

## Adherence to a strict medication protocol can reduce length of stay in hospitalized patients with Parkinson's Disease



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### ABSTRACT

**Background:** Patients with Parkinson's Disease (PD) are at higher risk of complications when admitted to the hospital. Delays in PD medications and use of contraindicated medications contribute to the increased risk and prolong their lengths of stay (LOS). Using a hospital-wide PD protocol, we aimed to ensure PD medications were placed with “custom” timing to resemble the home schedules, and also to avoid ordering or administering contraindicated medications. **Material and methods:** 569 patients admitted in 2017 and 2018, were reviewed retrospectively. Mean age was 76.5 (SD 10.6), 332 were males and 237 were females. Charts were reviewed to assess if A) PD medications were ordered with custom timing, B) if not, were the orders changed to custom timed C) if contraindicated medications were ordered, and D) if they were administered. We also assessed the actual/expected length of stay during this time period. Chi Square and post hoc analyses were done to compare time points. Poisson regression analysis was done to assess relative improvement of variables.

**Results:** There was a 2.7 fold increase in orders placed with custom timing in 2018 compared to 2017 (RR = 2.651, 95%CI: 1.860–3.780,  $p < 0.0001$ ), and a 3.2 fold increase in correction of non-custom orders in the same time period (RR = 3.246, 95%CI: 1.875–1.619,  $p < 0.0001$ ). We also observed a decrease in the actual/expected LOS ratio from 1.54 to 1.32 ( $p < 0.05$ ).

**Conclusion:** By utilizing an established platform for quality improvement, we were able to improve adherence to the home medication regimen timing in admitted PD patients. Our findings also suggests that adherence to a strict medication regimen protocol may decrease LOS for this patient population.

### 1. Introduction

One of the main treatment goals in patients with advanced Parkinson's Disease (PD) is to maintain quality of life by minimizing motor fluctuations and reducing troubling dyskinesias [1]. Finding an optimal medication regimen can be difficult and time consuming, and often requires frequent assessments and adjustments in the outpatient setting. These strict medication schedules are often overlooked when a patient with PD is admitted to the hospital [2–7].

The cause of these omissions is typically multifactorial. Most health care practitioners are unaware of the intricacies of PD care, the importance of adherence to medications and their dosing schedules, and the potential side effects of commonly used medications in PD patients [4,8]. In addition, awareness of the importance of timing of medications and of adherence to patients' “customized” schedules is not universal among hospital physicians [8,9]. (A customized schedule refers to medication orders that match the patients' home medication timing and not defaulted timed regimens such as qid or tid). Patients with PD who may require hospitalization are frequently admitted for medical or surgical diagnoses other than PD [8,10–12] and healthcare teams often overlook the PD diagnosis, as the primary complaint becomes the focus of treatment [8,13,14]. Furthermore, hospitals may not carry all PD medications on their formularies, and

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replacement of doses or substitution of medications can be harmful [15]. These treatment and knowledge gaps can result in delayed or missed medication doses, or administration of contraindicated medications which in turn can be detrimental to PD patients [2,3,5–8,13,16].

We recently initiated a protocol for improving medication management for PD patients admitted to the hospital [17]. Our objectives were to assess the effects of this hospital wide initiative on proper PD medications orders, the avoidance of contraindicated medications, and the resulting effects on length of stay in the 24 months following the implementation.

## 2. Methods

This retrospective observational cross-sectional study was approved by the Institutional Review Board of Hackensack University Medical Center (HUMC). As a chart review informed consent was not required.

### 2.1. Hospital-wide medication management protocol

A hospital wide protocol for improved safety and quality of care of inpatients with PD was implemented at HUMC in early 2017. The main aim of the initiative was improvement of medication management and avoidance of contraindicated medications as they are recognized as major safety gaps for this population. The efforts were directed to ensure PD medications were ordered according to the patients' home schedules, and thus the orders were entered with "custom" timing (to differentiate from the default times such as BID, TID, or QID for example). To support the initiative, a hospital wide, multi-faceted continuing educational program was also implemented. This program received formal Disease Specific care designation from The Joint Commission on Accreditation of Health care Organizations (JCAHO) in June 2018.

