

FOOD AND DRUG ADMINISTRATION
PATIENT-FOCUSED DRUG DEVELOPMENT
PUBLIC MEETING

Afternoon Session

Tuesday, September 22, 2015

8:57 a.m.

Food and Drug Administration
White Oak Campus
10903 New Hampshire Avenue
Silver Spring, Maryland 20903
(301) 796-9018

Reported by: Michael Farkas,
Capital Reporting Company

1 A P P E A R A N C E S

2 MEETING ROSTER:

3 SAUJANYA GIAMGONE, Office of Strategic Programs, FDA

4 DR. WILLIAM DUNN, Division of Neurology Products

5 DR. THERESA MULLIN, Office of Strategy Programs

6 DR. DAVE PODSKALNY, Division of Neurology Products

7 DR. ELLIS UNGER, Office of Drug Evaluation 1

8 DR. ERIC BASTINGS, Division of Neurology Products

9 DR. SUSANNE GOLDSTEIN, Medical Reviewer, Neurology Team

10 DR. KENNETH BERGMAN, Neurology Reviewer

11 DR. LEONARD CAPCALA, Medical Officer, Neurology Team

12 DR. PETER COMO, Division of Neurological and
Physical Medicine Devices

13 DR. LEU XU, Central Biologics

14 DR. MEGHANA CHALASANI, Office of Strategic Programs

15 GRAHAM THOMPSON, Office of Strategic Programs

16 PUJITA VAIDYA, Office of Strategic Programs

17 DR. SARA EGGERS, Office of Strategic Programs

18

19

20

21

22

1	C O N T E N T S	
2	AGENDA ITEM:	PAGE
3	AFTERNOON SESSION: Parkinson's disease	
4	SOUJANYA GIAMBONE, Introduction	5
5	WILLIAM DUNN, Opening remarks	7
6	THERESA MULLIN, Overview of Initiative	15
7	SUSANNE GOLDSTEIN, Background of disease/treatment	20
8	SOUJANYA GAMBONE, Facilitator, Topic 1	26
9	DAN LEWIS, Panelist, Topic 1	35
10	KARL ROBB, Panelist, Topic 1	39
11	TODD HEBB, Panelist, Topic 1	48
12	ROSA KIM, Panelist, Topic 1	52
13	BECKY HOUDE, Panelist, Topic 1	56
14	CHUCK ESPOSITO, Panelist, Topic 1	79
15	JUDY WHEATON, Panelist, Topic 1	83
16	SARA EGGERS, Facilitator, Topic 2	95
17	STEVE DeWITTE, Panelist, Topic 2	97
18	GARY RAFALOFF: Panelist, Topic 2	107
19	JENIFER RAUB, Panelist, Topic 2	113
20		
21		
22		

1 C O N T E N T S (Cont'd)

2	AGENDA ITEM:	PAGE
3	AFTERNOON SESSION: Parkinson's disease	
4	KEVIN KWOK, Panelist, Topic 2	119
5	BILL PATTERSON, Panelist, Topic 2	126
6	PUJITA VAIDYA, Facilitator, public comments	162
7	DR. ERIC BASTINGS, Summary and closing remarks	174

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

1 P R O C E E D I N G S

2 A F T E R N O O N S E S S I O N

3 MS. GIAMBONE: All right. Well, let's
4 go ahead and get started. Thank you all for being
5 here. My name is Soujanya Giambone, and I'm with
6 the FDA's Office of Strategic Programs. And I,
7 along with my colleague Sara Eggers, will be
8 facilitating this meeting today.

9 So, on behalf of all of my FDA
10 colleagues, I'd like to just say thank you so much
11 for being here and welcome you all. And we
12 genuinely appreciate that you're all here today to
13 share your perspectives with us.

14 What I'd like to do is go over the
15 agenda and then just a few housekeeping items, and
16 then we'll get started. So we're going to start
17 off this afternoon with some opening presentations
18 from my FDA colleagues. They'll provide an
19 overview for the Patient-Focused Drug Development
20 Initiative, background on Parkinson's disease and
21 treatment options. And then I'll come back and
22 provide an overview of the discussion format.

1 So we have two topics today that we're
2 going to be covering. Topic 1 is on the symptoms
3 of Parkinson's and how they impact you on a daily
4 life. And then Topic 2 is on patient's
5 perspectives on current approaches to treating
6 Parkinson's.

7 We'll have a panel discussion for each
8 topic, followed by a group discussion for each
9 topic. That will take us to the last half-hour of
10 the day, which we've reserved for Open Public
11 Comment.

12 Open Public Comment is a time for
13 anybody in the audience, not just patients or
14 caregivers, but anybody that wants to share some
15 thoughts that are outside of the scope of Topic 1
16 or Topic 2, you can sign up for Open Public
17 Comment. We'll take a look at break time and see
18 how many people have signed up and how much time
19 each speaker will have.

20 And then finally, we'll wrap up the day
21 with some closing remarks from FDA.

22 Some housekeeping items -- bathrooms are

1 back out in the lobby. If you go back out into
2 the lobby area and make a right and go all the way
3 down the hallway, you'll see the restrooms there.
4 And you'll also see that we have a kiosk that
5 serves basic sandwiches, drinks, and so forth
6 available for purchase. So please feel free to
7 get up and stretch, or get a snack, or whatever
8 you need to do. So we just want you to be
9 comfortable here.

10 And before we continue, can I have my
11 FDA colleagues please introduce yourselves?

12 DR. UNGER: Good afternoon, everyone.
13 My name is Dr. Ellis Unger. I'm Director of the
14 Office of Drug Evaluation 1, and our office
15 oversees the Division of Neurology Products.

16 DR. DUNN: I'm Dr. Billy Dunn. I'm the
17 Director of the Division of Neurology Products.

18 DR. BASTINGS: Good afternoon. I'm Dr.
19 Eric Bastings. I'm the Deputy Director of the
20 Division of Neurology Products.

21 DR. PODSKALNY: Hi, I'm Dave Podskalny.
22 I'm a clinical team leader in the Division for

1 Neurology Products.

2 DR. GOLDSTEIN: Hello. I'm Susanne
3 Goldstein. I'm a medical officer in the Division
4 of Neurology Product's teams.

5 DR. BERGMAN: Hi, I'm Ken Bergman. I'm
6 a medical officer and clinical reviewer,
7 neurology.

8 DR. KAPCALA: Good afternoon. My name
9 is Dr. Len Kapcala. I'm a medical officer in the
10 Division of Neurology Products.

11 DR. MULLIN: Hi, I'm Theresa Mullin.
12 And I direct the Office of Strategic Programs in
13 the Center for Drugs.

14 DR. COMO: My name is Dr. Peter Como.
15 I'm a medical clinical reviewer in the Center for
16 Devices and Radiologic Health in the Division of
17 Neurological and Physical Medicine Devices.

18 DR. XU: Good afternoon. I'm Lei Xu.
19 I'm the medical officer at the Center for
20 Biologics Office of Cell Tissue and Gene Therapy.

21 MS. GIAMBONE: Thank you. And we have
22 some colleagues over here.

1 DR. EGGERS: I'm Sara Eggers in the
2 Office of Strategic Programs.

3 DR. CHALASANI: Meghana Chalasani, same
4 office.

5 MR. THOMPSON: Graham Thompson, same
6 office.

7 MS. VAIDYA: Pujita Vaidya, same office.

8 MS. GIAMBONE: All right. Thank you.

9 And just two more comments. This
10 meeting is being recorded and transcribed. So
11 we'll have the meeting recording and transcript
12 available on the meeting website within a few
13 weeks after the meeting.

14 And then, I know there are several of
15 you that are joining us that joined us already for
16 the morning portion of the meeting, and you're
17 here again for the afternoon. We thank you for
18 joining us for both. So some of the following
19 presentations may be repetitive to you, but we
20 just wanted to let you know.

21 So, on that note, I'd like to turn it
22 over to Dr. Billy Dunn for his welcoming remarks.

1 DR. DUNN: Hi. How ya'll doing?

2 Welcome. For those of you who were here this
3 morning, welcome back. And I see a lot of new
4 faces in the crowd, and we're just about as full
5 as we were this morning. So I'm glad you're here.

6 Welcome to this meeting on Patient-
7 Focused Drug Development for Parkinson's Disease.
8 As I said, I'm Dr. Billy Dunn. I'm the Director
9 of the Division of Neurology Products in the
10 Office of New Drugs at the FDA. Our division
11 reviews a wide breadth of drugs for neurological
12 diseases, including Parkinson's disease.

13 This meeting is a very important one to
14 us, and as you heard during the introductions, as
15 a testament to that, we have the entirety of our
16 team responsible for reviewing Parkinson's disease
17 here to hear your opinions, to avail themselves of
18 the informative commentary that I know that you
19 will have for us, and to incorporate that into our
20 daily work here as we engage in drug development
21 for Parkinson's with sponsors in this area.

22 All these folks have specialized

1 training and have taken care of Parkinson's
2 disease patients and are keen to hear your input
3 today.

4 We had a great discussion this morning
5 on Huntington's disease. I know we'll have
6 another good discussion this afternoon.

7 Before we move on, I want to reiterate
8 some of the important points from the morning.
9 Some of them were already done. But I do want to
10 just emphasize, as I said, the Patient-Focused
11 Drug Development is very important to us, as
12 illustrated by this meeting. We fully understand
13 that Parkinson's disease is a serious condition.

14 And although we have treatments
15 currently approved to treat Parkinson's disease,
16 which many of you here in the room are going to be
17 familiar with, there's obviously a continuing,
18 strong need for development of therapies,
19 particularly for patients with advanced disease or
20 patients who have difficulty managing their
21 condition with currently available therapies, not
22 to mention the ultimate goal, which is to

1 ultimately find a cure for Parkinson's. That's
2 absolutely what we all are here to do.

3 Dr. Susanne Goldstein, who introduced
4 herself just a moment ago, will provide a bit more
5 background on Parkinson's disease, specifically,
6 in a few minutes, much of which may be familiar to
7 you. But it is important to ground the
8 discussion.

9 I do want to point out that it's FDA's
10 responsibility to ensure that the benefits of a
11 drug outweigh its risks. Therefore, what we hear
12 from you today about the different ways your
13 symptoms affect your daily life and what you value
14 in a treatment can help us understand how you view
15 those benefits and risks in relation to treatments
16 for Parkinson's disease.

17 That will directly inform our work when
18 we are faced with a drug which is effective, but
19 which may have certain risks associated with it
20 for Parkinson's disease as we consider the best
21 way to get it out there and write a label for it
22 and inform the population about the best way to

1 use it.

2 It's important to remember that FDA is
3 just one part of the drug development process.
4 This came up this morning. I had some questions
5 after the session that really illustrated that
6 it's not always transparent. A lot of the work
7 that we do is confidential. It's not always
8 transparent to what degree we are involved with
9 companies. We're very involved with companies,
10 but we are not the ones that initiate the clinical
11 trials.

12 Drug companies, often working with
13 researchers or patient communities, are the ones
14 who conduct these trials and eventually submit
15 their drug applications to the FDA for our review.
16 We work closely with them throughout the drug
17 development process, however.

18 That was a question that I faced this
19 morning, and I thought I'd just go ahead and bring
20 it up now, because I didn't have time to address
21 it in any great detail earlier.

22 But from the discovery phase, when

1 molecules or new antibodies or whatever it might
2 be are being researched in animals or considered
3 kind of theoretically, to the first introduction
4 into humans, to large-scale trials that are
5 intended to demonstrate clear evidence of
6 effectiveness, and right through approval and on
7 to post-marketing surveillance, we're with the
8 drug companies every step of the way.

9 So we're closely engaged, and we're
10 bringing our approach, which I think is a flexible
11 one, an open-minded one, and one which reflects
12 the needs of the community -- we're bringing that
13 to the table each and every day we meet with the
14 sponsors who are developing these drugs.

15 I want to thank all the representatives
16 from industry, academia, and others, as well, who
17 are here as a part of this meeting. For those of
18 you who are here representing the Parkinson's
19 disease community, you may not realize that there
20 are members of industry here who are also eager to
21 hear what you have to say. And I think your
22 comments will be equally valuable for them.

1 I guess that's about it. We had a few
2 more comments this morning, but I think in the
3 interest of time, we'll stop them here.

4 Dr. Theresa Mullin is going to step up
5 and give you a few comments about the broad effort
6 on Patient-Focused Drug Development. And again,
7 thank you for being here. We really look forward
8 to your comments today.

9 DR. MULLIN: Thank you, Billy, and
10 welcome, welcome to FDA's campus. And as I said
11 this morning, I just want to say that we're very,
12 very grateful that you're here.

13 And in hindsight, we're grateful that we
14 had the meeting today and not planned it for
15 tomorrow or the next day, given how the road
16 closures -- there are signs everywhere in the
17 Washington area about how the roads are going to
18 be closed. And it will probably be even more
19 difficult than usual to get here tomorrow or the
20 day after that. So that was a good move on our
21 part, though we didn't realize it.

22 I'm going to spend a minute to tell you

1 about this Patient-Focused Drug Development
2 Initiative. As you notice on the agenda, it says
3 this is a Parkinson's disease meeting, a public
4 meeting, as part of this Patient-Focused Drug
5 Development. And as Dr. Dunn observed or reminded
6 us all, you know, FDA and CDER in particular, and
7 CDR and CDRH, the medical products centers, are
8 focused on trying to ensure that the benefits
9 outweigh the risks in the review of products, and
10 even deciding whether or not to allow products to
11 stay on the market.

12 And the clinical context for weighing
13 benefit and risk are quite critical to that
14 weighing and that decision. So that if a disease
15 is quite severe and there are not a lot of good
16 treatments available, it affects our willingness
17 and patients' willingness as they tell us to
18 accept risks.

19 So, what we realized is that, you know,
20 we really needed a better way to get,
21 systematically collect the patients' perspective
22 because it's a most critical perspective on

1 benefit and risk, that patients are the ones who
2 will be experiencing any benefit that there is to
3 gain from the drug and will experience the harm.
4 And we had no good way to collect that widely
5 across the population affected by disease.

6 We have very good programs in the
7 patient representative programs that allow us to
8 talk to individuals, but not really do it in the
9 way we're going to do it today, which is to get a
10 broader perspective, a diverse perspective on what
11 it's like to live with the disease, how that
12 disease affects your life, and how well or not the
13 treatments that are currently available are
14 working for you.

15 This provides great insight for FDA in
16 terms of our consulting with companies throughout
17 drug development -- for example, from the CDER
18 perspective, which we do -- and it allows us to
19 weigh that, take that into consideration when an
20 application comes in for marketing review.

21 So this is one of what we committed to
22 do, 20 meetings over the course of five years of

1 the Prescription Drug User Fee. This
2 authorization we call PDUFA V. We're going to do,
3 it turns out, more than 20. But each is focused
4 on a different disease area and intended to gain
5 that kind of information over the course of the
6 discussion and the meetings.

7 When we started this effort three years
8 ago, we, working with the divisions, identified
9 about 40 diseases to ask the public which we
10 should focus on over the five years. We got about
11 4,500 comments on that. So we got even more
12 diseases identified through the public comments.
13 We had to take that and a very difficult task of
14 trying to figure out which we would focus on in
15 this first five years.

16 And we say "first five years" because
17 we've learned a lot in the course of doing this
18 effort that we can build on and provide
19 opportunities, in fact, for others to have these
20 meetings, as well.

21 So we had 16 diseases identified in the
22 first three years. And there you can see the list

1 of all the diseases we will be covering under this
2 initiative over the five-year period. And today,
3 we're having the meetings on Huntington's disease
4 this morning, and now we're going to have the
5 meeting on Parkinson's this afternoon. And each
6 has provided extremely beneficial and insight-
7 providing input to us.

8 Each of these meetings is tailored to
9 the particular issues related to the disease, but
10 they also have this common set of questions that
11 try to elicit the patient's and that patient's
12 family and caregiver's perspectives on the disease
13 and the current approaches to treatment. So we
14 start with these questions, and then often we
15 tailor and add additional questions of the review
16 division has identified other questions they want
17 to take this opportunity to put to you and ask you
18 to help us understand better.

19 For example, when we had a meeting on
20 HIV, we asked the patients how they would feel
21 about participating in cure research. Many of
22 them were on treatments that seemed to be working

1 well. Would they be willing to go off those
2 treatments to try a cure, a possible cure
3 treatment? And so, we asked sometimes about the
4 difficulties of participating in trials and things
5 related to other aspects of development.

6 We've learned a great deal from these
7 meetings. At the end, and after we close the
8 docket -- we leave our electronic docket open so
9 that we can get other input that patients may be
10 able to offer us or people who are unable to be
11 here can send in. And we analyze all that
12 information, as well as the transcript that we
13 have from the meeting, to develop this report.

14 And you'll see the ones that have been
15 developed already, on our website. If you were to
16 Google "voice of the patient," you will find your
17 way to this report. I usually find information on
18 FDA's website by Googling, myself. And you can
19 take a look at all this stuff we've done, in this
20 way. And we'll produce a report like that on
21 Parkinson's when we collect all the information
22 and analyze it as well, going forward.

1 These reports are very useful as a
2 reference to reviewers and others in terms of what
3 they contain. They try to really authentically
4 capture what you tell us today in the words that
5 you tell us so that we really do have it be your
6 voice that we're reflecting in these documents.

7 And we've also found that what we hear
8 in these meetings is prompting us to look at how
9 we can build on what we hear in these meetings to
10 maybe even move towards the development of more
11 systematic tools to collect information like this
12 in clinical trials.

13 So it's been extremely valuable for us.
14 So we're looking forward to engaging and hearing
15 what you want to tell us today. And with that,
16 I'll turn it to Susanne Goldstein to tell you more
17 about the background on Parkinson's.

18 (Pause.)

19 DR. GOLDSTEIN: Welcome. And again,
20 thank you very much for being here today, sharing
21 your time and your thoughts with us.

22 I just want to briefly go over the

1 background of Parkinson's disease, which many of
2 you are well aware of. And my remarks don't
3 necessarily reflect those of the FDA.

4 Parkinson's affects approximately 1
5 million people in the United States, which is
6 about a half a percent. For the population over
7 80 years old, this prevalence is up to about 10
8 percent. On average, people develop the symptoms
9 of Parkinson's disease in their 60s. However,
10 about 10 to 15 percent of patients develop their
11 symptoms less than age 40, and this we refer to as
12 "young-onset Parkinson's disease."

13 There's really no specific causative
14 factor that's known. Both genetics and the
15 environment probably play a role. Research has
16 suggested that genetics play a larger role in the
17 young-onset Parkinson's disease patients, whereas
18 the environment plays a greater role in the later
19 onset of the symptoms.

20 This is a little bit of a complicated
21 slide, but it's just to briefly touch on something
22 that's come up in research more recently, that

1 it's felt that the primary mechanism of neuro-
2 degeneration, loss of dopamine cells in
3 Parkinson's disease, is caused by program cell
4 death, or apoptosis. And both genetics and the
5 environment play a role in this.

6 There are two main symptom categories
7 that define Parkinson's disease. And classically,
8 most people are familiar with the motor symptoms -
9 - muscle stiffness; slowness of movement; tremors,
10 specifically a resting tremor; as well as gait and
11 postural instability.

12 Nonmotor symptoms, which we are now
13 recognizing much more so, include depression and
14 anxiety, difficulty with memory, which can happen
15 early on, something known as the disexecutive
16 syndrome, and in the advanced disease, sometimes
17 as dementia. Difficulty sleeping, falling asleep,
18 staying asleep, abnormal dreaming also are very
19 common in Parkinson's disease, as are
20 hallucinations, which can be from the disease
21 itself or from the treatments.

22 And I just want to touch on the

1 treatments. We have a lot of treatments here, and
2 I'll cover them briefly, that are mainly for the
3 motor symptoms. And levadopa is still the gold
4 standard, been around since the 1960s, and later
5 reformulated as carbidopa- levadopa, much better
6 tolerated. And it's available in a variety of
7 formulations -- Sinemet; Sinemet CR, which is
8 long-acting; Rytary, which is a combination of
9 short- and long-acting.

10 More recently, we've approved in the gel
11 infusion of carbidopa-levadopa, duopa, which is
12 directly infused into the gut for more advanced
13 Parkinson's disease.

14 There are other agents, like dopamine
15 agonists, which can mimic dopamine in the brain.
16 And there are drugs that can actually slow the
17 breakdown of dopamine so you would increase the
18 amount of dopamine the brain has, the more
19 sustained benefit. And these are the COMT
20 inhibitors and the MAOB inhibitors. Other agents,
21 such as anticholinergics and amantadine, can help
22 with the tremor and dyskinesias.

1 In terms of non-motor symptoms, there's
2 nothing that's FDA approved, but we do use or you
3 probably have experience with antidepressants and
4 anxiolytics, as well as neuroleptic drugs for the
5 depression, anxiety, and sleep.

6 We also have found some excellent
7 benefit, and probably some patients here may have
8 had this, with the deep-brain stimulation surgery,
9 particularly for motor symptoms of tremor,
10 stiffness, and slowness.

11 Nonpharmacological treatments are
12 probably equally important, particularly early in
13 the disease, but all throughout the disease.
14 Physical and occupational therapy are very
15 important, as are speech and swallowing for people
16 suffering from issues of that. Diet and exercise
17 are extremely important in maintaining functional
18 ability. And counseling, both for the patient,
19 caregiver, family, all very important.

20 And as a clinician, I found that support
21 groups were a great help to my patients, because
22 they could learn so much from each other in how to

1 deal with their daily lives.

2 So, at FDA, we are very aware, we're
3 keenly aware that there are unmet medical needs
4 still, both motor and nonmotor symptoms. And
5 that's why it's so important that we have meetings
6 like this today to hear your thoughts, to help
7 guide us in future research and development of
8 treatments. And again, thank you so much for
9 taking the time to be here.

10 MS. GIAMBONE: Thank you to my FDA
11 colleagues for your remarks.

12 And now what I'd like to do is just
13 provide an overview of the discussion format. So,
14 as I mentioned before, we have two topics that
15 we'll be reviewing. Topic 1 is on the symptoms
16 that matter most to you. So, in this topic, what
17 we're listening for is, what are the most
18 significant symptoms of Parkinson's and how do
19 they impact your daily life? How do they affect
20 your ability to do certain activities, or are you
21 unable to do certain activities because of these
22 symptoms?

1 Tell us how your symptoms have changed
2 or evolved over time. And how do they affect your
3 social interactions or your mood?

4 Topic 2 is on current approaches to
5 treating Parkinson's disease. So here we're
6 listening for, what is your current treatment
7 regimen? And both prescription therapies and
8 other therapies, as Susanne just mentioned. How
9 well are these treatments treating your
10 significant symptoms? And how do you know that it
11 is or is not working for you? What are the
12 biggest downsides to your treatments?

13 And then finally, we'd like to hear your
14 perspectives on what you look for in an ideal
15 treatment.

16 So first, we'll start with hearing from
17 a panel of patients and caregivers. And I've had
18 the honor and the pleasure of working with our
19 panelists for the last week-and-a-half. And I can
20 tell you they've worked so hard to put their
21 thoughts down. You're all incredibly courageous
22 people to do that and then come here and share

1 those stories with us. So, thank you for doing
2 that.

3 Our panel reflects a range of
4 experiences with Parkinson's disease. And each
5 panelist will have roughly five minutes to present
6 their remarks.

7 So then what we'll do is we'll broaden
8 the dialog, and we'll invite other patients and
9 caregivers in the audience to build on what
10 they've heard from the panel, share with us what's
11 similar in your life, but also what's different in
12 how you experience Parkinson's or how your loved
13 one experiences Parkinson's.

14 So, periodically, we'll ask some
15 questions along the way. And if you're
16 comfortable to do so, please raise your hand. And
17 we'll have some microphone runners around the
18 room. They'll come to you, and you can provide
19 your thoughts. Please state your name before
20 answering. It just makes it a little bit easier
21 in our transcript.

22 We'll also do some polling questions

1 along the way. And you should all have clickers,
2 for patients and caregivers and patient
3 representatives only, please. You should all have
4 the clickers at your table that you'll use to
5 answer the polling questions. And we'll test that
6 out in just a little bit.

7 So, the polling questions are not
8 scientific. It's completely voluntary for the
9 patients and patient representatives to respond.
10 And what it does is it just gives us some more
11 understanding of what perspectives are in the
12 room.

