aim 1**). We will then deploy our intervention and compare its impact on medication errors at 6 months (**Aim 2a**) and then again at 12 months, after a review and adaptive re-design (**Aim 2b**). We will further analyze the impact of reduced medication errors on patient outcomes (**Aim 3**) and the replicability of the intervention in the regional hospital setting (**Aim 4**).

Retrospective Study Outcomes

- **13%** with unplanned readmission within 30 days
- Median 7 days to unplanned readmission

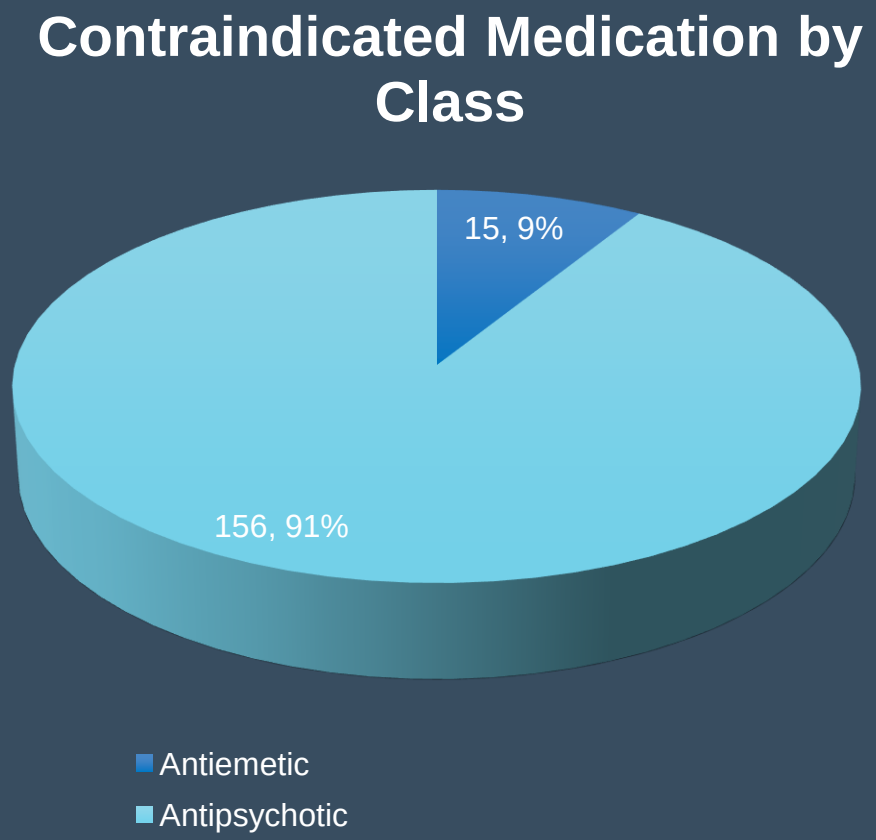
- **10%** died within 90 days of discharge
- Median 36 days to mortality

Contraindicated medications

- **10%** of hospital stays had at least one dose of contraindicated medication

- aripiprazole
- asenapine
- brexpiprazole
- chlorpromazine
- haloperidol
- lurasidone
- metoclopramide
- olanzapine
- paliperidone
- prochlorperazine
- promethazine
- risperidone
- ziprasidone