### 2.2. Joint Commission Disease Specific Certification

We used the Joint Commission program for Disease Specific Certification (JC DSC) [18] to institute our PD protocol based on the platform's established pathway for quality assessment and improvement [19]. The JC DSC requires the development of an interprofessional team of stakeholders, selection of performance parameters based on best clinical guidelines, regular and frequent assessment of these measures, and development of action plans to address variances if identified.

The key selected measures we chose were thought to be the most representative of the current best practices for the care of PD patients [15,20]. The main goals of the protocol were to ensure that PD medications were ordered in a "custom" fashion reflecting the individual outpatient schedules, and that contraindicated medications were not administered. Charts were reviewed on a daily basis, and errors or omissions were identified and rectified. The Parkinson's team met monthly to review the data and to implement actions when variances were identified.

### 2.3. Patients

Patients admitted to the hospital were flagged in the electronic health record (EHR) if their "problem list" included a diagnosis of Parkinson's Disease. To ensure we captured all such patients, ICD-10 codes of G20 and G21 were included, regardless of their admitting diagnosis. The problem list can be populated by physicians and nursing, and other healthcare providers involved in the care of the patient.

Inclusion criteria for chart review were the presence of the above codes either as primary or non-primary diagnoses. Excluded were patients who did not have these diagnoses included in their problem lists. 569 patients were included for review. Of these 290 patients were admitted to the hospital in 2017 and 279 in 2018. Table 1 summarizes the patient demographics, breakdown of patient entry points into the hospital, and the most common admitting diagnoses and units. Of the admitted patients, 31 were for deep brain stimulation surgeries in 2017 and 28 in 2018.

**Table 1**  
Patient characteristics.

	2017	2018
Patients with PD (n)	290	279
Age, mean (SD)	76.7 (10.5)	76.4 (10.65)
Breakdown by age (%)		
< 50	1.7	1.4
51–60	4.8	5.0
61–70	16.9	19.0
71–80	36.6	36.6
81–90	35.5	32.3
>91	4.5	6.1
Sex (%)		
Female	44.1	39.1
Male	55.5	60.9
Admitting diagnosis (%)		
Sepsis or other infection	14.2	16.6
Parkinson's Disease	7.2	8.4
Pneumonia	4.9	6.4
Cardiac	5.2	4.7
Renal	2.3	1.2
Orthopedic	3.1	3.5
Respiratory failure	0	2
Entry into hospital (%)		
ER	78.9	80.5
Elective surgery	11.9	11.6
Directly to floors	9	7.8
Admitting units (%)		
Intensive care	5.7	7.2
Medical floors	59	63.7
Surgical floors	7.9	6.1
Psychiatry	2.3	2.0
Admitting services (%)		
Cardiology	2.6	2.6
Family medicine	7.5	9
Internal medicine	21.6	27
Geriatrics	4	4.1
Neurosurgery	3.1	9.3
Oncology	0.5	2
Hospitalists	26	29.4
Psychiatry	2.5	2
Trauma	5.9	2.6
Surgical services	7.2	6.4

### 2.4. Educational program

Educational programs and care plans were developed to trigger the importance of adherence to the patient's home medication schedule, and avoidance of contraindicated medications when a PD patient was encountered. The educational program entailed a hospital-wide continuing effort utilizing: Unit based sessions for nursing, pharmacy, and allied health professionals; formal grand rounds for nursing, physicians, and other healthcare providers; designated care plans in the EHR; informational posters in medication dispensing areas reminding of the importance of timing and enumerating contraindicated medications; frequent e-learning modules; and educational webinars.

### 2.5. Data review

A daily list of PD patients admitted to the hospital was generated and reviewed by the PD care team. Orders for PD patients were evaluated. Errors were recorded as variances and the collected data were reviewed monthly with the PD care team and the variances analyzed. Finally, we assessed the length of stay for patients with Parkinson's Disease in this 24-month period.