13 For those of you on the Web, you can
14 also respond via the webcast. So speaking of the
15 Web, we have over 200 people joining us on the
16 webcast today. So that's incredible. Thank you so
17 much to all of you joining us on the Web. We
18 can't see you, but you're a very, very important
19 part of our meeting. And we'll be checking in
20 with you periodically. We'll summarize some of
21 the themes that we're hearing from on the Web. And
22 all of your comments from the Web will also be

1 incorporated into our summary report.

2 And then finally, we'll also go to the
3 phone towards the end of each discussion, to hear
4 from a few of the dial-in folks.

5 (Pause.)

6 MS. GIAMBONE: We also have a public
7 docket that will stay open for two months after
8 the meeting. And this electronic docket is just a
9 very important part of our meeting. It's anything
10 that you weren't able to, you know, either share
11 with us today or additional thoughts that come to
12 mind. Please go to the public docket and continue
13 to submit your written comments. They're
14 extremely important. They're all part of the
15 public record. And we'll go through each and
16 every one of them. And we incorporate those
17 comments into our summary report.

18 Anybody is welcome to comment in the
19 public docket, not just patients and caregivers.

20 We also want to share some additional
21 resources at the FDA that you may already know of.
22 First is FDA Office of Health and Constituent

1 Affairs. And their contact information is here.
2 And then finally, we also have -- within the CDER,
3 Office of Center Director, we have the
4 Professional Affairs and Stakeholder Engagement,
5 or PASE. And some of you, I think, have already
6 interacted with this group.

7 And again, all of this information will
8 be available on our meeting website. You know,
9 the slides and everything will be posted there.

10 Okay. So we'd just like to go over a
11 few ground rules for today. Today is really a day
12 to hear from patients and caregivers. So we
13 encourage you to contribute to the dialog. We are
14 looking forward to hearing as much as we can from
15 you. On that note, FDA is here to listen, along
16 with industry, academia, and other government
17 agencies. We think this meeting is going to be
18 very important to all of you also. We just ask
19 that you stay in listening mode.

20 Our discussion will focus on symptoms
21 and treatments on our topic questions. And we
22 understand that there are many, many aspects to

1 Parkinson's. So what we'll do is anything that's
2 outside the scope of Topic 1 or Topic 2, again,
3 please sign up for Open Public Comment, or submit
4 it to the public docket, you know, any additional
5 thoughts that come to mind.

6 The views expressed today are personal
7 opinions, and on that note, respect for one
8 another is paramount. And then finally, we're
9 going to be passing out evaluation forms toward
10 the end of the meeting. So let us know how the
11 meeting went for you today. And it really helps
12 us to see what we can improve upon for future
13 meetings.

14 All right. So, let's start with our
15 first polling question. So again, if we can have
16 our patients and patient representatives,
17 caregivers. All right. So, the first question
18 is, where do you live? A, within the D.C. metro
19 area; or B, outside of the D.C. metro area.

20 (Pause.)

21 MS. GIAMBONE: When you press it, it
22 should give you a little bit of a buzz, I think,

1 right?

2 (Pause.)

3 MS. GIAMBONE: And just to avoid double-
4 counting, if the patient is already responding,
5 the caregiver doesn't have to. But certainly, if
6 you would like to help and provide that input,
7 then the caregiver can submit the response on
8 their behalf.

9 Okay. So it looks like nearly 75
10 percent of you are from outside of the D.C. metro
11 area. So thank you again for making the travel to
12 come here. Twenty-five percent, local neighbors
13 we have here. So great to see you all, too.

14 Second question. Have you ever been
15 diagnosed as having Parkinson's disease? A for
16 yes, B for no.

17 (Pause.)

18 MS. GIAMBONE: Okay. So, two-thirds of
19 you in the room, roughly, have been diagnosed as
20 having Parkinson's disease. And 36 percent, no.

21 Next question. Are you A, male; or B,
22 female?

1 (Pause.)

2 MS. GIAMBONE: All right. So, almost an
3 even split here. It looks like we have more
4 females in the room, but good to see that we also
5 have a good portion of male perspectives in the
6 room.

7 Okay. Age. A, younger than 30; B, 30
8 to 40; C, 41 to 50; D, 51 to 60; E, 61 to 70; or
9 F, 71 or greater.

10 (Pause.)

11 MS. GIAMBONE: Okay. So it looks like
12 almost half of you responding are in the 61-to-70
13 age range, followed by the 51-to-60 age range.
14 And it actually, it looks like we have a good mix
15 of most of the age groups, so great to see that.

16 Okay. What is the length of time since
17 your diagnosis? A, less than five years ago; B,
18 five to ten years ago; C, ten to twenty years ago;
19 D, more than twenty years ago; or E, I'm not sure.

20 (Pause.)

21 MS. GIAMBONE: Okay. So, it looks like
22 we have several people that have been diagnosed

1 less than five years. And then, a large portion
2 of you diagnosed between five to ten years ago,
3 and then ten to twenty years ago. So again, a
4 good mix, it looks like.

5 Okay. And then on that note, could we
6 see what we're hearing on the Web?

7 MR. THOMPSON: Very, very similar
8 results. About 63 percent diagnosed, an even split
9 between male and female, similar age range, and 80
10 percent of people are either five to ten or less
11 than five years.

12 MS. GIAMBONE: Okay. Thank you very
13 much.

14 And now I'd like to turn it over to our
15 Panel 1 panelists to talk about their most
16 significant symptoms and daily impacts. So we'll
17 start with Dan.

18 MR. LEWIS: Hello. Thank you for this
19 opportunity to let the patients talk to the
20 doctors. It's a refreshing change. And we welcome
21 it. I'm fairly typical of each person's
22 individual profile with this disease. But I think

1 mine is fairly typical except for one thing, which
2 is the length of time.

3 I'm 71 years old. I was diagnosed when
4 I was 15. And my neurologist, Steve Rich
5 (phonetic), said that I was going to go slow and
6 would not rush into major dramatic changes, and he
7 was right. But after about eight years, I had
8 difficulty walking and balance, and freezing. So
9 we upped the Sinemet, and I was taking about --
10 Sinemet, 25-slash-100 every two hours.

11 I had terrible dyskinesia. So no one
12 would eat with me because I would knock over all
13 the glasses at the table. And I'm a lawyer. And
14 in the courtroom, I would have to take recess and
15 shoot myself with Apokyn to continue the cross
16 examination or argument before the judge.

17 Things were very, extremely difficult.
18 And my doctor, Dr. Rich, said, "How about a brain
19 implant?" And my first reaction was, the last
20 thing I want is a doctor messing around with my
21 brain. But I came around. And I had the
22 operation in 2005. And it was very successful for

1 me. I reduced the amount of Sinemet that I was
2 taking by 50 percent. And with the help of
3 amantadine, I didn't have any dyskinesia except a
4 slight, slight bit, but not enough to interfere
5 with any activities. So, it was very successful
6 for me.

7 And I run a support group for about 12
8 years now, 15 years. And we have a lot of
9 experience with DBS. And we've found that some
10 people don't do well with DBS at all, and that
11 large psychological problems occur and they get
12 very depressed. But I was lucky. I had none of
13 that.

14 Then, as my problems increased, I found
15 that the answer to most of my problems was not
16 with the doctors, unfortunately, and not with the
17 medicine, but with the exercise. Exercise is more
18 important than the pills we take, I think. So,
19 I'm in a regimen now. I do about 12 hours to 15
20 hours of supervised exercise aimed at Parkinson's.
21 Most of them are run by the Parkinson's Foundation
22 for the National Capitol Area. They're free, and

1 they're excellent.

2 And that has enabled me to be mobile. I
3 have ups and downs, periods of several months of
4 where I can walk without a walker and talk and be
5 understood. But other times, I have down times.
6 And throughout the whole time, I am doing
7 exercises. So they're not a total panacea. But I
8 have times where I have several months of good on-
9 time, and then off-time where I can't even
10 stabilize myself with a walker.

11 And the problems I have now that I need
12 to address medically are the things that DBS won't
13 help. And that is speech, sleep, and freezing and
14 falling -- balance, I'd say. So I would urge you
15 all, because the numbers are dramatic, the number
16 of people who have Parkinson's. And I think the
17 main is a little low. But we've been pushing
18 legislation at PAN to get -- see to do a real
19 survey of who has Parkinson's and who doesn't.
20 That will show how widespread Parkinson's really
21 is.

22 MS. GIAMBONE: Any final thoughts, Dan?

1 MR. LEWIS: Let me say, address the
2 impact of my situation. I can walk with a walker
3 and go to museums. I can fly. I can sit and
4 read. But I'm fearful of falling down and
5 breaking my hip. That is the fear that I think
6 many of us share, because once you break your hip,
7 recovery is slow and complicated, and you often
8 die.

9 So, it's something that is always in the
10 back of my mind. Am I going to fall? I have
11 fallen pretty regularly. Last week, I was in LA.
12 I fell, and I had to have five stitches. I
13 luckily fell in a way that didn't harm myself
14 permanently. But it's one of the things that you
15 all need to address, pharmacological devices, if I
16 could be so bold as to suggest such a thing with
17 the panel.

18 MS. GIAMBONE: Thank you so much, Dan.
19 We really appreciate it. Thank you.

20 Next, we have Karl.

21 (Pause.)

22 MR. ROBB: This is Parkinson's under

1 stress.

2 (Pause.)

3 MR. ROBB: Okay, I'm good.

4 MS. GIAMBONE: Karl, would you like for
5 me to read your comments? You have some excellent
6 comments down. Or we can come back to you if
7 you'd like.

8 MR. ROBB: I think I can do it. Just
9 give me one second.

10 MS. GIAMBONE: Okay. No problem.

11 DR. DUNN: Sir, let me reassure you that
12 don't let anything from our end cause you any
13 stress. We're thankful that you're here and very
14 eager to hear your comments. Take all the time
15 you need, okay?

16 MS. GIAMBONE: Yes.

17 MR. ROBB: I think I can go on. I'm
18 sorry.

19 Thank you. Thank you for this
20 opportunity. My name is Karl Robb. I'm 49 years
21 old. I've had Parkinson's since I was aged 17.
22 But I was diagnosed six years later. I'm an

1 Amazon bestselling author, a blogger, lecturer, an
2 advocate for and board member for the Parkinson's
3 Action Network.

4 I'm attempting to say that my slowness
5 of movement -- one second.

6 (Pause.)

7 MR. ROBB: I find that tasks take longer
8 and more effort. And the rigidity, range of
9 movement, poor flexibility have become more
10 difficult. Balance, ease of walking, and gait are
11 slowly becoming factors that I find most
12 challenging of all, the worst symptoms that I
13 encounter.

14 The most frustrating and annoying
15 factors, really the sheer unpredictability of when
16 certain symptoms crop up without forewarning.
17 Surprise. These factors can affect all factors of
18 daily living -- all factors of daily living.
19 Attempting to summarize some of the system is
20 massively intricate. It's not an easy feat.

21 So this changes your being, robs you of
22 your identity, forces you to become someone else.

1 Between the disease and the meds, you must
2 determine what are symptoms or side effects of
3 meds and what is truly Parkinson's. At age 30, I
4 made the very difficult decision to give up
5 driving. I didn't want to jeopardize or put
6 others at risk. So I wasn't sure as I could be in
7 better control.

8 Someone that's age 30 shouldn't have to
9 face something this difficult. On my best days, I
10 believe that I'm productive, mobile, and the meds
11 are working well. Even after two decades of
12 nearly the same dosage of meds, on the worst days,
13 I experience some balance problems, speech, and
14 probably experience dyskinesia as well. I never
15 really can tell when a good day is coming or not.

16 My ability to cope came at such a young
17 age, I have to make my peace with this illness as
18 something that must be dealt with, learned from,
19 and creatively worked around. It's trying at
20 times and hard to see this illness slowly creep up
21 on you. I imagine any illness fluctuates over
22 time. So, yes, I see variance from moment to

1 moment and day to day. I rarely, if ever, see two
2 that are alike. I try to make each a productive
3 day. I'm aware that stress is a major factor in
4 this illness.

5 Diet -- I think being a long-time
6 vegetarian has been a benefit. I find that when I
7 eat healthier, more natural foods, my digestion
8 improves and my whole body seems to function
9 better as well. Yoga has been excellent in
10 balancing and centering my mind and body. Greg
11 (phonetic) used to tell me so much about energy
12 and mindfulness. Sleep is crucial for PD
13 patients. I'm so grateful that I'm able to sleep
14 well.

15 Meditation, stress reduction, massage
16 and reflexology, and trying to learn patience have
17 all been helpful. Lastly, exercise can help
18 briefly, as well. But it can make balancing the
19 meds for the day even more difficult.

20 Stress, anxiety, crowds, and being
21 rushed all contribute to making my symptoms
22 worsen, such as like right now. When one loses

1 confidence in one's own body and knows that his or
2 her body will not respond as well as asked, you
3 wonder, search, seek for options and solutions.
4 It worries me that our best alternatives are
5 invasive solutions and dangerous drugs with side
6 effects, and that we don't look at something
7 that's truly a more organic and basic approach.

8 This illness affects the mind, body, and
9 spirit, and all three must be kept in balance for
10 fear they should fall as well. I'm worried that
11 there are fewer effective drugs and more patients
12 and that so little is understood about the aspects
13 of Parkinson's. It worries me to contribute less
14 and less to my family's care and not be able to
15 always help with household chores when I want to.

16 No two Parkinson's patients are exactly
17 alike. My observation in getting a handle on this
18 illness is a mystery. Parkinson's affects all
19 ages at all stages of their lives. Parkinson's
20 disease is an awkward disease on a social level
21 and a physical level. Since my diagnosis, nothing
22 in my life has ever been normal or predictable.

1 Before my diagnosis, I experienced tremors, poor
2 posture, balance issues, mobility problems,
3 dystonia, festination, padykinesia, and speech
4 issues.

5 When I began Sinemet over 25 years ago,
6 I experienced a miracle transformation in my
7 condition, as I saw my balance, gait, and overall
8 mobility condition improve. Moving forward, I
9 began experiencing dyskinesia, dyskinesias at one
10 point that would last for two hours, two
11 exhausting hours. Right now, I feel my greatest
12 challenge and struggle is timing and to stand the
13 potency of the meds as the pills wear off over the
14 day.

15 One of the hardest challenges throughout
16 the day is the delicate balance of mixing meds and
17 food over time. I'm very protein-sensitive, even
18 though I eat vegetarian. When traveling or going
19 out, it is never easy to know what to expect with
20 change in schedule.

21 For someone who's had this disease for
22 so long, my dosage of Sinemet, Requip, and

1 amantadine are all still quite low. But my window
2 of off-times is slowly creeping up. It has cost
3 me several friendships and given me many
4 friendships. But most of those relationships are
5 out of my control. I've lost friends who just
6 couldn't get their arms around this illness. I
7 accept that trying to understand Parkinson's
8 without living it on a daily basis is pretty much
9 impossible.

10 Parkinson's disease has brought me an
11 amazing community of close friends who understand
12 what I am experiencing and are there to support
13 me, as I do them. I have practiced (inaudible) for
14 16 years, with a master of it for three, and seen
15 a huge improvement over the time, over those 10
16 years in mental, physical, and spiritual ways.

17 I'm a long-term vegetarian, which has
18 improved my digestion, skin, and overall pill
19 uptake. Plus, I feel better without meat protein.
20 I do moderate exercise with walking, playing
21 Nintendo Wii until I sweat. I write almost every
22 day just to create something new every day.

1 My Sinemet continues to maintain most of
2 the efficacy needed on a good day. For movement
3 and balance, my Requip does most of the same.
4 Amantadine that I take has helped my balance.

5 To answer your question, too, about how
6 well your regimen is treating you, that's a tricky
7 question because I've had this so long I don't
8 know. I think that I'm doing well, for as long as
9 I have lived. So far, well enough, but I wouldn't
10 mind seeing more -- question 2A. So far, well
11 enough, but I wouldn't mind more help, and most of
12 my friends and readers need a lot more help.

13 I'm especially worried about my
14 caregiver, care partner, as I increase her
15 workload over time. Of course, side effects like
16 dyskinesia and the on-off effects are probably the
17 worst of the batch of my symptoms. I see the
18 insurance companies tell me which drugs are
19 maintenance and which drugs are not. I don't
20 think it should be up to them to tell me which are
21 significant and those that are not. If we need
22 our meds, we need our meds.

1 I don't know what a cure would mean,
2 whether that means all end to illness or reversing
3 it. But in my mind, the perfect treatment would
4 be a once-a-day pill, patch, or inhalant that
5 controls all symptoms, minus side effects and
6 without on-off at times. I'm a realist, but it is
7 fun to dream.

8 I'm hopeful for the future, developments
9 in therapies as well as drugs. Our community is
10 in dire need of assistance in slowing, stopping,
11 and even reversing this thief of a disease. Thank
12 you.

13 MS. GIAMBONE: Thank you so much, Karl.

14 Next, we have Todd.

15 MR. HEBB: PD for me is pathos-defiant.
16 Good afternoon, ladies and gentlemen. My name is
17 Todd Hebb. I am 63 years old. I have Parkinson's
18 disease.

19 I was diagnosed in November 2008. In
20 the seven years since, I have listened to
21 brilliant doctors, read stories about PD by
22 celebrated people, participated in clinical

1 research, joined a foundation, the Parkinson's
2 Disease Foundation, and am an advocate, and helped
3 form a nonprofit organization to raise money for
4 PWP services.

5 I'm here today to share my experience
6 with PD and specifically my symptoms as my disease
7 has progressed. Parkinson's disease is insidious.
8 Motor deficits are deceptively routine in the
9 scheme of old aging, stiffness, slowing, shaking,
10 and loss of balance. But finding these symptoms
11 in patients in their 30s and 40s and 50s, decades
12 before seniority, is unusual and frightening.

13 Upon these challenges, Parkinson's
14 disease often affects cognition -- memory,
15 executive function, and autonomic systems in the
16 human body.

17 Two years before I was diagnosed with
18 PD, I was having difficulty walking and
19 controlling my forward momentum. I was carrying
20 one end of a cabinet to install and could not
21 stop. My orthopedic surgeon recommended I see a
22 neurologist. I was first tested with the Hoehn

1 and Yahr rating scale, performing with ease the
2 simple motor coordination and reflex evaluations.
3 I felt reassured that I was not suffering a brain
4 disorder.

5 The neurologist then asked a question
6 that jolted me to attention, because I had not
7 mentioned this annoyance to anyone. He asked if
8 my handwriting had become smaller. I nearly
9 laughed at his precise deduction. Yes, my
10 handwriting had become Lilliputian.

11 It would start out relatively normal,
12 but by the sentence end, it was an illegible
13 scrawl. I had micrographia -- judgment: PD.

14 Another early symptom was emotional
15 sensitivity. Usually, when I was alone, that
16 would bring, without warning, episodes of tearful
17 weeping, linked to worry and anxiety about family,
18 as well as emotional welling associated with joy
19 and gratitude. I cried often at movies and at
20 music in the car, anyplace where emotions were
21 out. I considered the possibility that I was
22 evolving and maturing. I never thought of this as

1 pathological.

2 Shortly after my diagnosis, I learned of
3 emotional incontinence, a symptom not uncommon
4 with Parkinson's disease.

5 During the last seven years, I've
6 experienced a slow, but gradual worsening of motor
7 symptoms. The most difficult of these is
8 freezing, the sudden inability to move my legs, as
9 if they were set in blocks of hardened concrete.
10 This occurs most often when I'm at home, in
11 hallways, in closed quarters, usually coming off
12 my levadopa.

13 Often, this occurs when I'm trying to
14 hurry out to an appointment. And I'm severely
15 affected when standing in large crowds. This
16 condition presents the greatest risk of falling.

17 Sleep dysfunction, including daytime
18 sleepiness, contributes to impaired thinking, slow
19 reaction time, and fatigue. I've not had a
20 restorative sleep in many years. Initially,
21 restless leg caused an aching in my calves, which
22 took hours to walk off.

1 The medications helped, and then caused
2 sleep attacks, which are moments when my conscious
3 mind is switched off and I sort of go blind. This
4 has happened during casual conversations, while
5 watching TV. And you can imagine it's terrifying
6 for driving a car or operating machinery. Adding
7 to sleep problems, I have sometimes had vivid
8 dreams and act these out occasionally, which
9 contributes to my temperament.

10 Slowness, or bradykinesia, is my
11 condition most of the time. It is not just
12 physical change in movement, velocity, but a
13 pervasive slowing of thought patterns, like a
14 freezing of synapses. One way that I counteract
15 this condition is by using a positive intention
16 that requires a clear and undivided purpose. And
17 that's how I carry on.

18 Thank you, and my name is Todd Hebb.

19 MS. GIAMBONE: Thank you so much, Todd.

20 Next, we have Rosa.

21 MS. KIM: Hi. I'd like to thank FDA to
22 giving me opportunity to tell my experience. My

1 name is Rosa Kim. I'm research advocate with the
2 Parkinson's Disease Foundation and coordinator of
3 support group for Korean Americans with
4 Parkinson's disease in Chicago area.

5 I'm here on behalf of my mother, who
6 suffered from Parkinson's disease for six years
7 and passed away three years ago. My mother, a
8 schoolteacher, was a strong-willed and a most
9 loving and caring person. She was diagnosed
10 Parkinson's at age 81. Like most people, she had
11 symptoms such as insomnia, loss smell,
12 constipation, anxiety, and fear long before her
13 diagnosis. However, her first major symptoms were
14 stiffness and inability to move.

15 Mom raised the four of us by herself,
16 and she was very independent woman. Therefore,
17 when she could no longer walk or move, she felt
18 powerless. She felt like her humanity was taken
19 away and became very depressed. Soon after, she
20 developed speech problems and difficulty finding
21 words, which made her even more withdrawn.

22 Her degeneration was much faster than

1 most of Parkinson's disease patients. Around age
2 84, she became wheelchair-bound, and her mild
3 dementia started. Eventually, she lost ability to
4 do daily activities like dressing, bathing, feed
5 by herself, and go out for a walk. After that,
6 the nonmotor symptoms got worse, as well. She was
7 very embarrassed about her symptoms. And we often
8 had to cancel plans because her constipation,
9 diarrhea or stomach pain.

10 On good days, she was very responsive
11 and tried to help herself do little things like
12 holding a cup while she's drinking or trying to
13 use chopsticks to eat. Doing exercise and getting
14 out of the house helped her with flexibility and
15 mood.

16 She had bad days. When she was around
17 with lots of people, with noises, like parties,
18 and even family gathering. When she seemed
19 stressed, the medical didn't seem work well. And
20 her mind will be so distant and blank. Also, if
21 she woke up from a long nap, it would take her
22 some time to realize where she is and who she is.

1 Talking through it with her often helped.

2 One example how we could tell her
3 cognitive condition from day to day is, when I
4 call her, "Mom!" If she answers, "Yes?" then I
5 know her mind is somewhat clear. But when she
6 answers, "Yes, ma'am?" or smile and don't answer,
7 then I know she doesn't know who I am. So, then
8 we will have conversation based on that situation.

9 My mother spoke Korean and Japanese, and
10 limited English. After a couple of years, as her
11 disease progressed, she would answer us in
12 Japanese, which we do not speak. And she would
13 ask questions in Korean to her friend who only
14 speak Japanese. She sometimes started her
15 sentence in Korean and ended in English.

16 Other bad days, she had body aches.
17 Although we didn't know where the body aches were,
18 we could tell her by moaning out loud when we
19 moved her. We discussed with this doctor, and we
20 added pain medication before bathing or moving
21 activities to alleviate her pain.

22 My mother's greatest fear were losing

1 her independence, become dependent on her
2 children, and losing the respect of her peers.
3 Unfortunately, my mother had to realize and live
4 through many of these fears. I hope the FDA can
5 use us in Parkinson's disease support groups and
6 Parkinson's foundations as a resource for
7 developing better medicine in the future. Thank
8 you.

9 MS. GIAMBONE: Thank you so much, Rosa.

10 And finally, we have Becky.

11 MS. HOUDE: Hi. My name is Becky Houde,
12 and I'm from Princeton, Massachusetts. I'm 33
13 years old, and I have been living with Parkinson's
14 disease for 10 years.

15 My initial symptoms appeared when I was
16 23. I went to numerous doctors in Massachusetts,
17 all of who dismissed my symptoms and my fears,
18 stating that I was far too young to have
19 Parkinson's, especially given that I had no family
20 history of it. A year later, I moved south to
21 attend Duke Law School. It was there that I was
22 diagnosed with Parkinson's disease at the age of

1 24, one month after beginning law school and a
2 long way from home. Thank you.

3 By the time I was 30 years old, the
4 disease had progressed to the extent that deep
5 brain stimulation, or DBS, was necessary. The
6 three most significant symptoms that I deal with
7 are difficulty moving, dyskinesia, and cognitive
8 difficulties. Difficulty moving is one of the most
9 crippling symptoms that I have.

