# Patient Preferences for Device-Aided Treatments Indicated for Advanced Parkinson Disease

Thomas Marshall, PharmD, MS[1,*], Amy Pugh, BA[2], Angelyn Fairchild, BA[3], Steven Hass, PhD[4]

[1]AbbVie, Inc., North Chicago, IL, USA; [2]UCSF Medical Center, San Francisco, CA, USA; [3]Fairchild Research Analytics, Wilmington, NC, USA; [4]H.E. Outcomes, LLC, Boston, MA, USA

## ABSTRACT

**Background:** Effective treatment for advanced Parkinson disease (PD) uncontrolled with oral medication includes device-aided therapies such as deep brain stimulation (DBS) and continuous levodopa-carbidopa infusion to the duodenum via a portable pump. **Objective:** Our objective was to quantify patient preferences for attributes of these device-aided treatments. **Methods:** We administered a Web-enabled survey to 401 patients in the United States. A discrete-choice experiment (DCE) was used to evaluate patients' willingness to accept tradeoffs among efficacy, tolerability, and convenience of alternative treatments. DCE data were analyzed using random-parameters logit. Best-worst scaling (BWS) was used to elicit the relative importance of device-specific attributes. Conditional logit was used to analyze the BWS data. We tested for differences in preferences among subgroups of patients. **Results:** Improving ability to think clearly was twice as important as a 6-hour-per-day improvement in control of movement symptoms. After controlling for efficacy, treatment delivered via portable infusion pump was preferred over DBS, and both devices

were preferred to oral therapy with poor symptom control. Patients were most concerned about device attributes relating to risk of stroke, difficulty thinking, and neurosurgery. Avoiding surgery to insert a wire in the brain was more important than avoiding surgery to insert a tube into the small intestine. Some differences in preferences among subgroups were statistically, but not qualitatively, significant. **Conclusions:** This study clarifies the patient perspective in therapeutic choices for advanced PD. These findings may help improve communication between patients and providers and also provide evidence on patient preferences to inform regulatory and access decisions.

*Keywords:* best-worst scaling, conjoint analysis, deep brain stimulation, discrete-choice experiment, levodopa, Parkinson disease, patient preference.

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## Introduction

Parkinson disease (PD) is a chronic, progressive neurodegenerative movement disorder characterized by degeneration of dopamine neurons with resultant depletion of striatal dopamine. Most patients with PD are treated with oral levodopa therapy [1], a precursor for dopamine. Chronic oral levodopa therapy is associated with potentially disabling motor complications including motor fluctuations (i.e., an initial benefit after a levodopa dose, or "on" time, followed by a return of PD symptoms, or "off" time) and dyskinesia [1]. With disease progression, patients with PD experience decreases in the duration of effect of a levodopa dose [2] and increased periods of off time at the end of a dose [3]. Off time is associated with impairments in functioning and health-related quality of life and with poor patient utility [4]. Increases in the frequency of levodopa dosing, intended to

manage end-of-dose off time, can induce peak-dose dyskinesia [2]. In patients with advanced PD, maintaining an oral levodopa dose that satisfactorily controls transition periods between off time and on time, without inducing dyskinesia, is challenging.

For patients with advanced PD that is refractory to oral treatment, device-aided therapies such as deep brain stimulation (DBS) and continuous levodopa-carbidopa infusion to the duodenum via a portable pump can reduce the burden of motor complications. Currently, the standard DBS approach focuses on the subthalamic nuclei, which are stimulated by stereotactically introduced electrodes [3]. This approach improves motor symptoms [5] and reduces off time and dyskinesias [3,6,7]. However, DBS is not suitable for patients with dementia, cognitive decline, or depression [8,9]. Furthermore, complications with the surgical procedure, including stroke and intraventricular hemorrhage, can occur intraoperatively, postoperatively, or in the long-term [10].

Another device-aided treatment indicated for patients with advanced PD is continuous levodopa-carbidopa infusion via a portable pump. Levodopa-carbidopa intestinal gel is infused directly from a pump inserted into the jejunum via an outer transabdominal tube, with an inner intestinal tube extending to the duodenum. The intestinal tube is implanted by means of a percutaneous endoscopic gastrostomy [11,12] using local anesthesia [2,13]. This device-aided treatment yields more stable plasma concentrations than those that are achieved with oral levodopa, thereby improving motor fluctuations and dyskinesia [1,14–19]. Levodopa-carbidopa intestinal gel also has been found to improve quality of life [13,20,21] and functioning [3,22,23]. Levodopa-carbidopa is pharmacologically well tolerated and is not associated with the mental health contraindications of DBS. Nevertheless, complications with the surgical procedure (e.g., administration-site problems [3,20,24–26] and peritonitis [27]) and with the device (e.g., dislocation of the duodenal tube [13,20]) can occur.