### 2.6. Definition of analyzed variables

The measures tracked as part of our quality improvement protocol are as follows: Custom order placed on admission: Numerator: total number of PD patients with ALL PD meds ordered in "custom" format, denominator:

total number of PD patients who had orders for PD meds; Correction of non-custom orders: Numerator: total number of PD patients who had non-custom orders changed to custom orders, denominator: total number of PD patients with non-custom orders; Contraindicated medications ordered: Numerator: total number of PD patients with NO orders for contraindicated medications, denominator: total number of PD patients; Contraindicated medications Administered: Numerator: total number of PD patients who had NO contraindicated medications administered, denominator: total number of PD patients.

### 2.7. Expected and actual length of stay

Every patient admitted to the hospital regardless of admitting diagnosis has an automatic “expected” length of stay assigned to them. This number is calculated using a logistical regression of 60–70 characteristics including comorbidities for each patient based on LOS for patients with similar profiles across the country [21–23]. The *actual* length of stay is a measure of the true number of days a specific patient spent in the hospital. The ratio of “actual” to “expected” LOS is often used to represent comparisons that have been corrected for comorbidities. We utilized this ratio to compare the length of stay of our patient population.

### 2.8. Statistical analysis

Chi-square analyses were used to determine statistical significance across all time points. Eight time points corresponding to eight quarters were analyzed. Post-hoc chi-square analyses were then used to determine differences between individual time points and groups of time points (where applicable). Normality was evaluated using Shapiro-Wilk tests, and independent samples *t*-tests and Mann-Whitney *U* tests were used to determine significant differences between groups, where appropriate. Statistical analyses were performed using IBM SPSS Statistics for Windows, v24 (IBM Corp., Armonk, NY). Significance was set at  $p < 0.05$ .

In addition, to determine relative risk (RR) of improvement in performance measures, a Poisson regression analysis with repeated measures was conducted (month repeated over year 1 to year 2) using a generalized liner model with distribution and log link function using PROC GENMOD in SAS 9.4 (SAS Institute Inc., Cary, NC, USA) (95% Confidence interval, CI,  $p < 0.05$ ).

## 3. Results

### 3.1. Population characteristics

The majority of patients in this cohort entered the hospital via the emergency room (78.9% in 2017, and 80.5% in 2018). While many patients were admitted with the primary diagnosis of PD, most came to the hospital with non-PD complaints (92.8% in 2017 and 91.6% in 2018). Of the admitted patients, a majority were admitted to medical services (internal medicine, hospitalist, geriatrics) A smaller but not insignificant number were admitted to surgical services (16.2% in 2017 and 18.4% in 2018) (Table 1).

### 3.2. Custom order entry

290 patients were reviewed in 2017 and 279 in 2018. Thirty-seven of the patients in 2017 (12.8%) had PD medications ordered with custom timing. In 2018, 94 patients (33.8%) had PD medications ordered in a

customized fashion. Comparing the two years, PD medications for an admitted patients were 2.7 times more likely to be ordered in a customized schedule in 2018 than in 2017 (RR = 2.651, 95% CI: 1.860–3.780,  $p < 0.0001$ ) (Table 2). Importantly, a post-hoc analysis revealed that the custom order rate during 2018 Q2-Q4 combined was significantly higher than all previous quarters combined (39.9% vs. 13.3%;  $p < 0.001$ ) (Fig. 1A).

We also assessed the frequency with which orders that were initially placed with default timing (e.g. four times daily) were changed to orders with custom timing. Of the 253 patients who did not have PD medications ordered initially with custom timing in 2017, 35 were changed to a custom timed order (13.8%). In 2018, of the 184 patients who did not have PD medications ordered with custom timing, 61 were changed to a custom timed (33.2%). PD medications not ordered custom were 3.2 times likely to be changed to custom timed during the hospital stay in 2018 vs. 2017 (Rates: 34.4% vs. 9.3%; RR = 3.246, 95% CI: 1.875–1.619,  $p < 0.0001$ ) (Table 2). A post-hoc analysis revealed that the custom frequency change during 2018 Q2, Q3, and Q4 combined was significantly higher than that of all previous quarters combined (43.2% vs. 10.6%;  $p < 0.001$ ) (Fig. 1B).