10 When I was initially diagnosed,
11 difficulty moving meant that my left hand moved
12 slower than my right, and I walked with a slight
13 limp. Since my diagnosis nine years ago,
14 difficulty moving has increased exponentially and
15 now includes problems walking, eating, showering,
16 turning over in and getting out of bed, and at
17 times not being able to stand up without
18 assistance. I often have to get dressed while
19 lying on the floor.

20 Using the restroom is difficult, both
21 because my stomach muscles are often too cramped
22 to actually go to the bathroom, and also because I

1 have so much difficulties both standing up and
2 pulling up my pants.

3 I also suffer from dystonia, where my
4 entire upper body goes stiff, leading to a severe
5 back pain and neck pain and headaches. My mouth
6 is often forced open in a painful position, or my
7 mouth is forced closed with my tongue stuck out.

8 As for dyskinesia, I am very sensitive
9 to Parkinson's medications, and as a result, I
10 have extreme reactions to even tiny amounts of
11 medication. On some days, I just look like I've
12 had a lot of -- too much sugar. But at times, my
13 dyskinesia is so severe that it looks like I'm
14 having a seizure, and very painful.

15 Before undergoing DBS, I was expending
16 so many calories that I lost 15 pounds and I was
17 down to a weight of only 88 pounds. On a positive
18 note, having so much dyskinesia means that I can
19 always fully justify eating a lot of ice cream and
20 an extra helping of dessert.

21 When I'm dyskinetic, my left foot turns
22 in, causing me to walk on the outside of my foot.

1 The dyskinesia can cause me to slam the side of my
2 foot against the ground. As a result, not only
3 have I lost the ability to wear high heels, which
4 is something that I mourn deeply; I have also
5 fractured my foot on several occasions.

6 Cognitive difficulties have been
7 especially hard for me to deal with, as I recently
8 had to leave my job as a corporate attorney, a
9 position I held for the past five years and loved.
10 When I am off, I have difficulty understanding
11 simple questions, and it feels like I'm in a fog.
12 My concentration and ability to multi-task are
13 greatly affected. I often go from task to task
14 without ever actually completing anything.

15 As a result of these cognitive
16 difficulties, I suffer from anxiety whenever I
17 need to complete a particular task. In
18 preparation for this panel, we were also asked how
19 our lives were affected by Parkinson's. At the
20 risk of sounding overly dramatic, every aspect of
21 my life is affected by this disease. My life
22 revolves around my medication schedule. I take

1 Sinemet every one hour and seven minutes.

2 In addition to Sinemet, I take 14 other
3 types of Parkinson's or related medication
4 throughout the day, including 15 pills just at
5 nighttime.

6 My symptoms change frequently and
7 unpredictably. Not knowing how I'm going to react
8 to each dose of medication I take, as well as the
9 uncertainty of the length and severity of the
10 various off-and-on states, is what makes this
11 disease so hard to live with. Because of this, I
12 find myself confined to the house on many days. I
13 have to push myself to make plans with friends,
14 and when I do so, I often cancel at the last
15 minute because I get so anxious going out.

16 Leaving the house often triggers a panic
17 attack, where my whole body freezes and it becomes
18 difficult to breathe. My ability to cope with
19 these symptoms have definitely declined over time.
20 I used to be so hopeful that the DBS would
21 alleviate most of the symptoms. And while it has
22 had some success with decreasing the dyskinesia,

1 the severity and frequency of my off-times have
2 continued to increase.

3 As bad as the dyskinesia was, I find the
4 off times to be even more debilitating, as then
5 have to rely on others for help with basic tasks
6 such as dressing.

7 My biggest concern is not being able to
8 forecast what the progression of my disease will
9 be. It is incredibly scary not knowing how fast
10 and to what extent my disease will progress. I
11 fear that the people I love most in the world will
12 have to take care of me.

13 My family has all been there for me
14 through everything, and I do not want them to have
15 to worry about my care in the future. I'm engaged
16 to be married, and my fianchas stood by me through
17 brain surgery and through all of my ups and downs.
18 And I want to be there with him to build a family
19 and a happy life together.

20 With that said, I will continue to draw
21 my hope and strength from my family, the advocates
22 in this room, and the researchers around the globe

1 who are studying Parkinson's. And I know that one
2 day, together, we will find a cure.

3 MS. GIAMBONE: Thank you so much, Becky.

4 Can we please give our panelists a round
5 of applause?

6 (Applause.)

7 MS. GIAMBONE: I mentioned this earlier,
8 but it takes an extraordinary amount of courage
9 for coming here and sharing your stories with us.
10 So, thank you so much for doing that.

11 And what I'd like to do now is ask you,
12 for other patients and caregivers in the audience,
13 what you heard from the panel, do those
14 experiences resonate with you also? You can raise
15 your hand or nod your head. Does that sound
16 similar to your experiences? Yeah? Okay.

17 And on that note, I'd like to ask two
18 other questions. So, Todd, you brought up the
19 micrographia. And I was wondering if others in the
20 audience, is that something that you've
21 experienced? So, several hands raised for that.
22 And then, Karl and Becky touched upon just the

1 unpredictability of the Parkinson's. And was that
2 something also that you experienced, living with
3 that unpredictability? Okay. So a lot of head
4 nods. So thank you for sharing that.

5 Okay. So what we'd like to do now is a
6 polling question. So if you could get your
7 clicker out.

8 (Pause.)

9 MS. GIAMBONE: Okay. All right. So, of
10 all the symptoms that you have experienced because
11 of Parkinson's disease, which do you consider to
12 have the most significant impact on your daily
13 life?

14 And you can choose up to three: A,
15 motor symptoms such as slowed movement or tremor;
16 B, impaired balance and coordination; C,
17 constipation; D, sleep issues such as falling
18 asleep, staying asleep, or abnormal dreams; E,
19 cognitive impairment such as difficulty
20 concentrating or difficulty with complex tasks; F,
21 fatigue and loss of energy; G, difficulty
22 swallowing, or drooling; H, depression or anxiety;

1 or I, other symptoms not mentioned.

2 (Pause.)

3 MS. GIAMBONE: Okay. So, it looks like
4 the majority of you who responded identified A,
5 motor symptoms, as one of the most significant
6 symptoms that you're living with, followed by
7 impaired balance and coordination, and sleep
8 issues. And then it looks like we have, you know,
9 the other symptoms also highlighted here. In
10 addition to, several people chose other symptoms
11 not mentioned. So we'll be sure to touch upon
12 that in a little while also.

13 How about on the Web?

14 MR. THOMPSON: We had 55 percent say
15 motor symptoms; 55 percent also say fatigue and
16 loss of (inaudible) -- 36 percent say cognitive
17 impairment; 40 percent, sleep issues; and 40
18 percent, impaired balance. And all the rest are
19 20 or below.

20 MS. GIAMBONE: Okay. Thank you.

21 All right. So, now I'd like to invite
22 other patients and caregivers in the audience, and

1 certainly, panelists, please also share your
2 thoughts, too. Would somebody like to start us
3 off with how you or your loved one experiences the
4 motor symptoms and how that impacts your life?

5 (Pause.)

6 MS. GARRIDO-REVILLA: Thank you. My
7 motor symptoms and all my other symptoms are the
8 same as my brothers and sisters here with
9 Parkinson's. In some of them, I see my past; in
10 some of them, I see my future. And that's the
11 reason why I'm here.

12 I don't want to be -- I'm supposed to be
13 the caregiver of my children. My children are at
14 the point that -- they're only teenagers, and
15 they're beginning to help. I want that -- that's
16 not the right way to be a parent. I wish that
17 situation could change. I don't know how to
18 change it. That's why I'm here.

19 As for the current medications, there
20 are no medications. There are only symptoms. The
21 current things that we have available, and we're
22 running out of options, are like an aspirin to a

1 migraine. Sinemet and DBS, they all stop working.

2 We don't need to look any further.

3 And with all due respect, we're doing as
4 patients all we can right here today. And all the
5 patients that are present on the Internet, and all
6 the others that could not travel to be here
7 because of mobility reasons.

8 So we're here to ask the FDA, what else
9 can you do for us? We're here to do whatever we
10 can. We're here to participate in trials. We're
11 here to advocate. We're here to step up and raise
12 our hands. We speak about our experiences. Our
13 experiences are all the same. We're all past or
14 present and our future. But we need to do -- we
15 need more than a medication that was found in
16 1967.

17 Also, many resources have been spent on
18 so many other things. Man has been to the moon,
19 and how many of us are going to go to the moon?
20 So we want a medication, something better other
21 than 1967. I was born in 1964. And I'm still
22 waiting for something.

1 So please help us.

2 MS. GIAMBONE: Thank you so much. And
3 your name?

4 MS. GARRIDO-REVILLA: My name is Claudia
5 Garrido-Revilla.

6 MS. GIAMBONE: Thank you so much.

7 MS. GARRIDO-REVILLA: Thank you.

8 MS. GIAMBONE: Would anybody else like
9 to share? Yes, we have a comment back there.

10 MS. McCLEARY: Hi. My name is Kim
11 McCleary, and I'm here in two roles, one on behalf
12 of my mother, Karen Burk, who is 72 and has lived
13 with Parkinson's for 25 years. And what struck
14 me, I took some notes from her on Sunday about how
15 she would answer some of these questions.

16 And the motor symptoms is such a big
17 basket of issues in Parkinson's. And you've got
18 rigidity and dyskinesia, freezing, tremor, all of
19 these things that are kind of wrapped up in the
20 idea of motor symptoms, but I think would be more
21 varied among the people here in the room and
22 probably on the Web to describe, you know, what

1 their most problematic things are.

2 And certainly, over the course of her
3 25-year experience, it has shifted, as the woman
4 who just spoke was saying, that some are in the
5 past and some are in the future. But maybe we
6 could delve a little more into that particular
7 issue.

8 MS. GIAMBONE: Thank you, Kim.

9 We have one more comment here.

10 MR. KWOK: Yes. My name is Kevin Kwok.

11 One of my concerns is the actual diagnosis and
12 definition of our disease here. If we look
13 towards using motor symptoms, which is the primary
14 marker of disease, generally by the time we're
15 diagnosed it's far too late, because many of the
16 other symptoms have progressed so far.

17 And so what my concern is, or urging to
18 researchers and to the patient community, is to
19 talk about this myriad of symptoms collectively
20 and use measurement tools that actually take all
21 of them into consideration, not just motor
22 symptoms as your first primary diagnosis. Because

1 I think by then, we're actually missing the chance
2 to actually help many, many people. So, thank you
3 very much.

4 MS. GIAMBONE: Thank you, Kevin.

5 So that's a good point. Let's expand
6 upon this. I'd like to invite those of you who
7 want to respond to give us your experiences with
8 any of these issues, really. Is there a symptom
9 here that is most bothersome to you? And why is
10 it most bothersome to you?

11 (Pause.)

12 MS. OLSON: Hi. My name is Nancy Olson.
13 I'm here as a patient. I don't look like a
14 patient yet, but I am. And I'd like to challenge
15 the FDA to think about bringing together
16 traditional medicine with Eastern medicine,
17 because when I started with my symptoms that were
18 very, very slight, I'm just one of those people
19 that's very in tune with my body. And I knew
20 something was off.

21 I went to doctor after doctor after
22 doctor, and for years, and nobody could tell me

1 what was wrong. I finally went to the Myrna Brind
2 Center for Integrative Medicine at Thomas
3 Jefferson University Hospital in Philadelphia,
4 where they discovered I had an extreme overgrowth
5 of bacteria that's present in your intestinal
6 tract, but that doesn't belong there in large
7 quantities. And I had so much of it that it had
8 killed the good bacteria.

9 So recently, there's been some news on
10 the Parkinson's front to suggest that perhaps
11 Parkinson's starts in the gut. It was before my
12 diagnosis with Parkinson's that I was treating
13 with the Myrna Brind Center, when they discovered
14 this overgrowth of bacteria. And once they got
15 that under control, I felt a lot better.

16 It didn't prevent me from having
17 Parkinson's, which I was later diagnosed with,
18 because I knew that something was still wrong with
19 the motor symptoms and the olfactory, you know,
20 decline, and so forth. So I pretty much diagnosed
21 myself by the time I got the clinical diagnosis.

22 But I think there's a lot of merit to

1 some of the things that are being done on the
2 Eastern side of medicine, together with the
3 Western side. So I would challenge the FDA and
4 any -- I'm a retiree of the pharmaceutical
5 industry, worked in the industry for 45 years.

6 I would challenge the industry and the
7 government to bring those two thoughts and schools
8 of medicine together, because in my experience,
9 that was the magic bullet for me to get to my
10 diagnosis early. And by getting to my diagnosis
11 early, I've been able to keep my symptoms under
12 control with no medication, simply through
13 exercise and diet.

14 You may have noticed me getting up
15 earlier and going up against the wall. The
16 stiffness was overwhelming me, and I just don't
17 let it do that. When I need to move, I move,
18 whether I'm in church or at the FDA or in bed. My
19 husband says, you know -- I won't tell you what he
20 says.

21 (Laughter.)

22 MS. OLSON: But I get up and down at

1 night more than the average person. I walk around
2 the house, and I look out the window. Then my
3 legs are not hurting anymore, and then I go back
4 to sleep.

5 So, I think there's value in those two
6 schools of medicine putting their heads together,
7 which I think is kind of a trend anyway in the
8 medical field today in many arenas.

9 MS. GIAMBONE: Thank you.

10 MS. OLSON: So it's been very helpful to
11 me, and I would just raise that as a flag and say,
12 you know, don't forget about that piece.

13 MS. GIAMBONE: Um-hm. Thank you so much
14 for that thought. Thank you.

15 Yes. Let's go here, this gentleman.

16 MR. POSTOW: I'm Elliot Postow. And
17 I've had Parkinson's for seven years. And it
18 seems to me that from my experience, one of the
19 most underrated symptoms, one that bothers me a
20 lot, is the constipation-diarrhea symptom. And
21 that is probably not spoken about as much as
22 others because of societal reasons and personal

1 control over one's topics.

2 But not only is it important in and of
3 itself in its activity limitations, it is
4 important in that it affects the rate of
5 absorption of the L-dopa drugs that you're taking.
6 And it seems to me that we've made very little, if
7 any, progress in that area over that past 20
8 years.

9 MS. GIAMBONE: Thank you very much.

10 I'd like to ask -- I know that we heard
11 some of you mention that, you know, stress or
12 maybe not getting enough sleep can trigger some of
13 your symptoms. Would somebody like to comment on
14 additional triggers or how your symptoms change
15 day to day? Yes.

16 MS. LAZZARINI: Do I have the
17 microphone? My name is Alice Lazzarini. I've
18 been a patient with Parkinson's for about 11 years
19 now. I'm here in part representing the American
20 Parkinson's Disease Association, but also on my
21 own personal experience.

22 In retrospect, I think even before 11

1 years, my first presenting symptom was fatigue.
2 And I would just call to the FDA's attention
3 something that came up in this morning discussion
4 with the Huntington's as well, which is writing
5 off-label or repurposing a drug. I recently had
6 trouble getting refill for a drug I'd been taking
7 for nine years for -- it's indicated for
8 narcolepsy, not for Parkinson's disease. But it's
9 already been through the safety rigmarole of being
10 FDA approved.

11 And I was amazed, actually, that because
12 it's not indicated for Parkinson's disease, my
13 neurologist had to jump through hoops after hoop
14 after hoop to prove, in fact, that there's
15 documented evidence that fatigue is a difficulty
16 with Parkinson's disease. And it took me two
17 months to get this medication.

18 So consider at least some things that
19 are being repurposed or off-label would be
20 important to bring to the fore.

21 MS. GIAMBONE: Thank you so much.

22 Looks like we have a comment back here.

1 (Pause.)

2 MR. LINDERMAN: I am Charles Linderman
3 from Alexandria. And I want to address the other
4 symptoms up there that you don't -- where you
5 don't have any nomenclature for them. How would
6 you like to walk around with this contraption on?
7 Because the FDA has done nothing, and there is
8 nothing in the medical community, to help those of
9 us who have head-drop associated with Parkinson's.

10 And I can assure you, without this, my
11 chin would be on my chest. And that is not
12 something that one wants to have to live with for
13 the rest of their life. And I find that this is
14 an area in which the only alternative that's been
15 suggested to me has been surgery and an eight-
16 hours procedure at Johns Hopkins University
17 Hospital that would take a year to recover from
18 because they would fuse both the front and the
19 back of the neck and put titanium plates, rods,
20 and screws in my neck. And we've chosen not to do
21 that.

22 But I want to focus the FDA not just on

1 that portion of this, but to focus as well on what
2 Dan Lewis started out in his first comments, about
3 exercise. Because over 10 years ago, I made a
4 decision when I was first diagnosed that I was
5 going to fight this thing with a personal trainer,
6 and I have done so pretty effectively and still
7 compete in the all-adaptive rowing regatta that
8 takes place every year in Philadelphia.

9 MS. GIAMBONE: Thank you so much, sir.
10 And your name? Charlie. Okay. Thank you,
11 Charlie.

12 Could I check in with the Web and see if
13 there's any comments coming in? Okay. Okay.
14 Great.

15 So, let's take some more comments then.
16 Any of you like to comment? So we've heard some
17 mention on the fatigue, constipation, motor
18 symptoms. Other symptoms that you'd like to share
19 with us? Yes. Dan?

20 MR. LEWIS: I think we neglected to
21 address the cognitive issues, which are very
22 important. I suffer from very broad memory loss.

1 And for example, if you ask me, I wouldn't tell
2 you what I had for breakfast. And I forget
3 things. And it is very disruptive to a normal
4 life. We never -- I've lost my short-term memory.
5 And I can't recall names or places or proper
6 nouns.

7 The other thing I'd like to say is
8 stress is a killer. It really worsens all my
9 symptoms. And a lot of people I know through my
10 work with Parkinson's Foundation have the same
11 problem. They get involved in responsibilities,
12 and then their symptoms get worse. And so, the
13 responsibility of raising enough money to keep the
14 foundation open drove me to quit as chairman of
15 the board, because I guess it was just haunting me
16 and causing me to fall down, and other symptoms
17 were accentuated.

18 MS. GIAMBONE: Thank you very much, Dan.
19 Karl?

20 MR. ROBB: I just wanted to reiterate
21 that I think 60 percent of Parkinson's is stress.
22 But I also think -- also, I'm very fortunate that

1 I don't suffer from depression. But depression
2 seems very common in Parkinson's. And that's
3 something that needs to be addressed.

4 MS. GIAMBONE: Thank you very much.

5 Let's hear from --

6 MS. OKUN: Hi. I'm Sally from
7 PatientsLikeMe, Sally Okun. I wanted to just
8 report a symptom that we haven't heard about that
9 our patients do report on. About 32 percent are
10 reporting severe -- moderate to severe sexual
11 dysfunction. And again, that might be a sensitive
12 topic that in real encounters with physicians and
13 things might not come up. But in our community,
14 oftentimes those types of comments are actually
15 welcome and encouraged to be talked about.

16 So I think the number is high enough for
17 us to be thinking about that as an issue. Also,
18 the relationship -- the impact on relationships is
19 also related to that as well. Thank you.

20 MS. GIAMBONE: Thank you very much,
21 Sally.

22 What I'd like to do now is go over to

1 the phone. We do have two participants joining us
2 on the phone today. And they were identified as
3 panelists, but they couldn't make it here today.
4 So we want to make sure we give them just a few
5 minutes each to present their thoughts.

6 So we should have Chuck and Judy on the
7 phone. And, Operator, it looks like we're going to
8 start with Chuck. So, Chuck, are you there?

9 (Pause.)

10 CHUCK: Can you hear me?

11 MS. GIAMBONE: Yes. Chuck, we can hear
12 you.

13 MR. ESPOSITO: Okay. Good afternoon.
14 Greetings from the North Georgia mountains. My
15 name is Chuck Esposito, and I first reported my
16 symptoms to my PCP in the summer of 2004. And
17 like many Parkinsonians, I was originally
18 misdiagnosed. It was not until two years later
19 that I was properly diagnosed with idiopathic PD.

20 We Parkinsonians are different as
21 snowflakes. Although there are many similarities,
22 no two of us are exactly alike. In my case, the

1 three most bothersome symptoms are fatigue; EDS,
2 which is excess daytime somnolence; and LID, which
3 is levadopa-induced dyskinesia. Some of you have
4 recognized, the medications used to treat the PD
5 are more responsible for these disturbances than
6 the disease itself.

7 Despite these different symptoms, they
8 can affect different activities. And they can
9 vary not only from day to day, but from hour to
10 hour. Panel participants have commented on this
11 at the beginning.

12 For example, on a bad day when I'm
13 suffering from fatigue, EDS, LID, tremors,
14 bradykinesia, rigidity, dyspnea, which is
15 difficulty breathing, postural instability, et
16 cetera, I'm pretty miserable and I'm not
17 interested in moving very far from my recliner,
18 especially if I'm experiencing festination and
19 freezing.

20 The word "festination" comes from a
21 Latin word meaning "to hurry," which describes the
22 quickening and shortening of a normal stride,

1 which can occur as a hopping or shuffling gait.

2 Freezing was mentioned earlier by
3 participant Todd. This is something different
4 altogether. And this is experienced by about a
5 third of us. It's the sensation of suddenly
6 becoming stuck to the floor and temporarily unable
7 to walk. This is a potentially serious problem
8 because it increases the risk of falling forward,
9 which increases the risk of ending up in a
10 hospital bed with a broken hip, which increases
11 the risk of getting pneumonia, which increases the
12 risk of dying, as was mentioned by Dan.

13 Now, under such circumstances, the
14 proximal cause of death is generally regarded as
15 pneumonia. But the distal cause is, in fact, PD.

16 On a good day, when most of these
17 symptoms are absent or minimized, I can engage in
18 a fair number of activities and performances. At
19 the same time, there are some activities, for
20 example, motorcycling, which will forever remain
21 on the I-do-not-do-that-anymore list.

22 PD is a progressive disease. And, Lord

1 knows, Becky explained that to us. And that means
2 that the original symptoms will worsen as time
3 goes by. And also, symptoms which were not
4 originally apparent begin to emerge. The good
5 news, in my view -- and I know not everyone shares
6 this view -- is that the progression is generally
7 slow. The slow progression allows the time for
8 both the Parkinsonian and the care partner to
9 acclimate to the inevitable relentless
10 deterioration.

11 My closest family members are a day's
12 drive from here. And as my PD progresses, my
13 endurance declines, fatigue increases and reduces
14 how far I can drive in a day. So I just don't get
15 together with family or visit with friends as much
16 as I used to or as much as I'd like to.

17 In closing, I'd like to say I appreciate
18 the invitation to participate in FDA's Patient-
19 Focused Drug Development meeting. And I thank you
20 for your attention. Bye-bye.

21 MS. GIAMBONE: Thank you so much, Chuck.
22 I'm not sure if you could see, but several people

1 were nodding their heads as you were speaking. So
2 it sounds like what you said resonated with
3 several people in the room.

4 Okay. Next, we should have Judy. Judy,
5 are you there?

6 JUDY: Can you hear me?

7 MS. GIAMBONE: Yes. We can hear you.

8 MS. WHEATON: Okay. Good afternoon. My
9 name is Judy Wheaton (phonetic). I'm 65. And I
10 was diagnosed two years ago with Parkinson's. I
11 currently live in Arkansas. I've retired in
12 Arkansas as a researcher at a college in Texas.
13 I'd like to address three symptoms that
14 significantly impact me on a daily basis.

15 The first one is constipation. And I'm
16 not talking occasional constipation, but I'm
17 talking constant, chronic, everyday constipation.
18 It's more than just (inaudible). It's homebound
19 for several days each week just to address the
20 issue with medication and the aftereffects. I'm
21 currently taking Amitiza twice a day in order to
22 digest the food and pass the way.

1 I also have to watch my diet. I believe
2 it was Karl, one of the panelists, that mentioned
3 that he watches his diet. I think he said he was
4 a vegetarian. I have to really watch meat,
5 especially, maybe because it's harder to digest.
6 But it will take me several days to digest and
7 cause constipation, even with the meds.

8 The second symptom is not sleeping. And
9 I've heard several people talk about this.
10 Currently, my doctors prescribe a medication,
11 Ambien, but warned me that insurance companies
12 will not refill this medication on a monthly basis
13 because it's habit forming. My insurance allows
14 for 90 days of this medication per year. So, that
15 kind of leaves me to cut the tablets in half and
16 not take one every night.