Continuous levodopa-carbidopa infusion to the duodenum via a portable pump was approved by the Food and Drug Administration (FDA) in 2015 for use in the United States and has been used in a number of European countries for more than 10 years.

Some attributes of device-aided treatments for advanced PD—the requirement of surgery, potential complications, and inconvenience factors—could discourage some patients from using them. However, it is likely that patients with advanced PD would be willing to tolerate these potential disadvantages to achieve improvements in PD symptoms. Therefore, at the time patients begin to no longer have adequate symptom control on oral medication, neurologists should initiate a dialogue with their patients on the availability of device-aided treatments, while at the same time sharing the most relevant benefit and risk considerations. In the United States, the two treatments approved for the treatment of advanced PD with motor fluctuations are DBS and levodopa-carbidopa intestinal gel, both of which have a higher efficacy compared with oral medications. The attributes of both these treatments differ from those of oral medications (which are a suboptimal therapy); thus, patients' preference is a key consideration for the choice of therapy. To our knowledge, no previously published studies have quantitatively evaluated patient preferences among the attributes of device-aided treatments relative to oral treatments for advanced PD. The primary objective of this study was to quantify patient preferences for attributes of device-aided treatments for advanced PD in the United States and to estimate the relative importance of treatment attributes to patients. The study used a discrete-choice experiment (DCE) and a best-worst scaling (BWS) exercise, two forms of conjoint analysis, to quantify the relative importance to patients of efficacy, tolerability, and convenience attributes of alternative PD treatments.

## Methods

### Study Sample

Respondents were required to meet the following eligibility criteria: be aged 18 years or older; have a self-reported physician diagnosis of PD; currently be taking oral prescription medicine(s) to treat PD; be naive to device-aided advanced therapies to treat PD (i.e., not have undergone DBS to treat PD; not currently be receiving levodopa-carbidopa intestinal gel delivered by infusion pump to treat PD); never have taken medicine for Alzheimer disease or cognitive impairment (i.e., donepezil HCl, rivastigmine transdermal system, galantamine, galantamine HBr, or memantine HCl); and be able to read and understand English to provide informed consent and complete the survey instrument. The target sample size was 400, which exceeds the optimal minimum sample size recommended for DCE surveys [28].

Respondents were recruited via an email invitation through GfK, an international market research organization. Each respondent received panel points from GfK that totaled less than $10 and could be redeemed for merchandise as compensation for participating in the study. The study complied with the Declaration of Helsinki and was approved by an institutional review board in the United States.

### Survey Methods

We conducted a Web-enabled survey to elicit patient preferences for attributes of device-aided treatments for advanced PD. The survey included both a DCE and a BWS exercise.

#### Survey instrument

The survey instrument was developed to capture patients' individual characteristics and their experience with PD and current medications. The instrument presented device and treatment-outcome descriptions and included questions to test understanding of definitions and graphics.

The survey used a DCE to evaluate patients' willingness to accept tradeoffs among various treatment attributes. Patients were asked to choose the most preferred treatment profile among three treatment options: brain stimulator, medicine pump, and an oral medicine reference condition that did not vary across choice questions. The choice scenario was designed to mimic the choice patients often face when considering device-aided treatments; that is, a choice between continuing on an oral therapy that does not control motor and cognitive symptoms well and can cause dyskinesia and two very different device-aided treatments—DBS and continuous levodopa-carbidopa infusion. The device-aided treatment profiles had varying combinations of attribute levels (Table 1). The treatment attributes and attribute levels were designed to represent common treatment features that can be affected by device-aided treatments and that distinguish between the two device-aided treatments of interest in this study. The attribute levels were informed by available clinical literature. The relevance of the attributes and levels was reviewed by a clinical expert. The salience of the attributes and levels to patients when making this type of treatment decision was assessed through face-to-face pretest interviews (see below). The reference condition represented oral treatment with poor outcomes (i.e., "3 hours a day when the oral medicine is working and 13 hours a day when the oral medicine is not working, you have a lot of difficulty finding the right words when speaking, you have a lot of difficulty thinking clearly, [and] you have to take 3 pills every 2 hours [a total of 24 pills] when you are awake"). An example choice question is shown in Figure 1.

To further evaluate the strength of patients' preferences for specific device-aided treatments, the survey included two hypothetical direct-comparison questions. The first direct-comparison question (Fig. 2A) described a medicine pump with best levels of the attributes "ability to find the right words when speaking," "ability to think clearly," and "additional oral medicine you take." The brain-stimulator profile was shown with the worst levels of those three attributes but with a slightly better "effect on control of movement symptoms" than that of the medicine-pump profile. The second direct-comparison question (Fig. 2B) showed the brain-stimulator profile with the best levels of the attributes "ability to find the right words when speaking," "ability to think clearly," and "additional oral medicine you take." The medicine-pump profile was shown with the worst levels of those three attributes but with a slightly better "effect on control of movement symptoms" than that of the brain-stimulator profile.