### 3.3. Contraindicated medications

We assessed the frequency of orders for contraindicated medications in the hospitalized patients, as well as the frequency of administration of such medicines. Of the charts reviewed, 79.4% did not have orders for contraindicated medications, and 90.8% did not have these medications administered in 2017. In 2018, these numbers were 80.9% and 90.6% respectively (Fig. 1C,D). There was no significant difference from 2017 to 2018 for either of these comparisons ( $p = 0.355$ ), and ( $p = 0.548$ ). Poisson regression also did not show any significance comparing the two performance measures in 2017 and 2018. (RR = 1.028, 94% CI 0.969–1.091,  $p = 0.364$ , RR = 0.998, 95% CI = 0.938–1.061,  $p = 0.9426$ ) Table 2.

### 3.4. Length of stay (LOS)

In 2017, the expected LOS was 4.8 days vs an actual LOS of  $7.1 \pm 0.8$  days. In 2018, the expected LOS was 4.9 days vs an actual LOS of  $6.7 \pm 1.4$  days. There was a statistically significant correlation between time and actual/expected LOS ratio across the 24 months ( $R = -0.41$ ,  $p < 0.05$ ). Additionally, there was a significant difference between the LOS ratios in 2018 Q2–4 as compared to all previous quarters combined (1.32 vs 1.54,  $p < 0.05$ ) (Fig. 2).

## 4. Discussion

Adherence to home PD medication regimen and avoidance of contraindicated medications are important for the safety of PD patients admitted to the hospital [15,20]. The deficiencies observing this practice in hospitals have been demonstrated. Magdalinou et al. [6] reviewed 35 patients over the course of 14 months admitted through the ER and found that 74% of them had a medication error. Derry et al. [2] retrospectively reviewed 54 patients in the perioperative period and reported a 71% medication error rate and observed administration of dopamine blockers in 41% of these patients. In a review of 89 PD patients admitted to the hospital over a 24-month period, Hou et al. [5] discovered that only 23.6% of the patients had medications written with specific timing, and there was an 89.9% rate of medication errors in these patients. Martinez-Ramirez et al. [7]

**Table 2**  
Comparison of adherence to protocol measures.

Performance measure	Rate in 2017	Rate in 2018	Relative risk	95% confidence interval (CI)	p-Value
PD Meds ordered with custom timing	12.2%	33.1%	2.651	1.860–3.780	<0.0001
PD Meds orders changed to custom timing if initial order non-custom	9.3%	34.4%	3.246	1.875–5.619	<0.0001
PD charts without contraindicated medications ordered	79.4%	81.0%	1.028	0.969–1.091	0.3644
PD charts without contraindicated medications administered	90.8%	90.5%	0.998	0.938–1.061	0.9426