17 And you might be thinking, why don't I
18 take a different medication, one that can be
19 refilled monthly? But unfortunately, I also take
20 Ridmal for a heart disorder, and many of the sleep
21 aids interact with this medication.

22 Not sleeping at night leads me to the

1 third symptom. And I haven't heard it mentioned
2 yet. But it's inflammation. Currently, I have
3 tremors in the right side of my body only. And
4 they're controlled fairly well during the day with
5 the Parkinson's med. I take the carbidopa-
6 levadopa. I take three tablets a day of the 25-
7 100.

8 But when I don't sleep, my right arm
9 tremors all night. Well, after two or three
10 nights of this, it feels like my arm and my
11 shoulder have been severely overused. And I begin
12 to get pockets of inflammation in my arm and up to
13 my shoulder. The last year, I even developed an
14 infection in the bursa of my elbow from several
15 nights not sleeping and the constant movement in
16 the arm and the inflammation unchecked. Sleeping
17 at night really seems to aid in this entire
18 inflammation problem that I experience.

19 Thank you for letting me share just a
20 little bit of my Parkinson's story. And I
21 appreciate listening to all of yours.

22 MS. GIAMBONE: Thank you so much, Judy.

1 And again, I saw heads nodding when she was
2 speaking, also.

3 So, on that note, she brought up
4 inflammation, that not sleeping increases the
5 inflammation that she feels. Do others feel the
6 same way? Does that resonate with others?

7 (Pause.)

8 MS. GIAMBONE: Okay. The tremor she
9 mentioned, that not sleeping also increases the
10 tremor. Okay.

11 FDA panel, do any of you have any
12 questions that you'd like to ask?

13 DR. DUNN: I don't have a specific
14 question. I want to not only thank folks, but
15 reassure folks that a lot of what you're saying,
16 it's familiar to us. We hear you, and it's good
17 to hear the reiteration that things that we're
18 aware of, particularly some of the uncommon
19 things, or things that you may be concerned we are
20 not attentive to, I want to reassure you that it's
21 not the first time we're hearing much of this.

22 And so, that's good news, I think,

1 because some of these things are very difficult to
2 detect. They're concerning. They're hard to talk
3 about. There's a whole wide variety of them. But
4 I know that I speak for the team because we talk
5 about these things. These are very important
6 Parkinsonian symptoms. And we do pay a lot of
7 attention to these in our work with sponsors.

8 So, I thought I would just offer that up
9 as a bit of what I consider to be good news, that
10 we're all together collaboratively on the right
11 track and trying to not just pay attention to the
12 stand-out symptoms, but to the whole plethora of
13 symptoms that could occur in this disease.

14 MS. GIAMBONE: Thank you, Billy.

15 Okay. So let's get back to our
16 discussion here for a few more minutes. Anything
17 else that you'd like to share on how you're
18 experiencing these symptoms? Yes.

19 MR. CANNON: I'm Paul Cannon. I'm a
20 patient. One of the things you asked in the
21 questions, but didn't address in here, is social
22 withdrawal. I think like many of these symptoms,

1 it's actually insidious and probably has more of
2 an effect than we realize, especially in the
3 caregiver, in that context. So it seems like
4 social withdrawal and sleep can actually be
5 insidious. They don't seem so bad themselves,
6 necessarily, but I think it makes a lot of other
7 things worse.

8 MS. GIAMBONE: Um-hm. Social
9 withdrawal. Okay. Thank you.

10 Yes. Let's see. Okay. Looks like the
11 microphone right there.

12 MS. ROBB: I'm Angela Robb. I'm Karl's
13 wife. But I'm not only speaking as his caregiver,
14 as some of the things I'm about to say are
15 actually experience I had as a support group
16 leader and as a speaker on care-partner issues.

17 I think there's a lot that isn't said
18 about the nonmotor symptoms, particularly the
19 problems with executive dysfunction, or -- I can't
20 remember what the word was. But there's a lot of
21 things that I think affect caregivers and in the
22 workplace, that people with Parkinson's, you know,

1 being able to go through step by step.

2 If it's a 10-step task, and they get
3 lost in about 2 or 3. And then they start over.
4 And then they get lost again. And then they have
5 to go back again. And then they never complete the
6 task. Or they start a project and can never
7 finish a project.

8 Also, with that, that goes with what
9 Becky said about the anxiety. So, you know, you
10 get to step four and you can't remember. And you
11 go back, and you keep going and going. And then
12 on top of that, the stress associated from in the
13 workplace or even in a family situation with that.
14 A lot of people who, if you aren't immediate
15 family and living with a person with Parkinson's,
16 you won't understand that the cognitive
17 dysfunction or executive dysfunction has a huge
18 impact.

19 People think you're doing it on purpose.
20 Even outside of the home, some people will think
21 that you're purposely -- because they don't
22 understand it's actually a symptom of the disease

1 that's preventing you to think that way.

2 So I think there's a lot to be said for
3 that par. And there's not a lot of medications
4 and/or therapies that treat that component of the
5 disease. Thank you.

6 MS. GIAMBONE: Thank you very much.

7 Let's take a couple more comments before
8 we go back to the Web and the phone. So, go
9 ahead. We'll go here. Okay.

10 MS. GARRIDO-REVILLA: One very important
11 symptom that people or even doctors know very few
12 -- well, in my time -- dystonia. Some people call
13 it cramps. Some people call it like twitching or
14 focal dystonia or cervical dystonia or the cramps
15 in your feet. They're not cramps. They're
16 dystonia.

17 Dystonia -- it's a disease by itself.
18 And it also comes with some cases in Parkinson's.
19 That's my case. It was my first symptom. And
20 when I showed up, the doctors didn't know what was
21 going on. I had to take a photo of my foot and
22 show it to the doctor to see what was going on.

1 So one of the most important symptoms is
2 dystonia. And September is Dystonia Awareness
3 Month. So.

4 MS. GIAMBONE: Oh, okay. Good to know.
5 Thank you very much. Thank you for sharing that.

6 FEMALE PARTICIPANT: To add another
7 symptom to the others, on number I, one of the
8 symptoms that bothers me most is blood pressure
9 drops, so hypertension. It doesn't necessarily
10 happen when I first stand up, but if I've been
11 standing still for awhile, my blood pressure will
12 drop and I feel like the center of my head is very
13 cold and that I'm going to die.

14 It doesn't make me dizzy. It's not
15 predictable, as other people were saying. It's
16 one of the hardest things for me to manage, not
17 knowing when it's going to happen. And so, just
18 to add that to the list of other things that can
19 happen with Parkinson's.

20 MS. GIAMBONE: Okay. Thank you. Blood
21 pressure drops. Do others also experience that,
22 the blood pressure drops? Okay. I see several

1 hands raised there. Okay. Great. Thank you.

2 So, let's -- so, we have two callers on
3 the phone. Okay. Operator, could we have caller
4 number one, please?

5 THE OPERATOR: Yes. Sophie, your line
6 is open.

7 MS. GIAMBONE: Yes. Hello?

8 THE OPERATOR: Sophie Carter, your line
9 is open.

10 (Pause.)

11 MS. GIAMBONE: Okay. We can go to the
12 next caller then. Caller two?

13 THE OPERATOR: Vicky, your line is open.

14 MS. PERRY: Thank you, sir. My name is
15 Vicky Perry. I've had Parkinson's for over 30
16 years. And when I was first diagnosed, they had a
17 hard time diagnosing it. And online you're
18 supposed to go for research. And I kind of
19 question that because I felt that the quality of
20 the patient's life should also be taken into
21 consideration.

22 And so, now that is. And I'm so happy

1 to see that. I think there's a lot of good things
2 that happened since I was diagnosed as far as
3 doctors are now looking more at quality of life
4 and the whole person. And because it improved
5 that.

6 I have genetic Parkinson's. I have a
7 sister with it. I was diagnosed when I was six
8 months short of graduating from college. It was
9 frightening. I had no idea what this disease was.
10 I didn't know anything about it. But I was taken
11 care of by good doctors, and even truly understood
12 a little more as time went by.

13 And like I said, the people's studies
14 looked more to the quality of life patients
15 instead of saying, "Oh, it's just this. I have
16 this. I have money. In time, you'll have a
17 cure."

18 And, of course, 30 years later, that
19 never happened. But they have really been
20 focusing on the patients. And I think that's a
21 very good thing.

22 And there's different kind of

1 Parkinson's. There's another form that I have.
2 It's more lateral than it is like idiopathic
3 Parkinson's. And what that means is my symptoms
4 don't really appear clearly as most people. But
5 mine is more working on the inside, both through
6 my inner body up. So I'm now at the point that
7 I'm having difficulty remembering words. I have
8 lots of cognitive problems.

9 There's a lot of autonomic systems that
10 become involved. I have had the sweats for no
11 reason. I have difficulty swallowing and
12 difficulty remembering words. But I think my
13 neurologist is very helpful, and they're trying to
14 stay on everything.

15 There's a point where I was actually put
16 in the hospital a couple of times going into a
17 coma because I had too much stress in my system
18 and kind of everything fell through. And that's
19 when I got my DBS, and I had to fight through
20 that. And that's how I found out I had the genes
21 for Parkinson's disease.

22 And now I'm -- I think we have a lot to

1 be hopeful for. It's not all bad. As she said,
2 you have to look at the whole patient, I believe,
3 now, instead of just at the disease. So, we need
4 a cure.

5 MS. GIAMBONE: Thank you. Thank you so
6 much for sharing those thoughts.

7 So it looks like we touched upon most of
8 these symptoms that are highlighted here. And
9 other symptoms that you mentioned included
10 problems with sexual intimacy, we heard. We heard
11 low blood pressure. We heard head drop. We heard
12 sweats, on the phone, dystonia. So thank you for
13 bringing up all of these really great points that
14 are so helpful for us to hear.

15 So on that note, I'd like to go to
16 break. And we will take a 10-minute break. So
17 we'll see you all back here in 10 minutes.

18 (Whereupon, at 3:05 p.m., a recess was
19 taken, to reconvene at 3:25 p.m.)

20 DR. EGGERS: This is Sara Eggers again,
21 from the Office of Strategic Programs. I'm one of
22 Soujanya's colleagues. And I will be helping

1 facilitate the discussion in Topic 2.

2 Topic 2 is focused on the approaches to
3 treatment of Parkinson's disease. And as was
4 reiterated this morning, you know, it goes without
5 saying the complexity and the management of this
6 condition. And many things were started to be
7 raised this morning in the comments that we heard
8 about symptoms that aren't quite being addressed
9 as much as you would like in the current
10 treatments, about your experiences with treatment
11 so far.

12 So we're going to get into that
13 discussion more. We are trying to focus on -- the
14 input that we are getting today really helps FDA
15 in our role understand how we can advise drug
16 sponsors in terms of, where are the unmet needs?
17 What should we be focused on? What is it
18 important to patients about their disease and the
19 disease management that perhaps we could better
20 reflect in pharmaceutical treatments?

21 So that's what I'm going to ask some
22 questions to try to tease that out, as well as

1 what you look for in an ideal treatment.

2 To start our discussion, we have
3 panelists again, five, who will set the stage with
4 their comments and sharing their experiences. And
5 then we will move again into the open discussion.

6 So with that, we will start with Steve.

7 MR. DeWITTE: Thank you. Tough act to
8 follow, table 1. But we'll do our best over here.
9 Thank you to the FDA committee for allowing me to
10 be a panelist. Tonight I present my views
11 alongside this distinguished group of fellow
12 people with Parkinson's. It will be my wish to
13 capably represent our community on the current
14 approaches to treating Parkinson's disease.

15 I suspect the phrase "Parkinson's
16 disease affects everyone differently" will be used
17 repeatedly by my distinguished colleagues.
18 Therefore, I just wish to present treatments that
19 I use to manage my multitude of symptoms.

20 I think it's important to point out that
21 the degree of symptom relief varies moment to
22 moment. Variables such as temperature, diet,

1 amount of sleep, and anxiety, like we've talked
2 about, have an effect on the degree of symptoms
3 regardless of the treatment plan. Therefore,
4 there can be a high degree of self- dosing which
5 we as PWD's will administer to get the maximum
6 symptom relief during upcoming dose times.

7 As I share this treatment plan that I
8 use, I think it's important to include some
9 nonmedicative steps I've taken that have led me to
10 choose the complementary medication plan that I'm
11 under.

12 It begins by ensuring I'm well versed on
13 what's being recommended by the medical community
14 currently. One way I do this is through making
15 myself accessible to patient-led support groups
16 such as the Connected Advocates for Parkinson's
17 and the Make a Different Parkinson's Alliance
18 based in my home State of Connecticut. Go,
19 Huskies!

20 (Laughter.)

21 MR. DeWITTE: Patients' information
22 exchanges like Dr. Goldstein spoke of have been

1 very significant in my determining what treatment
2 plan I make for myself, as well as discussions
3 that I've had with my movement disorder
4 specialist. I attend forums, symposiums. I
5 listen to Webinars. And I receive the latest news
6 from disease-specific agencies such as the
7 Parkinson's Action Network, Michael J. Fox
8 Foundation, Parkinson's Disease Foundation, and
9 the Cure Parkinson's Trust of UK.

10 I built the treatment team that provides
11 me counsel and prescriptions for various symptoms.
12 They include rheumatoid specialists, an
13 occupational therapist, psychiatrist, physical
14 trainers and nutritionist, and others as needed.

15 Lastly, I gain much from my
16 participation in clinical trials. I've enrolled
17 in well over a dozen. I seek studies that have
18 investigators that have a history of being
19 transparent in their observations and their study
20 results. Some of these studies allow me to
21 maintain personal measures of disease progression
22 through brain imaging or cognition testing.

1 All this, and I haven't even started to
2 mention the medications that help me in my daily
3 life. Having just passed my first decade with the
4 disease, I've noticed that there have been some
5 disheartening advances. I've found it necessary
6 to increase my visitations to my movement disorder
7 specialist.

8 And likewise, my medication regimen has
9 changed. I generally take six -- my pills six
10 times a day, 20 pills a day altogether. The
11 medications that I'm on are the gold standard
12 carbidopa-levodopa; ropinirole, also known as
13 Requip XL. I take a laxative and a melatonin
14 supplement to help me sleep.

15 Under the category of alternative
16 treatments is exercise. I'm a believer in the
17 value of the intense-interval exercise training
18 programs, and have worked with a lot of the
19 research centers, especially the University of
20 Alabama in Birmingham, on passing out their gospel
21 of intense exercise.

22 I recently registered with a local PD

1 program led by Michelle Heisler, called BP. It
2 also is an intense exercise training program at
3 least once a week, and provides me relief from
4 stiffness and a greater response to my
5 medications, which in turn allows more on-time and
6 less tremors.

7 Last but not least is Tai Chi. I
8 approached this martial art form with much
9 skepticism. I remember it on a trip I took to
10 Hong Kong, watching workers outside their office
11 going through some beautiful moves that in no way
12 resembled any Bruce Lee's movies.

13 (Laughter.)

14 MR. DeWITTE: It will often help
15 alleviate stiffness and provide relief from poor
16 gait. In the State of Connecticut, it's even
17 awarded a grant to a Tai Chi instructor to help
18 prevent falls, specifically for seniors, after
19 seeing the cost savings that can be realized when
20 such a discipline is adopted.

21 Now, believing the value of exercising,
22 having it a regular part of my treatment plan has

1 been difficult, as is evidenced by my not-so-
2 chiseled frame. But I still continue to get out
3 there daily and get the exercise in, because I
4 know it's not only good for me, but it has an
5 impact on the disease.

6 Now, how have things changed? Well, as
7 I move into my second decade of PD, I found it
8 necessary to increase my medications. Some of the
9 medications have warnings related to dyskinesia
10 and compulsive addictive behaviors at the dosage
11 levels. And I mention that because we've talked a
12 lot about our symptoms, some of them driven by the
13 medications themselves.

14 Every three hours, I need to take my
15 meds. Before I leave home, I go through my
16 checklist -- watch, wallet, phone, keys, pills.
17 Administration of the medication is tedious and
18 requires a lot of focus. One must ensure that
19 daily needs are properly in hand, but not only
20 that, making sure that you have additional, in
21 case there's unforeseen conditions like weather,
22 as well as airline delays, roadwork -- you may

1 take another pill.

2 With the exception of exercise, none of
3 the treatments I have mentioned provide relief
4 from my irregular sleep patterns. These patterns
5 are in the forms of screaming in the night and
6 awakening at all hours. This obviously affects me
7 and my family's needed REM sleep, and leads to
8 fatigue much of the following day.

9 I've found the most effective medication
10 for this condition for me has been Provigil.
11 However, Provigil is not an approved medication
12 from my insurance provider, and it's extremely
13 cost prohibitive.

14 In total, my treatment plan is not as
15 effective as I would like. There's about two
16 hours in any one day in which my normal
17 functioning is halted. My family members and my
18 friends, especially my Basset hound, Benny,
19 becomes very frustrated by my lethargic state as
20 we wait for my level of energy to return to help
21 me resume my activities.

22 Relationships can be affected. Maybe

1 some of you will hear some of these remarks at
2 your home, things like, "Dad seems lazy today.
3 He's falling asleep in the couch." "All I asked
4 you to do is pick up some milk and bread. You
5 remembered to pick up your pills, but you couldn't
6 remember to pick up family groceries?" "He's
7 looking a little slow today. Better not give him
8 that assignment if you want it done before the end
9 of the day."

10 These are the kind of conversations that
11 are held around us all the time.

12 So I have thought about the factors that
13 prevent some of the disciplines that could prevent
14 me from having a better quality of life. In the
15 limited time we have left, I'd like just to
16 address the two factors I believe are important.
17 And that's access to PD-certified therapists to
18 assist with valuable exercise programs and the
19 cost to pay for it.

20 Most health coverages do not cover
21 exercise programs unless justified through
22 physical therapy. Most physical therapists and

1 fitness trainers fail to have specific experience
2 with Parkinson's disease, despite growing evidence
3 of the positive impact exercise has on managing
4 our disease.

5 But I am the eternal optimist.

6 Recently, we've had some new treatments come
7 trickling out of the very full research funnel. I
8 look at this as a sign that we are not far off for
9 an ultimate disease- modifying treatment, "the
10 magic pill."

11 Now, in lieu of this, I am working with
12 some greatly admired and dedicated advocates and
13 researchers on an exercise prescription. The
14 ideal treatment for me might begin with the point
15 of diagnosis. Shortly after delivering those
16 fateful words, "You have Parkinson's disease," the
17 MDS will present you a prescription that directs
18 you to a certified therapist and trainer.

19 And a treatment plan that's covered by
20 insurance might look like this: Three days of
21 disciplined, intense exercise; one day of exercise
22 alternatives, such as cycling, hiking, or dance;

1 two days of Tai Chi; and a little medication to
2 round it off.

3 DR. EGGERS: Do you have any final
4 thoughts, Steve, to wrap up what you would look
5 for in ideal pharmaceutical treatments, perhaps,
6 that they would better address?

7 MR. DeWITTE: I didn't address the
8 pharmaceutical, because I thought that was a very
9 deep subject. I thought with the medications that
10 are out there right now, exercise is still the
11 best option.

12 DR. EGGERS: Okay.

13 MR. DeWITTE: And I'd like to thank the
14 FDA for taking the time to listen to us, as well
15 as the industry and all the partners that are
16 here. Because it makes a difference. We're going
17 to do this together.

18 MALE PARTICIPANT: Exactly.

19 DR. EGGERS: Thank you, Steve. I was
20 told not to call him Steven.

21 (Laughter.)

22 DR. EGGERS: Next, we will move on to

1 Gary.

2 MR. RAFALOFF: Hello. I'm Gary
3 Rafaloff, from New Jersey. I'd like to thank the
4 FDA for inviting me to speak today. My journey
5 with Parkinson's began when I was diagnosed in
6 2012, almost four years ago. Yet looking back, my
7 symptoms actually began about four years prior to
8 that, in 2008.

9 That year, I began to have several
10 medical problems, which I now know are classic
11 Parkinson's pre- motor symptoms. I lost my sense
12 of smell. I developed shoulder issues. I began
13 to have REM sleep disorder. These were all
14 noticeable changes for me, but not debilitating.

15 However, I also developed at that time
16 dystonia in my foot, which caused extreme
17 cramping. This was so debilitating that it became
18 difficult for me to walk more than several blocks
19 before I had to stop to let the cramps ease up.

20 I spent four years going to multiple
21 doctors with various specialties, getting X-rays,
22 MRI's, CAT scans, and without either being cured

1 or properly diagnosed. Unfortunately, although we
2 know that Parkinson's disease begins several years
3 prior to the onset of more classic, hallmark
4 symptoms, we don't yet have any sort of early
5 biomarkers to diagnose the disease and
6 differentiate it from other neurological disorders
7 with similar early symptoms.

8 And we can't properly treat those who
9 aren't first accurately diagnosed. In my case, a
10 simple one- half dose of levadopa was all that was
11 needed to alleviate the symptoms that I suffered
12 with for four years and allowed me to walk again
13 without issue.

14 Like many PD patients, I use a variety
15 of treatments to control my symptoms and hopefully
16 slow the disease progression. I use several
17 drugs, including Sinemet, Azilect, and amantadine
18 for symptomatic relief. They clearly are helpful
19 for my foot dystonia, only mildly beneficial for
20 my tremor, and they are of no help at all for my
21 neck and back stiffness and pain.

22 I also take a variety of over-the-

1 counter supplements and vitamins, like many, with
2 the hope that it will either be antioxidative or
3 anti-inflammatory, and the result have some
4 interventional benefits and maybe disease
5 modifying.

6 However, there is such a lack of
7 research in this area, I have absolutely no
8 evidence either through research or my own
9 experience to know whether these supplements
10 actually help. There is a great need for more
11 formal clinical research in this area to help us
12 guide in nonprescribed supplements that may be
13 beneficial.

14 In addition to the drugs and
15 supplements, I try to be very active and exercise
16 as much as possible. I also perform Tai Chi daily
17 and Qigong regularly. I walk several miles every
18 day, and I try to get to the gym several times a
19 week. Outside of taking prescribed medication at
20 the proper time, daily exercise and activity, as
21 mentioned by others, is by far the most important
22 thing a Parkinson's patient can do to help control

1 symptoms and possibly slow progression.

2 As I mentioned in my previous comments,
3 the prescribed drugs that I take only work
4 moderately for me in controlling my major
5 symptoms. In addition, the main treatment for
6 Parkinson's, the so-called "gold standard,"
7 carbidopa-levadopa, has a limited life in its
8 usefulness before the side effect, dyskinesia,
9 becomes more of a problem than the actual symptom
10 it is treating.

11 For me, this has caused an ongoing
12 debate many PD sufferers share -- when to begin
13 levadopa treatment. Do I start early and get the
14 most benefit while still in my best physical and
15 mental condition? Or do I delay as long as
16 possible so as to put off the dreaded dyskinesia
17 side effect?

18 The primary alternatives to levadopa
19 would be treatment with dopamine agonists, such as
20 Mirapex, Requip, or Neupro. Unfortunately, these
21 have their own serious side effects, which can
22 include harmful compulsive behaviors, sleep

1 disorders, and hallucinations.

2 After four years, my main problem from
3 the drugs and supplements which I take are daily
4 cases of mild nausea, along with repeated bowel
5 issues of either constipation and diarrhea. I
6 also find it difficult to constantly follow the
7 varied time schedules, dosing levels, and routine
8 that each drug requires.

9 Along with scheduling problems are also
10 the issues of food. Some drugs are taken with
11 food; some drugs require an empty stomach. Some
12 drugs require not to take protein because they
13 have a negative impact on drug effectiveness.

14 And of course, for many of us there's
15 the economic side effect involved in the
16 significant cost of taking all of these
17 treatments. This cost may be painful, but it's
18 even worse when you only receive a moderate, or
19 even no relief; then the cost is exorbitant.

20 Looking to the future, I see two avenues
21 for new treatments to be successful, even without
22 a complete cure. First, I would like to see

1 better symptomatic treatments. Ideally, they
2 would provide more symptomatic relief with fewer
3 side effects, and in addition, would have ease of
4 use that could be either oral, nasal, or
5 sublingual, rather than intravenous or invasive.
6 It would also have longer periods of activity so
7 as to require more limited dosing times.

8 Finally, we need to realize the
9 uniqueness and individuality of our disease, and
10 that different treatments may affect us
11 differently and some of us may require different
12 items that others don't use.