Contraindicated Medications



Top 3

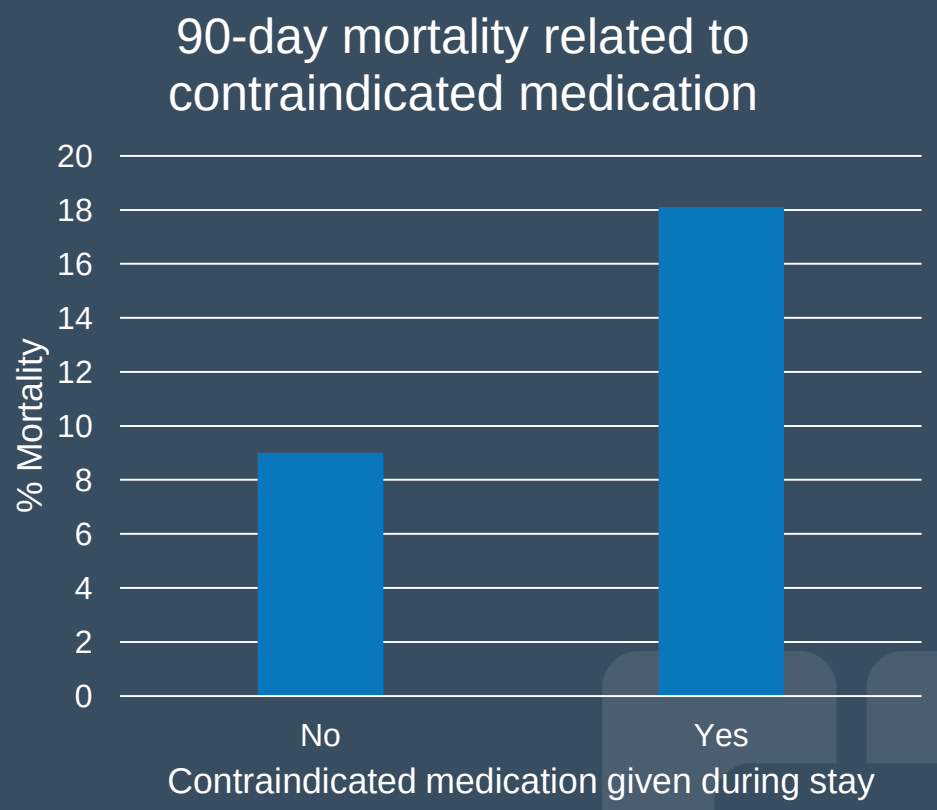
1) Haloperidol (34%)
2) Olanzapine/Zyprexa (23%)
3) Metoclopramide/Reglan (17%)

Others: aripirazole, risperidone, promethazine

Contraindicated meds

Following inpatient admissions where contraindicated medications were administered:

- Over **2X** odds of 90-day mortality
- **2X longer** length of stay
- **1.8X higher odds** of readmission or death within 30 days



Total levodopa daily dose differences

43% (of all hospital days) had a deviation from outpatient regimen
29% underdose, **14%** overdose

At least one day with underdose in total daily dose, **1.8X** readmission or death within 30 days, 14% higher odds of increased length of stay

Levodopa substitutions

- Different levodopa Compounds
  - Carbidopa/levodopa (Sinemet)
  - Controlled Release Carbidopa/levodopa (Sinemet CR)
  - Carbidopa/levodopa/ entacapone (Stalevo)
  - Carbidopa/levodopa XR (Rytary)
  - Inhaled carbidopa/levodopa (Inbrija)

- **19%** of hospital days had a levodopa substitution
- **22%** of hospital stays had at least one levodopa substitution

Outpatient/ home regimen

Carbidopa/levodopa 25/100mg extended release
Carbidopa/levodopa 50/200mg extended release

Most common substitutions in our data set

Hospital regimen

Carbidopa/levodopa 25/100mg immediate release

Levodopa timing differences and missed doses

- Average dosing administered >30 minutes from the time they were supposed to be given seen in:
- **47%** of all hospital days
- **72%** of all hospital stays
- Associated with **2X longer** length of stay

- **22%** (of all hospital days) with missed dose
- **1.4X** increased odds of 90-day mortality

Summary findings:

- **13%** with unplanned readmission within 30 days
- **10%** died within 90 days of discharge
- **22%** of hospital days with missed dose; **1.4X** 90-day mortality
- **10%** of hospital stays with contraindicated meds; **2X** longer length of stay, **2X** 90-day mortality
- **Haloperidol** (34%) is the most commonly prescribed
- **19%** of hospital days and **22%** of hospital stays with at least one levodopa substitution
- **47%** of hospital days, **72%** of hospital stays had levodopa timing deviations, **2X** longer length of stay

Conclusion

1. PWP are at risk during hospitalization due to frequent medication errors, exacerbation due to illness, and poor treatment choices in response to symptom exacerbation.
2. During hospitalization, PD medications should match stable home regimen when possible and given on time, every time.
3. Contraindicated medications should be avoided including most antipsychotics and antiemetics with antidopaminergic properties
4. Physicians, APPs, Nurses and Allied Care providers can proactively takes steps to reduce errors and reduce morbidity and mortality for PWPs during hospitalization
5. **Patients and care-partners can advocate for themselves deploying resources in the Aware in Care Kits.**

Take Home Messages

1. PWP are at risk during hospitalization due to frequent medication errors, exacerbation due to illness, and poor treatment choices in response to symptom exacerbation.
2. During hospitalization, PD medications should match stable home regimen when possible and given on time, every time.
3. Contraindicated medications should be avoided including most antipsychotics and antiemetics with antidopaminergic properties
4. PWP hospitalization challenged by getting PD expert care where most needed, and when needed.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