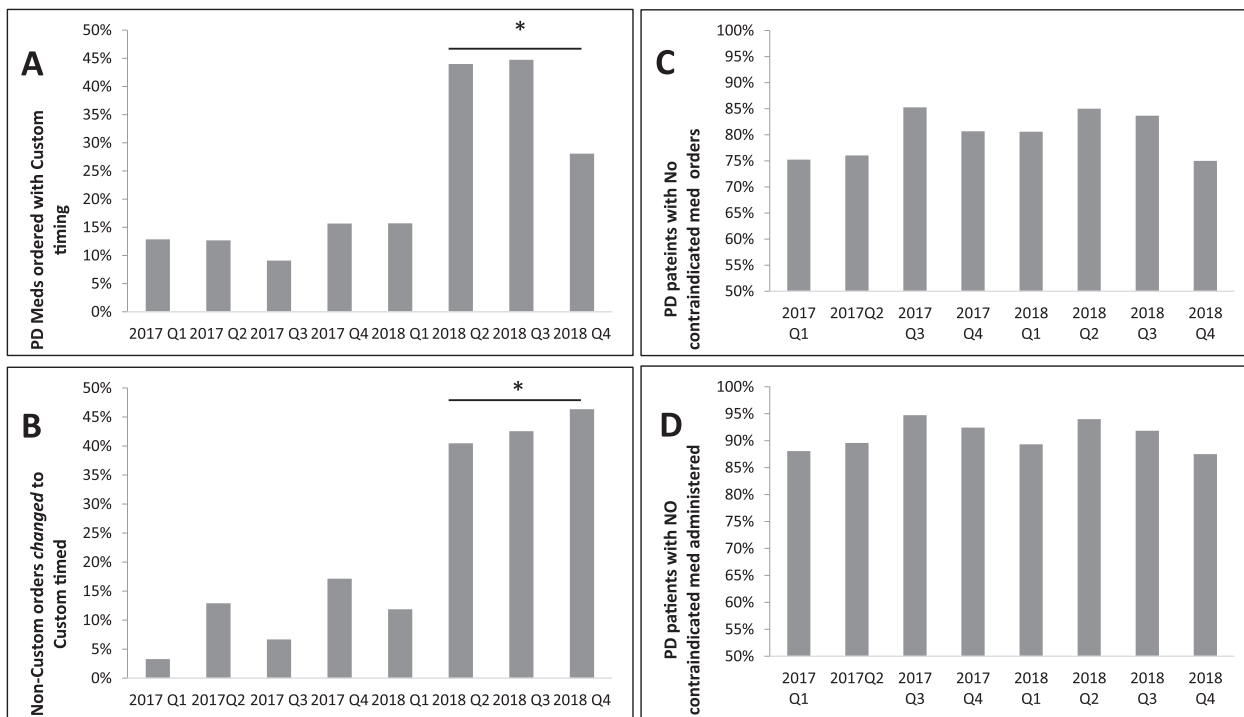


Fig. 1. A) Percentage of medications ordered with a customized time schedule. B) Percentage of medications initially not ordered in a customized schedule, *changed* to custom timing during hospital stay. C) Percentage of PD patients with no contraindicated medications prescribed. D) Percentage of PD patients with no contraindicated medications administered. \*p < 0.05.

reviewed 212 patients over a 27-month period and demonstrated that only 10.1% of medications were written in a specific time format and there was a nearly 72% rate of medication errors. Moreover, they observed an increase in length of stay when PD medications were delayed, or contraindicated medications were administered.

Errors in medication administration for PD patients admitted to the hospital occur as the result of several safety gaps. To be effective, a PD program must address all of these issues collectively, as omission in any single arm will diminish the potential for success. In addition, the efforts have to be hospital wide as patients are distributed throughout the hospital according to their primary diagnosis.

To this end, in addressing the care of this patient population, we utilized the JC-DSC platform. We have previously detailed the development and the structure of the protocol [17]. The JC-DSC is an excellent vehicle to identify, monitor and address the care of a specific patient population [19].

During the period studied, we observed a nearly threefold increase in the number of PD medications ordered in a custom fashion. And there was a statistically significant increase in orders placed with custom timing when comparing the later part of 2018 to the remainder of the study period. While much work remains to be done as the majority of orders are still being placed without custom timing, we are encouraged by the results. Firstly, as a potential reflection of the impact of education, we observed an increase in correction of non-custom orders to custom timed orders during this time period. We noted a related finding for orders for contraindicated medications, as most of these medications were NOT administered. While the comparatively lower number of these contraindicated orders likely reflects a more common understanding of the deleterious nature of these medications in the PD population, nevertheless it is reassuring to see the errors being identified by astute nursing and pharmacy staff, again as a potential effect of the educational components.