13 Second, and for me most importantly,
14 would be to discover disease-modifying
15 interventional treatments that can slow the
16 progression, if not totally cure it. As a
17 progressive illness, patients with Parkinson's
18 disease can usually live a normal life if taking
19 proper treatments in the early to mid-term years.
20 Currently, the life-altering period is probably
21 seven to ten years, at which point changes in
22 lifestyle become mandatory.

1 With interventional disease-modifying
2 drugs, along with new symptomatic treatments and a
3 proper exercise regimen, I truly believe most, if
4 not all, of us would be able to live active and
5 productive lives for many years beyond diagnosis.
6 Thank you for allowing me to speak today.

7 DR. EGGERS: Thank you very much, Gary.

8 And now I think it's Jennifer.

9 MS. RAUB: All right. Can everybody
10 hear me okay? Good. Hi. My name's Jenifer Raub.
11 I'm a patient advocate for Parkinson's and for
12 regenerative medicine. I have Parkinson's. I'm
13 57 years old. I was diagnosed seven to eight
14 years ago. But I do remember my first symptom at
15 35, with the hand flutter.

16 I'd like to thank the Patient-Focused
17 Drug Development Committee and the FDA for putting
18 a spotlight on Huntington's disease and
19 Parkinson's disease. There's approximately 7
20 million reasons why I am honored to speak with you
21 today.

22 Parkinson's disease is a progressive

1 disease, and my daily routine is always evolving.
2 Currently, I take carbidopa-levodopa, Neupro,
3 Azilect, and a handful of supplements morning and
4 night. I feel like my days are controlled by the
5 disease's needs.

6 Like so many of us with Parkinson's
7 disease, I've tried a plethora of therapeutics,
8 like biofeedback, acupuncture, physical therapy,
9 yoga, and more. I exercise rigorously daily,
10 sometimes twice daily. That seems to work the
11 best. I stretch throughout each day to stave off
12 the stiffness. I try to manage life's stressors
13 and keep my mind and body challenged and active.

14 Some days, these therapeutics aren't as
15 effective as others. Every day is a struggle with
16 the ups and downs of Parkinson's' Parkinsonian
17 symptoms. At the end of each day, I am exhausted
18 and sometimes frustrated, like I heard so many
19 others in this room.

20 I never know what tomorrow brings.
21 Another day filled with the same unpredictability?
22 Can I stand? How much pain will there be? How

1 long will the medications that are working today
2 continue to do so? Acceptance of this instability
3 is often frustrating.

4 I have days I'm reminded of the fact
5 that the medicines will not be effective forever.
6 Parkinson's is progressive, as I've said. Those
7 days I look at my children and grandchildren and
8 wonder -- oh, God, I don't want to cry -- how long
9 will the medications be effective? God. Sorry.

10 (Pause.)

11 DR. EGGERS: Take your time.

12 MS. RAUB: I'm watching you time me.

13 DR. EGGERS: No, no.

14 (Laughter.)

15 DR. EGGERS: I'll nudge you.

16 MS. RAUB: I'm onto you.

17 DR. EGGERS: Don't watch the clock.

18 MS. RAUB: My life has a new definition
19 of "normal." Parkinson's has redefined my family,
20 my friends, and marital relationships. Like Karl
21 and like all of us, Parkinson's has redefined me.
22 There is no cure for Parkinson's disease today.

1 And, yes, I've looked for alternative treatments
2 for my condition.

3 I do not want to be dependent on
4 medications for the remainder of my life --
5 medications with an undependable effectiveness and
6 side effects. I strongly believe there is great
7 promise in the near future for stem-cell therapy
8 for the treatment of Parkinson's disease,
9 specifically, induced pluripotent stem cells,
10 which are patient-specific and DNA-matched. These
11 cells are nonembryonic stem cells.

12 Stem cell therapy has been used in
13 Parkinson's. It has a 30-year history. I'm
14 sorry. Today, those in the study from decades ago,
15 using fetal cells, are now dying of natural
16 causes. And the dopamine cells at the time of
17 death were still viable.

18 Fast forward 30 years, and today a
19 simple skin cell can be made into a pluripotent
20 stem cell and, consequently, a dopamine-producing
21 neuron, the very thing that I'm missing and the
22 same thing that's missing in so many of us in this

1 room.

2 As I stated earlier, I'm a patient
3 advocate for Parkinson's, an advocate for all
4 regenerative medical research, and for Summit for
5 Stem Cell, working towards patient-specific stem
6 cell therapy. Currently, there are 10 patients in
7 a pilot study with their dopamine-producing
8 neurons already made and waiting. Parkinsonian
9 rodent model tests are completed, and within 18
10 weeks, all the rodents have regained strength and
11 movement. It's real. It's happening, and it's
12 happening now. Summit for Stem Cell hopes to file
13 an application with the FDA in 24 to 36 months.

14 I know the risks and the side effects of
15 the medications I take. I know the risks and the
16 side effects of the stem cell therapy. I'm
17 willing to take that risk. And most people I've
18 come into contact with would rather take that risk
19 than acquiesce to Parkinson's.

20 Let me, let us have the right to take
21 that risk, the right to choose how we fight the
22 symptoms of Parkinson's. I fight every day to

1 move. I am fighting for a life with my family.

2 I'm young-ish. I want a future with -- don't

3 laugh too hard over there.

4 (Laughter.)

5 MS. RAUB: I want a future with the
6 simple joy of being with my husband, my children,
7 and my grandchildren. I'm not crying -- I'm not
8 saying that.

9 Time is limited for someone with
10 Parkinson's. My time is limited. Give me a
11 chance. Give all of us a choice. I would like to
12 ask the FDA to consider supporting and furthering
13 this new and revolutionary field of regenerative
14 medicine that will change therapies and treatment,
15 not only for Parkinson's, but for so many diseases
16 that there is no cure for today. I'd like to thank
17 you for your time, and I appreciate you listening
18 to me.

19 DR. EGGERS: Thank you very much,
20 Jenifer.

21 MS. RAUB: Here. I'm shaking too much.

22 (Pause.)

1 DR. EGGERS: Now we have Kevin.

2 MR. KWOK: Can everybody hear me? My
3 name is Kevin Kwok. I'm from San Francisco. I'm
4 54 years old, and I am a Parkinson's patient. I
5 was diagnosed, I would say, in my mid- to late-
6 40s. It was not exactly sure when I started the
7 symptoms, but I did know that I lived with it for
8 a long time. And then, the ensuing denial was
9 many years after.

10 I'd like to give you a demonstration of
11 a fast-forward time-elapsed photography of what
12 Parkinson's could do for you. I elected DBS a few
13 years ago. And it changed my life. But it was
14 one of those decisions that I thought was very
15 harrowing at the time, and I almost backed out of
16 it at least a dozen times.

17 Without DBS, as I know a couple of my
18 colleagues on here on the panel have had DBS, I'm
19 basically disease-free, from a motor symptoms
20 standpoint. What I'd like to show you is what
21 happens when I turn it off, if I can.

22 (Laughter.)

1 MR. KWOK: Is it working? The white
2 button, right. I don't usually turn this off,
3 because I'm fearful that I'll jam and it will not
4 go back on.

5 (Pause.)

6 MR. KWOK: Thank you. So, this is my
7 symptoms. I'm off medications completely with DBS
8 for motor symptoms.

9 FEMALE PARTICIPANT: I think your
10 battery is dead inside of here.

11 FEMALE PARTICIPANT: Uh-oh.

12 MR. KWOK: Is it dead? It's all right.
13 We don't have to do show-and-tell.

14 FEMALE PARTICIPANT: Yeah. It would
15 have been cool, though.

16 MALE PARTICIPANT: You can describe it.
17 Some people won't see you, anyway.

18 MR. KWOK: I'll try to do a
19 demonstration live. I only have bradykinesia on
20 one side, my left side. And for the majority of
21 my disease, that was all that really bothered me,
22 I would say, from the motor symptoms side. But

1 what I'd like to emphasize, it's the non-motor-
2 symptoms side that really drove my decision to
3 have DBS, not the motor symptoms.

4 It's not working? That's all right.

5 So, you would normally see, if this
6 worked -- I'm glad it's locked on, not off.

7 (Laughter.)

8 MR. KWOK: -- is that off stimulation, I
9 would, in 30 seconds, my arm would curl almost
10 like a claw. And you would see someone very
11 decrepit on one side. And yet, right now, I'm
12 fine, if you look at all the UPDS symptoms on
13 here.

14 And so, I think that for me, a lot of
15 the things that I think about are very, very
16 different because of my staging of disease. I'm
17 very thankful that DBS has worked. My concerns of
18 not doing something which was considered science
19 fiction and Terminal-Man-like, Michael Crichton-
20 ish therapy, actually has proven to be something
21 that has been very, very beneficial in my life.

22 What I think about now, however, is the

1 things that DBS does not work on. It does not
2 work on many of the symptoms that I currently
3 have. As a Californian, a Northern Californian,
4 who is an obnoxious wine fan, I've lost my sense
5 of smell. That is a horrendous thing to have.
6 That's one of the least of my worries, however.

7 I still -- while my sleep has improved,
8 my sleep is not nearly quite as good as it used to
9 be. I worry about cognition, and I wonder if I'm
10 a candidate for Lewy body disease downstream.

11 I've gone through episodes of treatment
12 prior to DBS. I will tell you I was initially on
13 Sinemet, like all of you. And then with the
14 increasing doses, they started to add to the
15 cocktails of therapy. And then they started
16 adding dopamine agonists. I will tell you, for
17 some this works; for others, it's a very, very
18 dangerous drug.

19 And I actually -- many of the symptoms
20 of aberrant behavior -- I experienced many of
21 those things almost to the detriment of my family.

22 I still sense fatigue. And

1 occasionally, there's a dizziness when I stand.

2 And these are still some of the symptoms that I

3 have even after I'm off dopamine and my DBS is

4 working fully.

5 The things that I think about, however,

6 are really -- I would say I developed what I

7 consider themes of trying to improve my therapy.

8 So I've listed them. And these are not

9 necessarily just pharmacologist. My primary

10 concern right now is, how do I make these

11 beneficial effects that I've had with DBS last as

12 long as they can? It's really the durability.

13 DBS is oftentimes viewed as sort of

14 Medieval bleeding or leeches because we don't know

15 exactly how it works. All I can tell is it worked

16 for me. And so I've been involved in a clinical

17 trial now to look at beta-oscillation and

18 different patterns to see if there are electrical

19 surrogate markers instead of biochemical surrogate

20 markers.

21 So far, and this is something that just

22 came up last week, there's a detection that, even

1 though I don't show symptoms on the UPDRS rating
2 scale on my right side, but they're beginning to
3 show initial gaps in the beta-oscillation.

4 And my neurologist asked me at Stanford,
5 "Kevin, do you want us to power up your right side
6 now in addition to your left side?" I was one of
7 those patients who they said, "Well, while the
8 house is open and being renovated with your walls
9 open, why don't we wire for both sides, because it
10 is a progressive disease?"

11 So for me, I decided at the time, let's
12 not start dopamine and let's not begin because we
13 don't know enough about prevention with DBS. But
14 the delay in progression, from an electrical
15 standpoint, is one way I look at it. From a
16 pharmacologic -- and I think there's been a lot of
17 conversation on exercise being all part of it.
18 And this is the life that I live today to delay
19 progression.

20 My second theme is, how do we treat and
21 refocus on the nonmotor symptoms? I addressed
22 this in one of my questions earlier. But I

1 believe that the nonmotor symptoms are as equally
2 part of the complexities and a constellation of
3 disease, and we have to incorporate all of these.
4 And the current rating scales may not take into
5 effect the nonmotor symptoms.

6 I think a lot about the limitations of
7 current treatment. My experience with dopamine
8 agonists was something that I would not want a lot
9 of other people to experience. And I ask that we
10 be very vigilant on some of the side effects that
11 can happen there.

12 There's the aspect of prevention. I
13 think that some of these issues on finding
14 prodromal patients or those that have not yet
15 phenol-converted to be a lot of emphasis to be
16 found on how we could study and identify those
17 patients. I know from an industry standpoint,
18 that's not easy. But we can learn. We can learn
19 from cancer, where we start with end-stage
20 patients and progress to an earlier stage to show
21 maximum effect.

22 And then finally, of course, we'd love

1 for that holy grail, and that would be the cure.
2 But for patients like us in the room who already
3 have significant disease, cures may not
4 necessarily be in our horizon. But the
5 generations that will come, thanks to aggressive
6 research, aggressive support, and aggressive,
7 outspoken patients like our community, I think
8 will help us get towards this way, with the help
9 of the FDA.

10 So, on behalf of all of our patients, on
11 behalf of the different patient foundations that
12 I'm involved with, we thank you for the audience.
13 Because what we're doing here I think is very,
14 very important. Thank you very much.

15 DR. EGGERS: Thank you, Kevin.

16 And finally, we have Bill.

17 MR. PATTERSON: Hi. My name is Bill
18 Patterson. I am a 67-year-old retired computer
19 programmer who led a fairly sedentary life. And I
20 have Parkinson's disease.

21 From early in 2007, when I experienced
22 micrographia, some balance trouble, and foot drop,

1 and through the next three years, I progressively
2 experienced an undiagnosed and frightening
3 reduction of motor function on my right side,
4 despite visiting a neurologist two or three times
5 per year.

6 I knew I had a serious problem, and by
7 2010, I was limping badly, unable to type or use a
8 computer mouse with my right hand, and unable to
9 use my right foot and leg to drive. My
10 handwriting was small. I was significantly
11 depressed at that point. My sleep schedule was
12 chaotic, and I often would lie awake at night and
13 sleep during the day.

14 But on April 22nd, 2010, to get another
15 opinion, I went to what was, for me, a new medical
16 facility that was 100 miles from my home, at a
17 highly reputed medical school. I saw a
18 neurologist there who gave me the most thorough
19 neurological exam I can remember and gave me a
20 clinical diagnosis of early hemiparkinsonism.
21 This and the neurologist's prognosis scared me
22 into thinking that I could be, worst-case

1 scenario, at a nursing home in a few years and
2 possibly dead in five.

3 The fact that I had not been told any of
4 this before was particularly annoying. I decided
5 to learn as much as I could about PD. I scoured
6 the Internet, sought support groups, and began
7 seeing a movement- disorder specialist.

8 My research led me to Dr. Jay Alberts's
9 experiments at the Cleveland Clinic on the effect
10 of bicycling on PD symptoms. I also learned about
11 many animal-model experiments in which vigorous
12 aerobic exercise seemed to be neuroprotective --
13 that is, to slow the progress of the disease.

14 My movement disorder specialist started
15 me on a medication schedule that ramped up to two
16 tablets of 25-100 carbidopa-levadopa three times a
17 day. A couple of weeks later, selegiline at five
18 milligrams two times a day was introduced.

19 I found that, while I had more control
20 over my movements in general, I was experiencing
21 random writhing movements in my right leg, ankle,
22 and foot. I also did not like the nausea and

1 other weird feelings that I had. Additional
2 carbidopa was added, and it helped.

3 Over the next five years, different
4 strategies were tried. And for two of those
5 years, I was actually off of carbidopa-levadopa
6 entirely. Today, my anti- Parkinsonian
7 prescription medication consists of one- and-a-
8 half tablets of 25-100 milligram carbidopa-
9 levadopa, plus one tablet 25 milligrams carbidopa
10 three times per day, and the selegiline at, again,
11 the rate of 5 milligrams two times a day. This is
12 still less than was originally prescribed in the
13 beginning of my treatment.

14 I take coconut oil because some other
15 patients advised me that it helps fine motor
16 coordination in activities such as typing. My
17 typing speed is often good, but it varies, and I
18 have not isolated anything related to that
19 variance.

20 PD can result in reduced saliva. And
21 so, in consultation with my dentist, I have used
22 and expect to resume using Biotene mouthwash

1 during the day for dry mouth. And I use Act
2 mouthwash at night. I visit a hygienist every
3 four months instead of the usual six. And by the
4 way, I've lost a couple of teeth.

5 I have continued to bike on a stationary
6 machine almost daily through the last five-and-a-
7 half years at a cadence generally greater than 90
8 RPM for the 40 minutes that I stay on it. I feel
9 very fortunate to be able to do this. I track
10 specific measures of my exercising in a database.

11 I also practice Tai Chi and yoga. And
12 I've used personal trainers. I use weight
13 machines for strength, and I stretch regularly.
14 Now, there are side effects from the biking. One
15 is that I feel healthier. Another side effect is
16 I've lost weight.

17 But I developed cramps in my feet, and I
18 had to attack this myself. And I found a chapter
19 of a book that was available on the Internet from
20 a doctor who specialized in bicycling health. And
21 he identified several elements whose supplementing
22 can help. They're calcium magnesium and

1 potassium. I consulted with a dietician, got the
2 right dosing for myself. Doctors wouldn't give it
3 to me. And I started using it, and the cramps
4 went away.

5 I also developed pins-and-needles
6 feelings in my hands, and that's treated
7 effectively with anti- vibration gloves.

8 Now, I think my current treatment
9 regimen treats the symptoms fairly well. However,
10 the number of symptoms, exercises, substances, and
11 their interrelationships is overwhelming. At
12 times, it is hard to tell which combinations do
13 what.

14 Beyond mere symptom treatment is the
15 hope that some of these treatments are
16 neuroprotective. They do enable me to have a
17 fairly full life, but not as full as I would like.
18 During the first few years of this adventure, I
19 was employed full time. Now I'm retired, and that
20 makes things easier.

21 Importantly, I get around very well,
22 type, use a computer mouse, and drive with my

1 right leg and foot. And I'm able to enjoy my
2 family and friends. I've noticed some, but
3 comparatively little, progression of my symptoms
4 since my starting treatment five-and-a-half years
5 ago when compared to the progression experienced
6 in the first three years of undiagnosed PD. I
7 find this encouraging and suggested that my
8 treatments, including the aerobic exercise, have
9 slowed the disease progression.

10 One downside of my current treatments is
11 the time required, the time required for
12 exercising and related PD activities, such as
13 managing prescriptions and attending support
14 groups. It's significant. Now that I'm retired,
15 things are better.

16 I'm grateful for my treatment and the
17 research that supports it. An ideal treatment
18 would eliminate all these symptoms, and probably
19 the motor symptoms would be the worst that I have
20 now that would be tackled by an ideal treatment.
21 But if my cognition were impaired as well, I would
22 make that the first priority.

1 As bad as side effects of certain drugs
2 feel, they're usually not as bad as the conditions
3 being treated. Of course, if they were worse, you
4 probably wouldn't use them. Now, certainly fear
5 of the future is a real issue, and I think all of
6 us experience that.

7 And it's imperative that we learn more
8 about brain functions -- better knowledge and,
9 importantly, better distribution of that
10 knowledge. Remember that I went to neurologists
11 who weren't diagnosing me. And I was presenting
12 them symptoms.

13 The better distribution of knowledge may
14 enable not only better treatment of PD, but better
15 aging overall. And I don't think I can
16 overemphasize the importance of exercise in my
17 treatments. I feel good most of the time. Thank
18 you very, very much.

19 DR. EGGERS: Thank you, Bill.

20 So I want to give a round of applause to
21 the panelists.

22 (Applause.)

1 DR. EGGERS: As Theresa Mullin would
2 say, you guys are experts at what it's like to
3 live with your condition and the treatments. And
4 that came through very clearly.

5 We are going to now delve into a number
6 of the rich points that you raised. We won't be
7 able to address all of them. But you've talked
8 about the role of the pharmaceutical or the
9 surgical treatments, the role of exercise, the
10 role of all of the other therapies that you take
11 in addition to your treatment.

12 And I think, really insightful, you
13 talked about what is going on in you to make you -
14 - when you are deciding. You revealed to me your
15 decision-making processes, and I think that that's
16 really important to help us understand what's
17 important, what you're looking for in a treatment.

18 So that we have a little bit of context,
19 we are going to ask a polling question next, if
20 you can get out your clickers.

21 (Pause.)

22 DR. EGGERS: We're going to ask the

1 question, have you ever used any of the following
2 drug therapies to help reduce your symptoms of
3 Parkinson's disease? And check all that apply.
4 And I'm just going to let you read through this
5 list, because you would pronounce these treatments
6 much better than I would. So I'll give you some
7 time to read through these. Check all that apply
8 for you that you have tried or you're currently
9 doing.

10 (Pause.)

11 DR. EGGERS: Okay. It's not surprising
12 that everything, that at least some of you are
13 taking -- everything is mentioned here. Of
14 course, the carbidopa-levadopa being the primary
15 one, followed, I'm not going to try to pronounce C
16 and B.

17 We're not going to get into all of these
18 treatments. But before I actually -- before we do
19 that, are the results on the Web?

20 MR. THOMPSON: Results on the Web are
21 about almost exactly the same.

22 DR. EGGERS: Okay. Thank you. So,

1 sorry. I need my alarm clock. It's the only
2 thing that helps me keep us on time.

3 I'm going to actually turn to my
4 colleagues first and see if there's any of these
5 with what you're seeing here or represented in the
6 room or on the Web, any treatments that you would
7 like to ask more questions about, about their
8 effectiveness or their downsides or their -- or
9 what people have found, using those treatments.

10 DR. PODSKALNY: Sure. First, let me
11 say, as a former physical therapist, the exercise,
12 you're preaching to the choir. But as we see that
13 almost everyone has taken carbidopa-levadopa in
14 some form. And the team has worked very hard in
15 recent months to approve drugs like Rytary and
16 duopa.

17 If anyone -- and I'll throw this out
18 there to the people on the Web, too, so we cast a
19 larger audience, poll a larger audience. Has
20 anybody taken these medications recently and found
21 that they're effective in treating particular
22 aspects of their Parkinson's disease, that we

1 could maybe gain some feedback and understanding
2 of how people are finding these drugs to be
3 effective?

4 DR. EGGERS: Would you like them to
5 focus particularly on Duopa and Rytary, or any of
6 them?

7 DR. PODSKALNY: Well, we hear a lot
8 about the shortcomings of some of the drugs that
9 have been around for 20-30 years. So --

10 DR. EGGERS: So these newer ones?

11 DR. PODSKALNY: Yeah, the drugs that are
12 newer and maybe we have less experience with.

13 DR. EGGERS: Great. Thank you, Dave.
14 So, we'll start here.

15 MS. ROUDE: Thank you. I tried Rytary
16 earlier this year. And it didn't work for me at
17 all. It caused me to be angry all the time. I
18 was just upset. It didn't provide any benefits at
19 all. I didn't have any increased good time, and
20 my bad time, my off time was just increased
21 exponentially.

22 DR. EGGERS: Thank you, Rebecca.

1 And then, over here. Is it Kathy?

2 MS. HAGERBRANT: Is this on? Yeah.

3 Lynn Hagerbrant. You know, I've been on Neupro.

4 I'm an RN. My husband's a physician. And I've had

5 Parkinson's since November -- I was diagnosed

6 November of 2010.

7 But the Neupro that they put me on would

8 come off. I'm a nurse. And so, it would like

9 fall off. And then I wouldn't notice it. But

10 then, my symptoms would be coming back. So I

11 called the company. And they said they would mail

12 me out a new box, that a lot of times Neupro is

13 being stored in a warehouse over the summer and at

14 really high temperatures, and that it would lose

15 its ability to adhere to my skin.

16 So, I, ironically, had to go out to

17 dinner with somebody that had Parkinson's in the

18 city, and she was in really bad shape. And I

19 asked her what medication she was on, and she was

20 on Neupro, and her patch was falling off. So I

21 told her to do an emergency call to her

22 neurologist to get another medication onboard.

1 DR. EGGERS: Thank you.

2 Any other responses to Dave's question?

3 Right here. And then we'll go back there. Go
4 ahead, right here.

5 MR. DeWITTE: I just wanted to mention
6 that Requip has been very helpful, ropinirole has
7 been very helpful in helping with leg -- restless
8 legs syndrome at bedtime. And it helps to sleep.
9 Obviously, that's become a big issue.

10 DR. EGGERS: Okay. Thank you.

11 FEMALE PARTICIPANT: So, I don't take
12 duopa or things we're talking about. But one
13 thing that, one of my major concerns and main
14 frustration has been that the UPD -- the
15 medication results may be given to us as a 30
16 percent increase or decrease. And 30 percent of
17 what? When we look at the UPDRS, it may be one
18 point, two points different. I don't think most
19 people are aware of that.

20 DR. EGGERS: Okay. Thank you.

21 Right here.

22 MR. CANNON: This is Paul Cannon. I

1 haven't taken (inaudible) yet. I'm interested in
2 it. But apparently, the qualification
3 requirements are still quite stringent, I think
4 with cost being an issue as well. That's
5 potentially why you're not seeing as much uptake
6 of that as you might have expected to.

7 DR. EGGERS: Okay. So raising the point
8 of access issues and cost issues, which we've
9 heard throughout our discussion earlier in Topic
10 1.

11 Any of the other treatments that --
12 especially if the panelists didn't touch upon
13 them, that have had a really noticeable positive
14 effect? And when you describe it, if you could
15 tell us what that effect was and what change you
16 saw.

17 MS. ROBB: Unfortunately, my comment is
18 not that. But I wanted to make a mention why you
19 might not be hearing from people is because, once
20 they have a regimen that works really well,
21 they're not very keen in changing medications.
22 We're going through this now with -- you know, we

1 want a little more on time efficacy in Karl's
2 regimen.

3 And it's like a back-and-forth -- it's
4 like a tennis match with the neurologist, debating
5 the pros and cons of each medication and the
6 doses, and the hesitation to change something that
7 seems to be working, especially with the Rytary.
8 I know because the dosing is different. Although
9 it's a different delivery mechanism than standard
10 Sinemet and certainly much better than I've heard
11 Sinemet CR was, which Karl had a lot of difficulty
12 with.

13 So I think you're hearing some
14 hesitation, because once somebody finds a really
15 good regimen, they usually stick with it until
16 there's a major disruption and they need to change
17 their medication.

18 DR. EGGERS: Okay. So let's build on
19 this. And can someone tell us, someone who was
20 hesitant about changing, say what was the trigger
21 point for you? What was the disruption that
22 caused you to seek another option? Oh, lots of

1 hands raising on this one. Okay, we'll start
2 here, and then we'll go back there.

3 MR. PATTERSON: In the two years that I
4 was off of Sinemet -- this is Bill Patterson -- my
5 doctors did start me on Mirapex partway through
6 that. But it got to a point where at one time I
7 had a laptop computer on my lap and I was taking
8 notes in a lecture, and I had a sleep attack and
9 lost the laptop, which went to the floor.

10 I thought that was -- I was really glad
11 that it happened there and not somewhere else,
12 where there was more at stake. And we stopped
13 that particular regimen and increased the Sinemet.

14 DR. EGGERS: Okay. Right here, and then
15 back. And then Ellis Unger has a question.

16 MS. GOULD: Thank you. Hello. My name
17 is Sherrie Gould. I actually am a clinician at
18 Scripps Clinic in La Jolla, California. And when
19 Rytary came out, we were very excited the FDA
20 approved this very long-acting type of carbidopa-
21 levadopa.

22 So I definitely do give patients, if

1 they're willing to do it, especially the ones that
2 are very frequently dosed. As you've heard here
3 in the room, there are many of these patients that
4 need to take their medicine maybe even a half or a
5 quarter every hour, every hour and seven minutes,
6 whatever the case is.

7 The drug has definitely helped improve
8 the quality of their life, because they don't have
9 to live every hour to hour on just regular what we
10 call carbidopa-levadopa. So Rytary, I would have
11 to say, in about 60 percent of the patients I give
12 it to, they love it. Forty percent, it just
13 doesn't work. You know, who knows why that is?
14 And they felt better on their old regimen. But I
15 just wanted to give you feedback on that.

16 We've not done anything -- we have no
17 patients on Duopa. It seems a little invasive.
18 We can't -- anyway, and it's a very tedious
19 medication to actually prescribe. Patients seem
20 to stay in the hospital to get titrated
21 appropriately, et cetera. So that's not a drug
22 that we've tried in our clinic.

1 DR. EGGERS: Okay. Going to the back.

2 MR. LINDERMAN: Following up on the
3 comment on Mirapex, I was on Mirapex two or three
4 years ago on a three-times-a-day times a 1.5
5 milligram tablet. And that put me over the edge
6 psychologically, and I began to do some things
7 that somebody would not want to do, impulsive
8 behavior such as responding to Internet requests
9 for money from India and that kind of crap.

10 When I -- and it also has made my feet
11 swell to the point that I can hardly find a pair
12 of shoes that will fit. And even now today, I'm
13 down to three times a day, a point -- a half-a-
14 milligram on the Mirapex, and the feet are still
15 somewhat swollen, though the impulsive behavior
16 seems to have gone.

17 And I would also stress, in terms of
18 physical trainers, when I found my trainer, I had
19 been with him for a couple of years before I was
20 diagnosed. And I went to him the afternoon after
21 I'd received my diagnosis. And my wife had not
22 gone with me to the doctor's that morning, so he

1 was the first person that I felt I could trust
2 that I could talk to about what the neurologist
3 had said to me.

4 And he looked at me in the face and
5 said, "Are you going to lie down and die with this
6 thing? Or are you going to stand up and fight
7 it?" And together, we have fought it for the last
8 decade. And I can tell you, when I am doing a
9 legs workout, I feel the difference in my body,
10 and the dopamine production is clearly on and
11 moving forward very aggressively. And I don't
12 feel the same thing when we do an upper body
13 workout as much. But working hard on the legs
14 does do that. And I feel similarly.

15 The other thing the exercise has brought
16 out is that it's given me the option, with my
17 neurologist's blessing, to take an extra dosage of
18 Sinemet either before or during the workout,
19 because I was finding that the Sinemet would wear
20 off in the middle of a workout sometimes. And
21 when you're out in the middle of a river rowing,
22 that's not a good thing to have happen.

1 DR. EGGERS: Thank you very much,
2 Charlie.

3 And Ellis has a question.

4 DR. UNGER: I do. We heard one comment
5 about orthostatic hypotension. And I just
6 wondered if there were others in the audience who
7 have had symptoms from what we call orthostatic
8 hypotension. And if so, you know, what are the
9 symptoms and what have you done about them?

10 DR. EGGERS: Okay. So, I think the
11 comment about the low blood pressure was here --
12 or it was back there. Okay. So we'll let you
13 start, if you would like to respond.

14 FEMALE PARTICIPANT: Well, the symptoms
15 that I would have would happen after I had been
16 standing still for awhile. So, they happened
17 first -- I'm a nurse- midwife. They happened
18 first when I was standing in the OR and when I was
19 cooking. And what happened was, this is weird,
20 the center of my head felt cold, and I felt like I
21 was going to die.

22 I did not feel dizzy. And it took a

1 long time to identify it as orthostatic
2 hypotension because it didn't have the dizziness
3 or lightheaded, faint component to it. But
4 finally, I just got a blood pressure cuff and
5 started checking.

6 DR. EGGERS: And are you treating it in
7 any way? Are you taking any medications for that?

8 FEMALE PARTICIPANT: No. I figured out
9 sort of what the triggers are. So it's much worse
10 when it's hot outside. So I do not stand still
11 when it's hot outside. I've had to stop working,
12 so I'm on disability. If I drink huge amounts of
13 fluid before I have to do something like exercise,
14 that helps. But then I have the problem with
15 urgent continence. And if I increase my salt
16 intake, that helps too.

17 And also, if I know I'm going to be in a
18 position, I get out of it as soon as I can and I
19 lie down and sleep. And that will make it go
20 away.

21 DR. EGGERS: Okay. Thank you.

22 Anyone taking a medication?

1 MS. GARRIDO-REVILLA: Yes, I'm sorry.
2 I'm not taking a medication, but I do understand
3 what she says about orthostatic hypotension. It
4 happens to me whenever I forget, I miss my dose of
5 Mirapex. I feel my blood pressure down, or I
6 completely pass out. I have landed in the ER
7 several times because of that. And just they keep
8 me -- they warn me, I have to remember all my
9 doses, because that's one of the things that
10 happen.

11 DR. EGGERS: Thank you.

12 One more comment on experience with
13 managing the orthostatic hypotension? Oh, right
14 here. Okay.

15 FEMALE PARTICIPANT: I've been treated
16 for hypertension, just a central hypertension,
17 with drug therapy since I was in my mid-30s. And
18 it was always well managed with very little drug.

19 Prior to -- post my diagnosis for PD,
20 there were instances where if I got up very
21 quickly from a lying-down position or sitting, and
22 I jerk my head, my blood pressure would drop to

1 the point where I would almost pass out. I would
2 get dizzy, and everything would go kind of sort of
3 yellow, like I was about to pass out. But if I
4 just braced myself and kept real still for a
5 couple of minutes, a few seconds, actually, it
6 would pass.

7 And if I checked my blood pressure right
8 after that, it was spiking high and low. So
9 they've titrated my medication for the
10 hypertension down a bit. And that seems to have
11 helped it. I still have to be very careful rising
12 up from a lying-down position too quickly.

13 Like when I get up in the morning, I sit
14 up in bed, swing my legs over, and sit there
15 before I actually stand and begin walking.
16 Because that's when I was experiencing it the
17 most. I would get right up, walk out of -- you
18 know, sit up and stand up and then walk into the
19 bathroom. And like by the time I go through the
20 bathroom doorway, I was dizzy.

21 But it seems to be managed by decreasing
22 the drug.

1 DR. EGGERS: Thank you so much, Nancy,
2 right?

3 Okay. So, Leonard has a question.

4 DR. KAPCALA: Almost one-third of the
5 respondents noted that they were using other drug
6 therapies not mentioned. So I'd like to hear
7 about, what are those other drug therapies?

8 DR. EGGERS: Okay. So if you could just
9 briefly go through and say what those are, and why
10 you're taking them. Anyone? Okay. We'll start
11 here.

12 MALE PARTICIPANT: Thorazine, which is a
13 calcium channel blocker normally used for
14 hypertension. And there's been some research being
15 done now as a possible neuroprotective use for it.
16 So I use that.

17 DR. EGGERS: Okay.

18 MR. KWOK: I'm experimenting with --
19 through my neurologist with Atomoxetine for
20 fatigue and also possibly for cognition
21 improvement.

22 DR. EGGERS: Any others? Okay, one more

1 here, and then we'll take two more. And then
2 Peter has a question.

3 MS. HOUDE: I use lamotrigine. It's to
4 stabilize my mood, but it also helps with the
5 dyskinesia. And I recently started Vitamin E
6 treatment.

7 DR. EGGERS: Okay. Thank you.

8 FEMALE PARTICIPANT: Because I was
9 improperly diagnosed initially, I was on the
10 scopolamine patch for awhile. And I felt great on
11 the scopolamine patch. When I was correctly
12 diagnosed, they took me off of it and my symptoms
13 got worse instantly. But they won't give it back
14 to me.

15 DR. EGGERS: Okay. Okay. So, Peter, do
16 you have a question? And then we're going to move
17 on to a broader topic.

18 DR. COMO: Sure. A number of the
19 panelists have told us that they have DBS systems
20 implanted. I was just curious. A, did you
21 experience any complications from the surgery
22 itself? And B, are you experiencing any side

1 effects of your DBS stimulation?

2 DR. EGGERS: We heard from Kevin.
3 Anyone else? So we'll come here, and then Kevin,
4 and then you can.

5 MS. HOUDE: I had DBS three years ago.
6 And it was originally for my dyskinesia. So my
7 doctor, we went through the surgery. And then
8 they decided to change the location of the probe
9 halfway through the surgery. So the -- so there
10 was a complication in the surgery itself. But
11 since then, I have had -- I've had increased off
12 times. My dyskinesia has been reduced, but with
13 the battery, it's quite painful in my chest
14 sometimes.

15 DR. EGGERS: Thank you.

16 MR. KWOK: It's a little humorous, but
17 originally, because I only had one-sided disease,
18 they got the leads switched off. And they were
19 for the first three months innervating the wrong
20 leads. And I couldn't understand why it wasn't
21 working.

22 There is an interesting thing with DBS.

1 So there is a microlesion effect. So you
2 initially feel almost like a placebo-like positive
3 benefit that seems to go away, which should -- I
4 think masks sometimes the efficacy of DBS in the
5 early days.

6 I'm happy to report that I'm also
7 involved in the closed-loop trials right now to
8 look at new neurotransmitters that might actually
9 be, you know, smart transmitters that use some
10 sort of biofeedback. And I'm looking forward to
11 that as being an innovation that will help, one,
12 prolong the battery life, but, two, hopefully
13 prolong the disease as well, the benefits on the
14 disease as well.

15 DR. EGGERS: Thank you. So we are going
16 to -- we're a bit tight on time. We do have an
17 Open Public Comment, but I understand that we can
18 probably cut into our Open Public Comment time.
19 And to do so, we'll even ask the open public
20 commenters to really stay on time with their open
21 public comments.

22 So we can dig in. I think we have

1 probably about 10 more minutes that we can spend
2 on this. I do want to get a Web summary, and we
3 have a couple of people on the phone.

4 But before -- while we're doing that,
5 I'm going to put up the next polling question. We
6 don't get to talk about these, but we do recognize
7 their importance, of the other therapies besides
8 the pharmaceutical. So just, we won't be able to
9 discuss them. I think there's been some really
10 eloquent descriptions about some of these. But it
11 would be helpful to see, in the room, what the
12 reflection of it in the room of how important
13 these are to you, what you're using.

14 So you can use your clickers. Besides
15 your drug therapies, what other therapies have you
16 used to help reduce your symptoms of Parkinson's
17 disease? Check all that apply.

18 (Pause.)

19 DR. EGGERS: Okay. So, I think you're
20 reiterated a take-home point of the afternoon is
21 the importance of these other therapies to you.
22 It looks like many of you are doing most or all of

1 these things as part of the management of your
2 condition.

3 Is there any summary on the Web,
4 anything that's been new or something we haven't
5 heard that you can pull out?

6 MR. THOMPSON: Going back to Rytary,
7 there is one person had an experience with it,
8 said they attempted several different dosages and
9 could never find anything that would smooth out
10 the tremors, and also experienced a lot of
11 dyskinesia using it. One person who was talking
12 about Sinemet and suggesting that a lot of the
13 symptoms that people were talking about may be
14 side effects of taking Sinemet.

15 And then we had one person who was
16 speaking about the need for better education and
17 understanding of medical staff during
18 hospitalization incidents or in rehab settings,
19 because people are occasionally not receiving the
20 correct care.

21 DR. EGGERS: All right. So we have time
22 to take a couple of people on the phone. And on

1 the phone, we'll ask you to really focus in on
2 something that you may think will surprise the
3 folk -- well, maybe not the folks in the room,
4 that would surprise FDA about your experiences
5 with particular treatments.

6 Operator, can we have a caller, please?

7 (No audible response.)

8 DR. EGGERS: Operator, can we have our
9 first caller?

10 THE OPERATOR: Your line is open.

11 MR. AIMES: Hello.

12 DR. EGGERS: Yes. Can we -- what's your
13 name?

14 MR. AIMES: Carl Aimes.

15 DR. EGGERS: Hi, Carl.

16 MR. AIMES: How are you all?

17 DR. EGGERS: Good.

18 MR. AIMES: I am calling from Phoenix,
19 Arizona. I am a Parkinson's patient diagnosed in
20 early 2008. I am active in the Parkinson's
21 community here locally and trying to get involved
22 nationally as often as I can. I applaud all of

1 the participants today, along with the FDA, for
2 getting this group together and hearing what we're
3 experiencing. And hopefully, we can improve
4 things.

5 And one thing that I'd like to suggest
6 is that, when I was first diagnosed, I was told
7 that it was a life sentence versus a death
8 sentence. You can live with Parkinson's disease
9 for a long time. So with that in mind, I
10 obviously -- just daily challenges that we all
11 experience with Parkinson's disease. And I think
12 the thing we have to really be quite the fighters
13 for dealing with it and what-not.

14 But with different medications that
15 we're all taking and the ability to keep track of
16 what's being effective, works, and what's not, I
17 think it would be very helpful to have some type
18 of a database link, or doctor's office, that would
19 tie into the FDA and be able to, as we go to our
20 doctors and we're maybe given a new prescription,
21 we're able to record that we started our new
22 prescription.

1 We're able to record, from home
2 basically, how it's affecting us. And then when
3 we go to our doctor's appointment, they can follow
4 -- the doctor's appointment six months later,
5 three months later, or whatever it is, is the
6 ability to have more of a history of -- obviously,
7 we're doing it from memory, because obviously our
8 memories aren't very good.

9 So I think it would be very helpful to
10 have more of -- with the technology out there to
11 develop it, we'd have more of a link that the FDA
12 and how we can tie in our day-to-day activities
13 with our -- how things are helping us or not. And
14 more like, get to know the patient more on a
15 personal basis. And I just think that would be
16 very, very helpful for us.

17 DR. EGGERS: Okay. Thank you, Carl.
18 So, you're identifying an unmet need for support
19 with the complex management and really linking the
20 information together.

21 MR. AIMES: Yes.

22 DR. EGGERS: Thank you for that.

1 Do we have -- we can have one more
2 caller.

3 THE OPERATOR: Your line is open.

4 SUE: Good afternoon. My name is Sue.
5 I have had Parkinson's disease --

6 DR. EGGERS: Sue, Sue, I'm going to
7 interrupt you for a second. Are you on the
8 speakerphone?

9 (Pause.)

10 DR. EGGERS: Sue, we're having some hard
11 time hearing you. If you're on speakerphone --

12 SUE: Can you hear me? Yes, I'm on the
13 speakerphone.

14 DR. EGGERS: Okay. We have a little bit
15 of a reverb. It's difficult to hear. Let's try
16 again.

17 SUE: Can you hear me now?

18 DR. EGGERS: Yes, that's great.

19 SUE: Okay. I have had Parkinson's
20 disease for 14 years. My two daughters, ages 50
21 and 52, also have the disease. My question has to
22 do with not with what the FDA can do regarding

1 treatment, but what the FDA can do regarding
2 prevention.

3 Research teams led by some of the most
4 highly respected authorities in the cause of
5 Parkinson's disease, including William Langston,
6 Scientific Director of the Parkinson's Institute
7 in Sunnyvale, California, have shown glyphosate,
8 the main ingredient in Round-Up, and permethrin,
9 which is imbedded in much of the outdoor clothing
10 sold by stores such as REI, have been shown to
11 cause Parkinson's disease.

12 I question why the FDA continues to
13 allow these toxic agents to be sold.

14 DR. EGGERS: Well, thank you very much
15 for your question. There we go. Thank you very
16 much, Sue, for your question. I'm going to ask
17 you to hang up now, Sue, because it reverberates.
18 Okay. Thank you, Sue.

19 I think it is -- that's a very big
20 question that goes a bit beyond what we can
21 address today. But I will take this opportunity,
22 though, to ask those questions through the docket

1 so that we know what is important to you. What
2 are the big questions you have on your mind?
3 Because they are all important, even if we can't
4 address them all, all today or through this
5 meeting. So, thank you.

6 With that, we have really concluded our
7 Topic 2 discussion, our discussion with -- to wrap
8 up the discussion with the participants. I want
9 to sincerely thank you on behalf of our colleagues
10 for the thoughts you sent in. Many of you sent in
11 comments. We identified -- it was a tough
12 decision to identify panelists, to folks to
13 service the panelists. But we have all the
14 comments you submitted, and we will be -- we have
15 reviewed those, so that is all useful input that
16 we will incorporate into our report as well.

17 I cannot emphasize enough the importance
18 of the docket. It is your chance to, you know --
19 you didn't get to talk as much as you wanted to
20 today; I know this. So the docket is your chance
21 to make sure that your full story and your full
22 thoughts are shared with us. And we do read

1 those.

2 There are evaluation forms at the back
3 table. So, please let us know how we're doing on
4 these meetings and how well you feel your voice is
5 being heard and your perspectives are being
6 reflected here.

7 And with that, I will again ask for a
8 round of applause, especially from FDA, for your
9 courage and your thoughtfulness and really your
10 expertise in your condition.

11 (Applause.)

12 DR. EGGERS: Thank you.

13 MS. VAIDYA: Hello, everyone. I'd like
14 to thank you all for coming here today. We're now
15 moving into the Open Public Comment session.
16 Please keep in mind that we will not be responding
17 to your comments, but they will be transcribed.
18 They will be a part of the public record.

19 Since we would like this process to be
20 transparent, we encourage you to note any
21 financial interests that you may have related to
22 your comment.

1 So we've collected sign-in during
2 registration and at the break. We have six people
3 who have signed up and roughly 20 minutes, I
4 believe, 15 to 20 minutes. So I suggest that we
5 all stick to the two minutes per person comment
6 time. And then I'll be keeping track of time up
7 here.

8 I'll run through the speakers really
9 quickly, and then we'll move on to the comment
10 session. So first, we will have Sally Okun.
11 Next, Paul Cannon, Sherrie Gould, Lynn Hagerbrant,
12 Charles Linderman, and then Jeanne Loring.

13 So first, could we have Sally Okun,
14 please?

15 MS. OKUN: Thank you very much, and let
16 me just disclose that I am an employee of
17 PatientsLikeMe. And I will be talking a little bit
18 about that experience.

19 I just wanted to let you know that we
20 will be submitting to the public docket a survey
21 that really overviews about 170 of our patients
22 who have been surveyed with the exact questions

1 that have been discussed here today. So we have
2 some insights from at least over 150 patients that
3 have really given us their deep thoughts on these
4 questions.

5 But I also wanted to say that we have an
6 ongoing community of over 10,000 Parkinson's
7 patients that are telling us about their
8 experiences of daily life, with symptoms and
9 treatments and side effects, on a regular basis.

10 Just one comment, I was looking up the
11 information that you asked about, some of the
12 newer treatments. In our forum, we have a thread
13 that's just on some of those newer treatments,
14 with about 17 pages of posts and conversations
15 about it, representing about 300 different
16 individual patients talking about their
17 experiences.

18 So I think there's an opportunity to
19 systematize some of the data collection, and we'd
20 be happy to support that in any way that we can.
21 We will supply all of this to the public docket as
22 well. So thank you so much for the meeting today

1 and all of the patients and caregivers here today.

2 MS. VAIDYA: Thank you, Sally.

3 Could we have Paul Cannon next?

4 MR. CANNON: So, I'm Paul Cannon. In
5 addition to being a patient and a drug developer
6 and a scientist, I'm also the Program Manager at
7 23andMe. And I've also submitted to the docket a
8 summary of the questionnaire that we've produced
9 of our community. It's about the same size,
10 actually, 9,000 patients, and about 1,700 replies.

11 It's a document that's already in the
12 docket. If anybody wants to look it up or if they
13 want to contact me, I'll be happy to share it --
14 many of the things that we've already heard in the
15 room today, which is consistent and good. I think
16 it says that the community online are putting it
17 together, an actual useful resource for patients
18 and the outcomes, and should be used as broadly as
19 possible. We're happy to work with people to do
20 that.

21 My only other comment is, looking around
22 the room, I think we all have to work on the

1 ethnic representation in the research and in the
2 support groups. As we see, it's clearly an issue
3 that we all have to deal with, I think.

4 MS. VAIDYA: Thank you, Paul.

5 Next, we have Sherrie Gould.

6 MS. LORING: Yeah, Sherrie and I are
7 switching. I'm Jeanne Loring. I'm a professor at
8 the Scripps Research Institute in La Jolla,
9 California. I'm the Director of the Stem Cell
10 Program there. And as such, I'm part of the
11 Summit for Stem Cell Program that was mentioned
12 earlier by Jenifer Robb.

13 What we're doing, briefly, is taking
14 skin cells from patients with Parkinson's disease.
15 We're using a technique called "reprogramming" to
16 turn those cells into pluripotent stem cells,
17 which are identical to embryonic stem cells, but
18 they come from individual people. And so they
19 carry exactly the same DNA as that person. We
20 could do that with any of you.

21 We take those pluripotent stem cells and
22 turn them into dopamine neurons, which you all

1 know are what die in Parkinson's disease. We're
2 making the precise kind of neurons that is present
3 in the substantia nigra.

4 Right now, we've done a great deal of
5 the preclinical work. We've shown that cells
6 we've taken from patients cure a rat model. So,
7 and there are rather spectacular results. They
8 are equivalent and, in fact, in a lot of ways
9 better than the NIH-funded studies using fetal
10 tissue in the 1990s and 2000s, which had mixed
11 effects, and some patients were improved and some
12 didn't.

13 Those who improved are now in -- much
14 older, of course. And they have had 20 years in
15 some cases without any requirement for any kind of
16 drug therapy. They are not cured. But they have
17 no symptoms. And they get no worse with time.

18 So we're hoping that we can improve upon
19 those results by using these patient-specific
20 pluripotent- stem-cell-derived dopamine neurons.

21 MS. VAIDYA: Thank you so much, Jeanne.

22 Next, could I have Sherrie Gould, then?

1 MS. GOULD: So again, my name is Sherrie
2 Gould. I'm a nurse practitioner at Scripps
3 Clinic. And work very closely and kind of started
4 the Summit for Stem Cell, which is a fundraising
5 group of Parkinson's patients that our sole
6 purpose is to raise money for this research that
7 brings so much hope to people with Parkinson's.