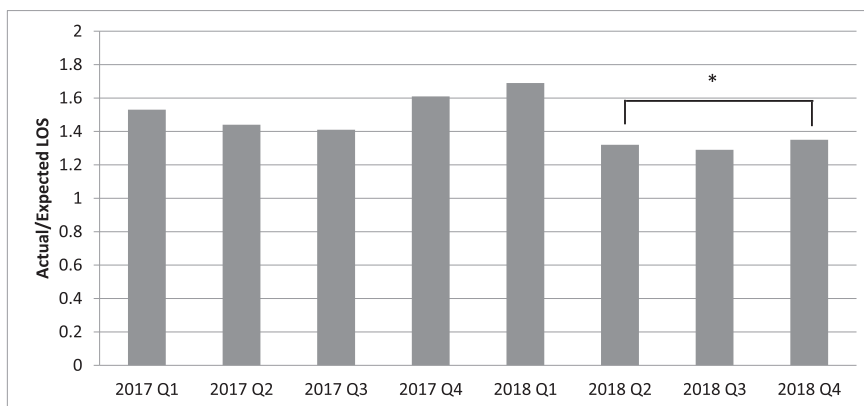


Fig. 2. LOS Actual/Expected Ratio Q1 2017 to Q4 2018. When comparing Q2–4 2018 to the prior time period, there was a significant decrease in actual/expected LOS.\* p < 0.05.



Secondly there may be cost savings overall with even modest increases in compliance. In our patient population, we observed an 8% decrease in comparing the **actual** LOS for the two years. It is possible that this number can increase as we saw the significant reduction toward the end of the second year as the protocol was more successful. According to the American Hospital Association, the average daily cost of hospitalization in the US in 2016 for non-profit hospitals was \$2488 [24]. This cost can be significantly higher in certain US regions. The overall cost savings to hospitals can also provide a financial justification, in addition to the improvement of care, for adherence to such protocols.

#### 4.1. Limitations

The conclusions reached by this study have to be tempered by some limitations. First this is a retrospective review, and a future prospective study to confirm the observations is needed. Secondly, studies have demonstrated that the errors in the hospitals occur both as a result of improper orders for PD medications (lack of compliance with patients' home regimen) as well as delays in administering these medications once orders have been placed. Our initiative has been focused on ensuring medications *orders* are placed according to patients' home schedules. This study did not assess timing delays in *administration* of medication. While we hope that our educational efforts have highlighted the importance of timing for PD medications throughout the hospital, the lack of data regarding this important factor can be considered a shortcoming of this manuscript. In addition, because we relied on any provider to identify the patients as having PD, it is unlikely that the subtlety of distinguishing between idiopathic and atypical PD was observed or even was known, and as such the number of atypical PD patients here maybe under-represented. This may result in an imperfect list in a pure sense, however the protocol has likely benefited atypical patients as well. Atypical PD patients may also be maintained on PD medications, and susceptible to the same errors particularly with antidopaminergic medications.

#### 5. Conclusion

While other studies have demonstrated the deleterious effect of medication mismanagement in the inpatient PD population, this is the first study to demonstrate **an active** adherence to a hospital wide protocol can improve proper PD medication ordering and decrease the length of stay for this patient population. Clearly additional studies are needed to replicate our findings in different settings and in a prospective manner. Our study draws attention to the importance of awareness of medication timing and avoidance of contraindicated medications in inpatients with PD.

#### CRediT authorship contribution statement

**Hooman Azmi:** Conceptualization, Visualization, Methodology, Formal analysis, Writing - original draft, Investigation. **Lisa Coccoziello:** Methodology, Software, Validation, Data curation, Formal analysis, Project administration, Writing - review & editing. **Themba Nyirenda:** Methodology, Formal analysis, Writing - review & editing. **Claudia Douglas:** Project administration, Supervision, Resources, Writing - review & editing. **Blessy Jacob:** Validation, Data curation, Supervision, Writing - review & editing. **Jewell Thomas:** Validation, Data curation, Supervision, Writing - review & editing. **Donna Cricco:** Data curation, Writing - review & editing. **Giuseppina Finnerty:** Data curation, Supervision, Validation, Writing - review & editing. **Kirsten Sommer:** Data curation, Supervision, Validation, Writing - review & editing. **Anthony Rocco:** Methodology, Software, Validation, Supervision, Project administration, Writing - review & editing. **Randy Thomas:** Resources, Writing - review & editing, Project administration. **Patrick Roth:** Resources, Methodology, Writing - original draft, Writing - review & editing. **Florian P. Thomas:** Resources, Methodology, Writing - original draft, Writing - review & editing.

#### Declaration of competing interest

None.

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