8 You know, sit here for a number of
9 hours. I see, I spend my entire workday seeing
10 nothing but people with Parkinson's disease for
11 the last 10 years. I'm the one that prescribes
12 over and over, and more and more and more drugs.

13 I really would like to have this
14 opportunity to ask the FDA, as we approach you in
15 a couple of years with the proper studies, et
16 cetera, that you'll take that quantum leap to
17 think of something outside of drug therapy, to
18 actually fill the bucket back up, to actually
19 replace the cells that are missing and dying in
20 people with Parkinson's.

21 So, we have a lot of work ahead of us.
22 We're working with an FDA consultant right now, so

1 on a monthly basis, and raising the money on our
2 own. We've raised over \$2 million, which has been
3 fantastic, all by just community philanthropy.

4 So, there is hope. I'm telling this
5 group of people out here there is hope. In the
6 future, there is a hope for you. We really
7 believe Parkinson's disease is the lowest-hanging
8 fruit for this type of therapy. It has the
9 greatest chance of success, because the main one
10 cell type that is missing and dying in people with
11 Parkinson's is, of course, the dopamine-producing
12 neuron. And we can make those from your skin.

13 So, thank you very much. I appreciate
14 the time.

15 (Applause.)

16 MS. VAIDYA: Thank you, Sherry.

17 Next, we have Lynn Hagerbrant.

18 MS. HAGERBRANT: I want to introduce
19 myself again. I'm Lynn Hagerbrant. Do you mind
20 if I sit down? I wanted to -- when I was
21 diagnosed back in November 2010, my neurologist
22 said to me, "Lynn, whatever you do, don't go on

1 the Internet and look up Parkinson's disease."

2 And she said, "In addition, do not go to a support
3 group."

4 So in my area, there was -- the face of
5 Parkinson's is different. It was usually somebody
6 much older than myself. So, I'm a nurse, and I
7 knew better. I used to be a critical care nurse.
8 And I did put my head in the sand, and I did not
9 look on the Internet. Sometimes, after my husband
10 would go to bed, I would sneak on and like look
11 some things up and get really afraid.

12 But my mission at this point is, I
13 turned everything around. And how I turned
14 everything around is, about a year ago, I met a
15 wonderful couple at Partners in Parkinson's, the
16 Michael J. Fox event in New York City. And I met
17 a couple that lived near me. And we formed a
18 support group that has over 65 members of young
19 onset. And it is one of the most significant
20 things I've ever done in my life.

21 And I now know that it's very important
22 to be in a support group. It's very important to

1 talk about this. And now my flyer is in a
2 neurologist's office so that when somebody else is
3 diagnosed like myself, they're given the
4 information and they're given the direction to go
5 into.

6 And two more quick things. The face of
7 Parkinson's is not really apparent because there
8 are men that are worried about losing their jobs,
9 men and women. And there's fear in coming out
10 about it. So I think there's a lot of issues
11 around young onset Parkinson's. That's what I
12 want to say.

13 Oh, and then one other thing. One of my
14 members contacted me that he was -- his wife asked
15 for a divorce. And she said that Parkinson's
16 treatment is too expensive, and she wants to
17 protect her assets. And so there's a lot of work
18 to be done with the young onset Parkinson's.
19 Thank you.

20 MS. VAIDYA: Thank you, Lynn.

21 Last, we have Charles Linderman.
22 Charles, where are you? Oh, here.

1 MR. LINDERMAN: Back here with the jet
2 pack on.

3 MS. VAIDYA: I see you.

4 MR. LINDERMAN: I hope the FDA leaves
5 here with at least one clear message, that for the
6 people that have spoken today, from the male side,
7 exercise is highly important. And I would hope
8 that if -- that in addition to all the drug
9 therapies that you're working on, that you come
10 out with some kind of clear protocol by which the
11 neurological providers can look somebody in the
12 eye and say, "This is what you need to be doing in
13 terms of exercise to reduce the effects of this
14 long-term degenerative disease."

15 And don't give me the line and malarkey
16 that I've heard other -- Dr. Shulman over at the
17 University of Maryland -- that you can choose any
18 kind of exercise you want so long as you enjoy it.
19 But rather, let's be specific and tell people what
20 exercises, what kinds, what intensity will provide
21 for the results that will give them relief and
22 give them a longer life.

1 That, to me, is something you can do
2 without a great deal of cost to the government.
3 And I certainly am encouraged by what I've heard
4 from La Jolla this afternoon. And I want to talk
5 to you guys afterwards.

6 But let's focus, since cures seem a ways
7 away yet, let's focus on what will help life
8 rather than getting down into the microcosms and
9 micro levels of genetics and other things, where
10 it would seem you're simply splicing cells further
11 and further and getting no closer to a result that
12 will help all of us.

13 Thank you for this forum. I've
14 appreciated it.

15 MS. VAIDYA: Thank you, Charles.

16 So, finally, I'd like to ask everyone to
17 please leave the clickers on the tables before you
18 leave. We'll pick them up afterwards. Also the
19 evaluation forms, you can leave them on the table
20 or outside at the registration table, and we'll
21 pick them up later.

22 So lastly, could I please call Dr. Eric

1 Bastings to the stand for our closing?

2 DR. BASTINGS: Yes, good afternoon. So
3 I'm Eric Bastings. I'm the Deputy Director of the
4 Division of Neurology Products and the Office of
5 New Drugs at the FDA.

6 I want to thank all of you for
7 participating in the discussion this afternoon,
8 and for sharing your personal experience with
9 Parkinson's. There is really no substitute for
10 hearing directly from you about the disease, about
11 how it impacts your life, and about what aspects
12 of the disease you believe new treatments should
13 be targeted to.

14 So there was a lot of information that
15 was shared this afternoon. And I will try to take
16 the next few minutes to summarize some of the key
17 information that I've heard.

18 In terms of symptoms, persons with
19 Parkinson's experience a variety of symptoms. But
20 the most disabling reported by many is the off-
21 time, and in particular, the unpredictability of
22 the off-time, and as a consequence, the fear of

1 falling and having difficulties moving and being
2 stuck somewhere while you experience off-time.

3 Another big problem is, of course,
4 dyskinesia that comes often as a complication of
5 the various treatments.

6 In addition to the various motor
7 symptoms, a lot of you mentioned the nonmotor
8 symptoms of Parkinson's. And in particular, sleep
9 is a problem for many people. Cognitive
10 difficulties and memory loss are experienced by
11 about 30 percent of people with Parkinson's. And
12 it's certainly an important area to target for new
13 therapies.

14 We heard of other symptoms, such as
15 constipation and fatigue, and also depression and
16 anxiety, which can be the result of some of the
17 symptoms or could be related to Parkinson's by
18 itself.

19 We also heard about sexual dysfunction
20 and the impact on relationships of the disease.
21 And we are aware of the impact of Parkinson's on
22 your life, how it robs your identity, the impact

1 it can have on your ability to drive a car, and
2 the fear of losing your independence. So we
3 certainly got the message for all of that.

4 In terms of treatment, we discussed a
5 number of nondrug therapies, and we certainly got
6 the message that exercise is very important. We
7 heard bicycle exercising is an option that's done
8 by some of you. But certainly, various forms of
9 exercise have been very useful to many of you.

10 Other nondrug treatment, hearing that
11 yoga, support groups are very important. And most
12 of you make a lot of use of these groups. And I
13 really can see the impacts that it can have on
14 your lives. Meditation, counseling, massage are
15 other options.

16 In terms of treatment, many of you take
17 a large number of drugs -- 15, 20, sometime more.
18 And I hear some of you take it as often as every
19 hour, sometime maybe three hours. But I hear it's
20 very difficult to keep a routine of using these
21 various drugs and make sure you have the drug
22 available if needed.

1 So in terms of perfect treatment, beside
2 a cure, which is certainly the goal that we all
3 share, and I hope we get there -- beside a cure, a
4 very important option would be to have a treatment
5 that you take just once a day that controls most
6 of your symptoms without too many side effects and
7 without the fluctuations that you experience and
8 without the off periods. So less-frequent
9 treatments with fewer side effects are certainly
10 desired by many.

11 I heard suggestion to have a dosage
12 form, again that allows fewer dosing times. So
13 it's really a common theme, having a treatment
14 that you don't have to take every hour or every
15 three hours and that works around the clock.

16 So again, I want to thank all of you for
17 coming today. I think the feedback you gave us is
18 invaluable. And I can assure you that the FDA
19 team here will continue to do everything it can to
20 support the research and the identification of new
21 drugs for the treatment of Parkinson's. So, thank
22 you for coming.

1 (Applause.)

2 (Whereupon, the FDA Public Meeting of

3 Patient- Focused Drug Development was

4 adjourned.)

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19


20

21

22

1 CERTIFICATE OF NOTARY PUBLIC

2 I, MICHAEL FARKAS, the officer before whom the
3 foregoing proceeding was taken, do hereby certify
4 that the proceedings were recorded by me and
5 thereafter reduced to typewriting under my
6 direction; that said proceedings are a true and
7 accurate record to the best of my knowledge,
8 skills, and ability; that I am neither counsel
9 for, related to, nor employed by any of the
10 parties to the action in which this was taken;
11 and, further, that I am not a relative or employee
12 of any counsel or attorney employed by the parties
13 hereto, nor financially or otherwise interested in
14 the outcome of this action.

15 

16
17 MICHAEL FARKAS
18 Notary Public in and for the
19 State of Maryland
20

21 My commission expires: 6/27/2018

22 Notary Registration No.: 256324

<hr/> <p style="text-align: center;">\$</p> <hr/> <p>\$2 169:2</p> <hr/> <p style="text-align: center;">1</p> <hr/> <p>1 2:7 3:8,9,10,11,12,13 ,14,15 6:2,15 7:14 22:4 26:15 32:2 35:15 97:8 140:10</p> <p>1,700 165:10</p> <p>1.5 144:4</p> <p>10 22:7,10 46:15 56:14 76:3 95:17 117:6 154:1 168:11</p> <p>10,000 164:6</p> <p>100 85:7 127:16</p> <p>107 3:18</p> <p>10903 1:14</p> <p>10-minute 95:16</p> <p>10-step 89:2</p> <p>11 73:18,22</p> <p>113 3:19</p> <p>119 4:4</p> <p>12 37:7,19</p> <p>126 4:5</p> <p>14 60:2 159:20</p> <p>15 3:6 22:10 36:4 37:8,19 58:16 60:4 163:4 176:17</p> <p>150 164:2</p> <p>16 18:21 46:14</p> <p>162 4:6</p> <p>17 40:21 164:14</p> <p>170 163:21</p>	<p>174 4:7</p> <p>18 117:9</p> <p>1960s 24:4</p> <p>1964 66:21</p> <p>1967 66:16,21</p> <p>1990s 167:10</p> <hr/> <p style="text-align: center;">2</p> <hr/> <p>2 3:16,17,18,19 4:4,5 6:4,16 27:4 32:2 89:3 96:1,2 161:7</p> <p>20 3:7 17:22 18:3 64:19 73:7 100:10 163:3,4 167:14 176:17</p> <p>200 29:15</p> <p>2000s 167:10</p> <p>2004 79:16</p> <p>2005 36:22</p> <p>2007 126:21</p> <p>2008 48:19 107:8 156:20</p> <p>2010 127:7,14 138:6 169:21</p> <p>2012 107:6</p> <p>2015 1:8</p> <p>20-30 137:9</p> <p>20903 1:15</p> <p>22 1:8</p> <p>22nd 127:14</p> <p>23 56:16</p> <p>23andMe 165:7</p> <p>24 57:1 117:13</p> <p>25 45:5 67:13 85:6 129:9</p> <p>25-100 128:16</p>	<p>129:8</p> <p>256324 179:22</p> <p>25-slash-100 36:10</p> <p>25-year 68:3</p> <p>26 3:8</p> <p>2A 47:10</p> <hr/> <p style="text-align: center;">3</p> <hr/> <p>3 89:3</p> <p>3:05 95:18</p> <p>3:25 95:19</p> <p>30 34:7 42:3,8 57:3 92:15 93:18 116:18 121:9 139:15,16 175:11</p> <p>300 164:15</p> <p>301 1:16</p> <p>30s 49:11</p> <p>30-year 116:13</p> <p>32 78:9</p> <p>33 56:12</p> <p>35 3:9 113:15</p> <p>36 33:20 64:16 117:13</p> <p>39 3:10</p> <hr/> <p style="text-align: center;">4</p> <hr/> <p>4,500 18:11</p> <p>40 18:9 22:11 34:8 64:17 130:8</p> <p>40s 49:11 119:6</p> <p>41 34:8</p> <p>45 71:5</p> <p>48 3:11</p> <p>49 40:20</p>	<hr/> <p style="text-align: center;">5</p> <hr/> <p>5 3:4 129:11</p> <p>50 34:8 37:2 159:20</p> <p>50s 49:11</p> <p>51 34:8</p> <p>51-to-60 34:13</p> <p>52 3:12 159:21</p> <p>54 119:4</p> <p>55 64:14,15</p> <p>56 3:13</p> <p>57 113:13</p> <hr/> <p style="text-align: center;">6</p> <hr/> <p>6/27/2018 179:21</p> <p>60 34:8 77:21 143:11</p> <p>60s 22:9</p> <p>61 34:8</p> <p>61-to-70 34:12</p> <p>63 35:8 48:17</p> <p>65 83:9 170:18</p> <p>67-year-old 126:18</p> <hr/> <p style="text-align: center;">7</p> <hr/> <p>7 3:5 113:19</p> <p>70 34:8</p> <p>71 34:9 36:3</p> <p>72 67:12</p> <p>75 33:9</p> <p>79 3:14</p> <p>796-9018 1:16</p> <hr/> <p style="text-align: center;">8</p> <hr/> <p>8:57 1:9</p> <p>80 22:7 35:9</p>
---	---	--	---

<p>81 53:10 83 3:15 84 54:2 88 58:17</p> <hr/> <p style="text-align: center;">9</p> <hr/> <p>9,000 165:10 90 84:14 130:7 95 3:16 97 3:17</p> <hr/> <p style="text-align: center;">A</p> <hr/> <p>a.m 1:9 aberrant 122:20 ability 25:18 26:20 42:16 54:3 59:3,12 60:18 138:15 157:15 158:6 176:1 179:8 able 20:10 30:10 43:13 44:14 57:17 61:7 71:11 89:1 113:4 130:9 132:1 134:7 154:8 157:19,21 158:1 abnormal 23:18 63:18 absent 81:17 absolutely 12:2 109:7 absorption 73:5 academia 14:16 31:16 accentuated 77:17 accept 16:18 46:7 Acceptance 115:2</p>	<p>access 104:17 140:8 accessible 98:15 acclimate 82:9 accurate 179:7 accurately 108:9 aches 55:16,17 aching 51:21 acquiesce 117:19 across 17:5 act 52:8 97:7 130:1 action 41:3 99:7 179:10,14 active 109:15 113:4 114:13 156:20 activities 26:20,21 37:5 54:4 55:21 80:8 81:18,19 103:21 129:16 132:12 158:12 activity 73:3 109:20 112:6 actual 68:11 110:9 165:17 actually 24:16 34:14 57:22 59:14 68:20 69:1,2 74:11 78:14 88:1,4,15 89:22 94:15 107:7 109:10 121:20 122:19 129:5 135:18 136:3 142:17 143:19 149:5,15 153:8 165:10 168:18 acupuncture 114:8 add 19:15 91:6,18 122:14</p>	<p>added 55:20 129:2 addictive 102:10 adding 52:6 122:16 addition 60:2 64:10 109:14 110:5 112:3 124:6 134:11 165:5 170:2 172:8 175:6 additional 19:15 30:11,20 32:4 73:14 102:20 129:1 address 13:20 38:12 39:1,15 75:3 76:21 83:13,19 87:21 104:16 106:6,7 134:7 160:21 161:4 addressed 78:3 96:8 124:21 adhere 138:15 adjourned 178:4 administer 98:5 Administration 1:2,12 102:17 admired 105:12 adopted 101:20 advanced 11:19 23:16 24:12 advances 100:5 adventure 131:18 advise 96:15 advised 129:15 advocate 41:2 49:2 53:1 66:11 113:11 117:3 advocates 61:21</p>	<p>98:16 105:12 aerobic 128:12 132:8 Affairs 31:1,4 affect 12:13 26:19 27:2 41:17 80:8 88:21 112:10 affected 17:5 51:15 59:13,19,21 103:22 affecting 158:2 affects 16:16 17:12 22:4 44:8,18 49:14 73:4 97:16 103:6 afraid 170:11 aftereffects 83:20 afternoon 1:6 3:3 4:3 5:2,17 7:12,18 8:8,18 9:17 11:6 19:5 48:16 79:13 83:8 144:20 154:20 159:4 173:4 174:2,7,15 afterwards 173:5,18 against 59:2 71:15 age 22:11 34:7,13,15 35:9 42:3,8,17 53:10 54:1 56:22 aged 40:21 agencies 31:17 99:6 agenda 3:2 4:2 5:15 16:2 agents 24:14,20 160:13 ages 44:19 159:20</p>
---	---	--	--

<p>aggressive 126:5,6 aggressively 145:11 aging 49:9 133:15 ago 12:4 18:8 34:17,18,19 35:2,3 45:5 53:7 57:13 76:3 83:10 107:6 113:14 116:14 119:13 132:5 144:4 152:5 170:14 agonists 24:15 110:19 122:16 125:8 ahead 5:4 13:19 90:9 139:4 168:21 aid 85:17 aids 84:21 aimed 37:20 Aimes 156:11,14,16,18 158:21 airline 102:22 Alabama 100:20 alarm 136:1 Alberts's 128:8 Alexandria 75:3 Alice 73:17 alike 43:2 44:17 79:22 all-adaptive 76:7 alleviate 55:21 60:21 101:15 108:11 Alliance 98:17 allow 16:10 17:7</p>	<p>99:20 160:13 allowed 108:12 allowing 97:9 113:6 allows 17:18 82:7 84:13 101:5 177:12 alone 50:15 alongside 97:11 already 9:15 11:9 20:15 30:21 31:5 33:4 74:9 117:8 126:2 165:11,14 alternative 75:14 100:15 116:1 alternatives 44:4 105:22 110:18 altogether 81:4 100:10 am 38:6 39:10 46:12 48:17 49:2 55:7 58:8 59:10 69:14 75:2 105:5,11 113:20 114:17 118:1 119:4 126:18 142:17 145:8 156:18,19,20 163:16 173:3 179:8,11 amantadine 24:21 37:3 46:1 47:4 108:17 amazed 74:11 amazing 46:11 Amazon 41:1 Ambien 84:11 American 73:19 Americans 53:3</p>	<p>Amitiza 83:21 among 67:21 amount 24:18 37:1 62:8 98:1 amounts 58:10 147:12 analyze 20:11,22 and/or 90:4 and-a 129:7 Angela 88:12 angry 137:17 animal-model 128:11 animals 14:2 ankle 128:21 annoyance 50:7 annoying 41:14 128:4 answer 29:5 37:15 47:5 55:6,11 67:15 answering 28:20 answers 55:4,6 anti 129:6 131:7 antibodies 14:1 anticholinergics 24:21 antidepressants 25:3 anti-inflammatory 109:3 antioxidative 109:2 anxiety 23:14 25:5 43:20 50:17 53:12 59:16 63:22 89:9 98:1 175:16</p>	<p>anxiolytics 25:4 anxious 60:15 anybody 6:13,14 30:18 67:8 136:20 165:12 anymore 72:3 anyone 50:7 136:17 147:22 150:10 152:3 anyplace 50:20 anything 30:9 32:1 40:12 59:14 87:16 93:10 129:18 143:16 155:4,9 anyway 72:7 120:17 143:18 Apokyn 36:15 apoptosis 23:4 apparent 82:4 171:7 apparently 140:2 appear 94:4 appeared 56:15 applaud 156:22 applause 62:5,6 133:20,22 162:8,11 169:15 178:1 application 17:20 117:13 applications 13:15 apply 135:3,7 154:17 appointment 51:14 158:3,4 appreciate 5:12 39:19 82:17</p>
--	---	--	---

<p>85:21 118:17 169:13</p> <p>appreciated 173:14</p> <p>approach 14:10 44:7 168:14</p> <p>approached 101:8</p> <p>approaches 6:5 19:13 27:4 96:2 97:14</p> <p>appropriately 143:21</p> <p>approval 14:6</p> <p>approve 136:15</p> <p>approved 11:15 24:10 25:2 74:10 103:11 142:20</p> <p>approximately 22:4 113:19</p> <p>April 127:14</p> <p>area 7:2 10:21 15:17 18:4 32:19 33:11 37:22 53:4 73:7 75:14 109:7,11 170:4 175:12</p> <p>arenas 72:8</p> <p>aren't 89:14 96:8 108:9 114:14 158:8</p> <p>argument 36:16</p> <p>Arizona 156:19</p> <p>Arkansas 83:11,12</p> <p>arm 85:8,10,12,16 121:9</p> <p>arms 46:6</p> <p>art 101:8</p> <p>asleep 23:17,18 63:18 104:3</p>	<p>aspect 59:20 125:12</p> <p>aspects 20:5 31:22 44:12 136:22 174:11</p> <p>aspirin 65:22</p> <p>assets 171:17</p> <p>assignment 104:8</p> <p>assist 104:18</p> <p>assistance 48:10 57:18</p> <p>associated 12:19 50:18 75:9 89:12</p> <p>Association 73:20</p> <p>assure 75:10 177:18</p> <p>Atomoxetine 150:19</p> <p>attack 60:17 130:18 142:8</p> <p>attacks 52:2</p> <p>attempted 155:8</p> <p>attempting 41:4,19</p> <p>attend 56:21 99:4</p> <p>attending 132:13</p> <p>attention 50:6 74:2 82:20 87:7,11</p> <p>attentive 86:20</p> <p>attorney 59:8 179:12</p> <p>audible 156:7</p> <p>audience 6:13 28:9 62:12,20 64:22 126:12 136:19 146:6</p> <p>authentically 21:3</p> <p>author 41:1</p>	<p>authorities 160:4</p> <p>authorization 18:2</p> <p>autonomic 49:15 94:9</p> <p>avail 10:17</p> <p>available 7:6 9:12 11:21 16:16 17:13 24:6 31:8 65:21 130:19 176:22</p> <p>Avenue 1:14</p> <p>avenues 111:20</p> <p>average 22:8 72:1</p> <p>avoid 33:3</p> <p>awake 127:12</p> <p>awakening 103:6</p> <p>awarded 101:17</p> <p>aware 22:2 26:2,3 43:3 86:18 139:19 175:21</p> <p>Awareness 91:2</p> <p>away 53:7,19 131:4 147:20 153:3 173:7</p> <p>awhile 91:11 146:16 151:10</p> <p>awkward 44:20</p> <p>Azilect 108:17 114:3</p> <hr/> <p style="text-align: center;">B</p> <hr/> <p>back-and-forth 141:3</p> <p>backed 119:15</p> <p>background 3:7 5:20 12:5 21:17 22:1</p> <p>bacteria 70:5,8,14</p>	<p>bad 54:16 55:16 61:3 80:12 88:5 95:1 133:1,2 137:20 138:18</p> <p>badly 127:7</p> <p>balance 36:8 38:14 41:10 42:13 44:9 45:2,7,16 47:3,4 49:10 63:16 64:7,18 126:22</p> <p>balancing 43:10,18</p> <p>based 55:8 98:18</p> <p>basic 7:5 44:7 61:5</p> <p>basically 119:19 158:2</p> <p>basis 46:8 83:14 84:12 158:15 164:9 169:1</p> <p>basket 67:17</p> <p>Basset 103:18</p> <p>Bastings 2:8 4:7 7:18,19 174:1,2,3</p> <p>batch 47:17</p> <p>bathing 54:4 55:20</p> <p>bathroom 57:22 149:19,20</p> <p>bathrooms 6:22</p> <p>battery 120:10 152:13 153:12</p> <p>beautiful 101:11</p> <p>became 53:19 54:2 107:17</p> <p>Becky 3:13 56:10,11 62:3,22 82:1 89:9</p> <p>become 41:9,22 50:8,10 56:1 94:10 112:22</p>
--	--	--	--

<p>139:9 becomes 60:17 103:19 110:9 becoming 41:11 81:6 bed 57:16 71:18 81:10 149:14 170:10 bedtime 139:8 begin 82:4 85:11 105:14 110:12 124:12 149:15 beginning 57:1 65:15 80:11 124:2 129:13 begins 98:12 108:2 behalf 5:9 33:8 53:5 67:11 126:10,11 161:9 behavior 122:20 144:8,15 behaviors 102:10 110:22 believe 42:10 84:1 95:2 104:16 113:3 116:6 125:1 163:4 169:7 174:12 believer 100:16 believing 101:21 belong 70:6 beneficial 19:6 108:19 109:13 121:21 123:11 benefit 16:13 17:1,2 24:19 25:7 43:6 110:14 153:3 benefits 12:10,15</p>	<p>16:8 109:4 137:18 153:13 Benny 103:18 Bergman 2:10 8:5 beside 177:1,3 besides 154:7,14 best 12:20,22 42:9 44:4 97:8 106:11 110:14 114:11 179:7 bestselling 41:1 beta-oscillation 123:17 124:3 better 16:20 19:18 24:5 42:7 43:9 46:19 56:7 66:20 70:15 96:19 104:7,14 106:6 112:1 132:15 133:8,9,13,14 135:6 141:10 143:14 155:16 167:9 170:7 beyond 113:5 131:14 160:20 bicycle 176:7 bicycling 128:10 130:20 biggest 27:12 61:7 bike 130:5 biking 130:14 Bill 4:5 126:16,17 133:19 142:4 Billy 7:16 9:22 10:8 15:9 87:14 biochemical 123:19 biofeedback 114:8 153:10</p>	<p>Biologics 2:13 8:20 biomarkers 108:5 Biotene 129:22 Birmingham 100:20 bit 12:4 22:20 28:20 29:6 32:22 37:4 85:20 87:9 134:18 149:10 153:16 159:14 160:20 163:17 blank 54:20 bleeding 123:14 blessing 145:17 blind 52:3 blocker 150:13 blocks 51:9 107:18 blogger 41:1 blood 91:8,11,20,22 95:11 146:11 147:4 148:5,22 149:7 board 41:2 77:15 body 43:8,10 44:1,2,8 49:16 55:16,17 58:4 60:17 69:19 85:3 94:6 114:13 122:10 145:9,12 bold 39:16 book 130:19 born 66:21 bothered 120:21 bothers 72:19 91:8 bothersome 69:9,10 80:1 bowel 111:4</p>	<p>box 138:12 BP 101:1 braced 149:4 bradykinesia 52:10 80:14 120:19 brain 24:15,18 36:18,21 50:3 57:5 61:17 99:22 133:8 bread 104:4 breadth 10:11 break 6:17 39:6 95:16 163:2 breakdown 24:17 breakfast 77:2 breaking 39:5 breathe 60:18 breathing 80:15 briefly 21:22 22:21 24:2 43:18 150:9 166:13 brilliant 48:21 Brind 70:1,13 bring 13:19 50:16 71:7 74:20 bringing 14:10,12 69:15 95:13 brings 114:20 168:7 broad 15:5 76:22 broaden 28:7 broader 17:10 151:17 broadly 165:18 broken 81:10 brothers 65:8</p>
---	--	--	--

<p>brought 46:10 62:18 86:3 145:15</p> <p>Bruce 101:12</p> <p>bucket 168:18</p> <p>build 18:18 21:9 28:9 61:18 141:18</p> <p>built 99:10</p> <p>bullet 71:9</p> <p>Burk 67:12</p> <p>bursa 85:14</p> <p>button 120:2</p> <p>buzz 32:22</p> <p>Bye-bye 82:20</p> <hr/> <p style="text-align: center;">C</p> <hr/> <p>cabinet 49:20</p> <p>cadence 130:7</p> <p>calcium 130:22 150:13</p> <p>California 142:18 160:7 166:9</p> <p>Californian 122:3</p> <p>caller 92:3,12 156:6,9 159:2</p> <p>callers 92:2</p> <p>calories 58:16</p> <p>calves 51:21</p> <p>campus 1:13 15:10</p> <p>cancel 54:8 60:14</p> <p>cancer 125:19</p> <p>candidate 122:10</p> <p>Cannon 87:19 139:22 163:11 165:3,4</p> <p>capably 97:13</p>	<p>CAPCALA 2:11</p> <p>Capital 1:21</p> <p>Capitol 37:22</p> <p>capture 21:4</p> <p>car 50:20 52:6 176:1</p> <p>carbidopa 24:5 85:5 129:2,8,9 142:20</p> <p>carbidopa- levadopa 24:11 100:12 110:7 114:2 128:16 129:5 135:14 136:13 143:10</p> <p>care 11:1 44:14 47:14 61:12,15 82:8 88:16 93:11 155:20 170:7</p> <p>careful 149:11</p> <p>caregiver 25:19 33:5,7 47:14 65:13 88:3,13</p> <p>caregivers 6:14 27:17 28:9 29:2 30:19 31:12 32:17 62:12 64:22 88:21 165:1</p> <p>caregiver's 19:12</p> <p>caring 53:9</p> <p>Carl 156:14,15 158:17</p> <p>carry 52:17 166:19</p> <p>carrying 49:19</p> <p>Carter 92:8</p> <p>case 79:22 90:19 102:21 108:9 143:6</p>	<p>cases 90:18 111:4 167:15</p> <p>cast 136:18</p> <p>casual 52:4</p> <p>CAT 107:22</p> <p>categories 23:6</p> <p>category 100:15</p> <p>causative 22:13</p> <p>cause 40:12 59:1 81:14,15 84:7 160:4,11</p> <p>caused 23:3 51:21 52:1 107:16 110:11 137:17 141:22</p> <p>causes 116:16</p> <p>causing 58:22 77:16</p> <p>CDER 16:6 17:17 31:2</p> <p>CDR 16:7</p> <p>CDRH 16:7</p> <p>celebrated 48:22</p> <p>cell 8:20 23:3 116:12,19,20 117:5,6,12,16 166:9,11 168:4 169:10</p> <p>cells 23:2 116:9,11,15,16 166:14,16,17,21 167:5 168:19 173:10</p> <p>center 8:13,15,19 31:3 70:2,13 91:12 146:20</p> <p>centering 43:10</p> <p>centers 16:7 100:19</p>	<p>central 2:13 148:16</p> <p>certain 12:19 26:20,21 41:16 133:1</p> <p>certainly 33:5 65:1 68:2 133:4 141:10 173:3 175:12 176:3,5,8 177:2,9</p> <p>CERTIFICATE 179:1</p> <p>certified 105:18</p> <p>certify 179:3</p> <p>cervical 90:14</p> <p>cetera 80:16 143:21 168:16</p> <p>chairman 77:14</p> <p>Chalasani 2:14 9:3</p> <p>challenge 45:12 69:14 71:3,6</p> <p>challenged 114:13</p> <p>challenges 45:15 49:13 157:10</p> <p>challenging 41:12</p> <p>chance 69:1 118:11 161:18,20 169:9</p> <p>change 35:20 45:20 52:12 60:6 65:17,18 73:14 118:14 140:15 141:6,16 152:8</p> <p>changed 27:1 100:9 102:6 119:13</p> <p>changes 36:6 41:21 107:14 112:21</p> <p>changing 140:21 141:20</p> <p>channel 150:13</p>
---	--	---	---

<p>chaotic 127:12</p> <p>chapter 130:18</p> <p>Charles 75:2 163:12 171:21,22 173:15</p> <p>Charlie 76:10,11 146:2</p> <p>check 76:12 135:3,7 154:17</p> <p>checked 149:7</p> <p>checking 29:19 147:5</p> <p>checklist 102:16</p> <p>chest 75:11 152:13</p> <p>Chi 101:7,17 106:1 109:16 130:11</p> <p>Chicago 53:4</p> <p>children 56:2 65:13 115:7 118:6</p> <p>chin 75:11</p> <p>chiseled 102:2</p> <p>choice 118:11</p> <p>choir 136:12</p> <p>choose 63:14 98:10 117:21 172:17</p> <p>chopsticks 54:13</p> <p>chores 44:15</p> <p>chose 64:10</p> <p>chosen 75:20</p> <p>chronic 83:17</p> <p>Chuck 3:14 79:6,8,10,11,15 82:21</p> <p>church 71:18</p> <p>circumstances 81:13</p>	<p>city 138:18 170:16</p> <p>classic 107:10 108:3</p> <p>classically 23:7</p> <p>Claudia 67:4</p> <p>claw 121:10</p> <p>clear 14:5 52:16 55:5 172:5,10</p> <p>clearly 94:4 108:18 134:4 145:10 166:2</p> <p>Cleveland 128:9</p> <p>clicker 63:7</p> <p>clickers 29:1,4 134:20 154:14 173:17</p> <p>clinic 128:9 142:18 143:22 168:3</p> <p>clinical 7:22 8:6,15 13:10 16:12 21:12 48:22 70:21 99:16 109:11 123:16 127:20</p> <p>clinician 25:20 142:17</p> <p>clock 115:17 136:1 177:15</p> <p>close 20:7 46:11</p> <p>closed 15:18 51:11 58:7</p> <p>closed-loop 153:7</p> <p>closely 13:16 14:9 168:3</p> <p>closer 173:11</p> <p>closest 82:11</p> <p>closing 4:7 6:21 82:17 174:1</p>	<p>closures 15:16</p> <p>clothing 160:9</p> <p>cocktails 122:15</p> <p>coconut 129:14</p> <p>cognition 49:14 99:22 122:9 132:21 150:20</p> <p>cognitive 55:3 57:7 59:6,15 63:19 64:16 76:21 89:16 94:8 175:9</p> <p>cold 91:13 146:20</p> <p>collaboratively 87:10</p> <p>colleague 5:7</p> <p>colleagues 5:10,18 7:11 8:22 26:11 95:22 97:17 119:18 136:4 161:9</p> <p>collect 16:21 17:4 20:21 21:11</p> <p>collected 163:1</p> <p>collection 164:19</p> <p>collectively 68:19</p> <p>college 83:12 93:8</p> <p>coma 94:17</p> <p>combination 24:8</p> <p>combinations 131:12</p> <p>comes 17:20 80:20 90:18 175:4</p> <p>comfortable 7:9 28:16</p> <p>coming 42:15 51:11 62:9 76:13 138:10 162:14 171:9 177:17,22</p>	<p>comment 6:11,12,17 30:18 32:3 67:9 68:9 73:13 74:22 76:16 140:17 144:3 146:4,11 148:12 153:17,18 162:15,22 163:5,9 164:10 165:21</p> <p>commentary 10:18</p> <p>commented 80:10</p> <p>commenters 153:20</p> <p>comments 4:6 9:9 14:22 15:2,5,8 18:11,12 29:22 30:13,17 40:5,6,14 76:2,13,15 78:14 90:7 96:7 97:4 110:2 153:21 161:11,14 162:17</p> <p>commission 179:21</p> <p>committed 17:21</p> <p>committee 97:9 113:17</p> <p>common 19:10 23:19 78:2 177:13</p> <p>communities 13:13</p> <p>community 14:12,19 46:11 48:9 68:18 75:8 78:13 97:13 98:13 126:7 156:21 164:6 165:9,16 169:3</p> <p>Como 2:12 8:14 151:18</p> <p>companies 13:9,12</p>
--	--	---	---

<p>14:8 17:16 47:18 84:11</p> <p>company 1:21 138:11</p> <p>comparatively 132:3</p> <p>compared 132:5</p> <p>compete 76:7</p> <p>complementary 98:10</p> <p>complete 59:17 89:5 111:22</p> <p>completed 117:9</p> <p>completely 29:8 120:7 148:6</p> <p>completing 59:14</p> <p>complex 63:20 158:19</p> <p>complexities 125:2</p> <p>complexity 96:5</p> <p>complicated 22:20 39:7</p> <p>complication 152:10 175:4</p> <p>complications 151:21</p> <p>component 90:4 147:3</p> <p>compulsive 102:10 110:22</p> <p>computer 126:18 127:8 131:22 142:7</p> <p>COMT 24:19</p> <p>concentrating 63:20</p> <p>concentration 59:12</p>	<p>concern 61:7 68:17 123:10</p> <p>concerned 86:19</p> <p>concerning 87:2</p> <p>concerns 68:11 121:17 139:13</p> <p>concluded 161:6</p> <p>concrete 51:9</p> <p>condition 11:13,21 45:7,8 51:16 52:11,15 55:3 96:6 103:10 110:15 116:2 134:3 155:2 162:10</p> <p>conditions 102:21 133:2</p> <p>conduct 13:14</p> <p>confidence 44:1</p> <p>confidential 13:7</p> <p>confined 60:12</p> <p>Connected 98:16</p> <p>Connecticut 98:18 101:16</p> <p>cons 141:5</p> <p>conscious 52:2</p> <p>consequence 174:22</p> <p>consequently 116:20</p> <p>consider 12:20 63:11 74:18 87:9 118:12 123:7</p> <p>consideration 17:19 68:21 92:21</p> <p>considered 14:2 50:21 121:18</p>	<p>consistent 165:15</p> <p>consists 129:7</p> <p>constant 83:17 85:15</p> <p>constantly 111:6</p> <p>constellation 125:2</p> <p>constipation 53:12 54:8 63:17 76:17 83:15,16,17 84:7 111:5 175:15</p> <p>constipation- diarrhea 72:20</p> <p>Constituent 30:22</p> <p>consultant 168:22</p> <p>consultation 129:21</p> <p>consulted 131:1</p> <p>consulting 17:16</p> <p>contact 31:1 117:18 165:13</p> <p>contacted 171:14</p> <p>contain 21:3</p> <p>Cont'd 4:1</p> <p>context 16:12 88:3 134:18</p> <p>continence 147:15</p> <p>continue 7:10 30:12 36:15 61:20 102:2 115:2 177:19</p> <p>continued 61:2 130:5</p> <p>continues 47:1 160:12</p> <p>continuing 11:17</p> <p>contraption 75:6</p> <p>contribute 31:13</p>	<p>43:21 44:13</p> <p>contributes 51:18 52:9</p> <p>control 42:7 46:5 70:15 71:12 73:1 108:15 109:22 128:19</p> <p>controlled 85:4 114:4</p> <p>controlling 49:19 110:4</p> <p>controls 48:5 177:5</p> <p>conversation 55:8 124:17</p> <p>conversations 52:4 104:10 164:14</p> <p>cooking 146:19</p> <p>cool 120:15</p> <p>coordination 50:2 63:16 64:7 129:16</p> <p>coordinator 53:2</p> <p>cope 42:16 60:18</p> <p>corporate 59:8</p> <p>correct 155:20</p> <p>correctly 151:11</p> <p>cost 46:2 101:19 103:13 104:19 111:16,17,19 140:4,8 173:2</p> <p>couch 104:3</p> <p>counsel 99:11 179:8,12</p> <p>counseling 25:18 176:14</p> <p>counter 109:1</p> <p>counteract 52:14</p>
---	---	---	---

<p>counting 33:4 couple 55:10 90:7 94:16 119:17 128:17 130:4 144:19 149:5 154:3 155:22 168:15 170:15,17 courage 62:8 162:9 courageous 27:21 course 17:22 18:5,17 47:15 68:2 93:18 111:14 125:22 133:3 135:14 167:14 169:11 175:3 courtroom 36:14 cover 24:2 104:20 coverages 104:20 covered 105:19 covering 6:2 19:1 CR 24:7 141:11 cramped 57:21 cramping 107:17 cramps 90:13,14,15 107:19 130:17 131:3 crap 144:9 cream 58:19 create 46:22 creatively 42:19 creep 42:20 creeping 46:2 Crichton 121:19 cried 50:19 crippling 57:9</p>	<p>critical 16:13,22 170:7 crop 41:16 cross 36:15 crowd 10:4 crowds 43:20 51:15 crucial 43:12 cry 115:8 crying 118:7 cuff 147:4 cup 54:12 cure 12:1 19:21 20:2 48:1 62:2 93:17 95:4 99:9 111:22 112:16 115:22 118:16 126:1 167:6 177:2,3 cured 107:22 167:16 cures 126:3 173:6 curious 151:20 curl 121:9 current 6:5 19:13 27:4,6 65:19,21 96:9 97:13 125:4,7 131:8 132:10 currently 11:15,21 17:13 83:11,21 84:10 85:2 98:14 112:20 114:2 117:6 122:2 135:8 cut 84:15 153:18 cycling 105:22</p> <hr/> <p style="text-align: center;">D</p> <hr/>	<p>D.C 32:18,19 33:10 Dad 104:2 daily 6:3 10:20 12:13 26:1,19 35:16 41:18 46:8 54:4 63:12 83:14 100:2 102:3,19 109:16,20 111:3 114:1,9,10 130:6 157:10 164:8 Dan 3:9 35:17 38:22 39:18 76:2,19 77:18 81:12 dance 105:22 dangerous 44:5 122:18 data 164:19 database 130:10 157:18 daughters 159:20 Dave 2:6 7:21 137:13 Dave's 139:2 day 6:10,20 14:13 15:15,20 31:11 42:15 43:1,3,19 45:14,16 46:22 47:2 55:3 60:4 62:2 73:15 80:9,12 81:16 82:14 83:21 85:4,6 100:10 103:8,16 104:9 105:21 109:18 114:11,15,17,21 117:22 127:13 128:17,18 129:10,11 130:1 144:13 177:5 days 42:9,12</p>	<p>54:10,16 55:16 58:11 60:12 83:19 84:6,14 105:20 106:1 114:4,14 115:4,7 153:5 day's 82:11 daytime 51:17 80:2 day-to-day 158:12 DBS 37:9,10 38:12 57:5 58:15 60:20 66:1 94:19 119:12,17,18 120:7 121:3,17 122:1,12 123:3,11,13 124:13 151:19 152:1,5,22 153:4 dead 120:10,12 128:2 deal 20:6 26:1 57:6 59:7 166:3 167:4 173:2 dealing 157:13 dealt 42:18 death 23:4 81:14 116:17 157:7 debate 110:12 debating 141:4 debilitating 61:4 107:14,17 decade 100:3 102:7 145:8 decades 42:11 49:11 116:14 deceptively 49:8 decided 124:11 128:4 152:8 deciding 16:10</p>
---	---	---	--

<p>134:14 decision 16:14 42:4 76:4 121:2 161:12 decision-making 134:15 decisions 119:14 decline 70:20 declined 60:19 declines 82:13 decrease 139:16 decreasing 60:22 149:21 decrepit 121:11 dedicated 105:12 deduction 50:9 deep 57:4 106:9 164:3 deep-brain 25:8 deeply 59:4 deficits 49:8 define 23:7 definitely 60:19 142:22 143:7 definition 68:12 115:18 degeneration 23:2 53:22 degenerative 172:14 degree 13:8 97:21 98:2,4 delay 110:15 124:14,18 delays 102:22 delicate 45:16</p>	<p>delivering 105:15 delivery 141:9 delve 68:6 134:5 dementia 23:17 54:3 demonstrate 14:5 demonstration 119:10 120:19 denial 119:8 dentist 129:21 dependent 56:1 116:3 depressed 37:12 53:19 127:11 depression 23:13 25:5 63:22 78:1 175:15 Deputy 7:19 174:3 describe 67:22 120:16 140:14 describes 80:21 descriptions 154:10 desired 177:10 despite 80:7 105:2 127:4 dessert 58:20 detail 13:21 detect 87:2 detection 123:22 deterioration 82:10 determine 42:2 determining 99:1 detriment 122:21 develop 20:13 22:8,10 158:11</p>	<p>developed 20:15 53:20 85:13 107:12,15 123:6 130:17 131:5 developer 165:5 developing 14:14 56:7 development 1:3 5:19 10:7,20 11:11,18 13:3,17 15:6 16:1,5 17:17 20:5 21:10 26:7 82:19 113:17 178:3 developments 48:8 devices 2:12 8:16,17 39:15 DeWITTE 3:17 97:7 98:21 101:14 106:7,13 139:5 diagnose 108:5 diagnosed 33:15,19 34:22 35:2,8 36:3 40:22 48:19 49:17 53:9 56:22 57:10 68:15 70:17,20 76:4 79:19 83:10 92:16 93:2,7 107:5 108:1,9 113:13 119:5 138:5 144:20 151:9,12 156:19 157:6 169:21 171:3 diagnosing 92:17 133:11 diagnosis 34:17 44:21 45:1 51:2 53:13 57:13 68:11,22</p>	<p>70:12,21 71:10 105:15 113:5 127:20 144:21 148:19 dial-in 30:4 dialog 28:8 31:13 diarrhea 54:9 111:5 die 39:8 91:13 145:5 146:21 167:1 diet 25:16 43:5 71:13 84:1,3 97:22 dietician 131:1 difference 106:16 145:9 different 12:12 18:4 28:11 79:20 80:7,8 81:3 84:18 93:22 98:17 112:10,11 121:16 123:18 126:11 129:3 139:18 141:8,9 155:8 157:14 164:15 170:5 differentiate 108:6 differently 97:16 112:11 difficult 15:19 18:13 36:17 41:10 42:4,9 43:19 51:7 57:20 60:18 87:1 102:1 107:18 111:6 159:15 176:20 difficulties 20:4 57:8 58:1 59:6,16 175:1,10 difficulty 11:20</p>
---	---	---	--

<p>23:14,17 36:8 49:18 53:20 57:7,8,11,14 59:10 63:19,20,21 74:15 80:15 94:7,11,12 141:11 dig 153:22 digest 83:22 84:5,6 digestion 43:7 46:18 dinner 138:17 dire 48:10 direct 8:12 direction 171:4 179:6 directly 12:17 24:12 174:10 Director 7:13,17,19 10:8 31:3 160:6 166:9 174:3 directs 105:17 disability 147:12 disabling 174:20 discipline 101:20 disciplined 105:21 disciplines 104:13 disclose 163:16 discover 112:14 discovered 70:4,13 discovery 13:22 discuss 154:9 discussed 55:19 164:1 176:4 discussion 5:22 6:7,8 11:4,6 12:8 18:6 26:13 30:3</p>	<p>31:20 74:3 87:16 96:1,13 97:2,5 140:9 161:7,8 174:7 discussions 99:2 disease 3:3 4:3 5:20 10:7,12,16 11:2,5,13,15,19 12:5,16,20 14:19 16:3,14 17:5,11,12 18:4 19:3,9,12 22:1,9,12,17 23:3,7,16,19,20 24:13 25:13 27:5 28:4 33:15,20 35:22 42:1 44:20 45:21 46:10 48:11,18 49:2,6,7,14 51:4 53:2,4,6 54:1 55:11 56:5,14,22 57:4 59:21 60:11 61:8,10 63:11 68:12,14 73:20 74:8,12,16 80:6 81:22 87:13 89:22 90:5,17 93:9 94:21 95:3 96:3,18,19 97:14,16 99:8,21 100:4 102:5 105:2,4,9,16 108:2,5,16 109:4 112:9,18 113:18,19,22 114:1,7 115:22 116:8 120:21 121:16 122:10 124:10 125:3 126:3,20 128:13 132:9 135:3 136:22 152:17 153:13,14 154:17 157:8,11</p>	<p>159:5,20,21 160:5,11 166:14 167:1 168:10 169:7 170:1 172:14 174:10,12 175:20 disease/treatment 3:7 disease-free 119:19 disease-modifying 112:14 113:1 diseases 10:12 18:9,12,21 19:1 118:15 disease's 114:5 disease-specific 99:6 disexecutive 23:15 disheartening 100:5 dismissed 56:17 disorder 50:4 84:20 99:3 100:6 107:13 128:7,14 disorders 108:6 111:1 disruption 141:16,21 disruptive 77:3 distal 81:15 distant 54:20 distinguished 97:11,17 distribution 133:9,13 disturbances 80:5 diverse 17:10 division 2:4,6,8,12</p>	<p>7:15,17,20,22 8:3,10,16 10:9,10 19:16 174:4 divisions 18:8 divorce 171:15 dizziness 123:1 147:2 dizzy 91:14 146:22 149:2,20 DNA 166:19 DNA-matched 116:10 docket 20:8 30:7,8,12,19 32:4 160:22 161:18,20 163:20 164:21 165:7,12 doctor 36:18,20 55:19 69:21,22 90:22 130:20 152:7 doctors 35:20 37:16 48:21 56:16 84:10 90:11,20 93:3,11 107:21 142:5 157:20 doctor's 144:22 157:18 158:3,4 Doctors 131:2 document 165:11 documented 74:15 documents 21:6 done 11:9 20:19 71:1 75:7 76:6 104:8 143:16 146:9 150:15 167:4 170:20 171:18 176:7</p>
--	---	--	--

<p>doorway 149:20</p> <p>dopamine 23:2 24:14,15,17,18 110:19 116:16 122:16 123:3 124:12 125:7 145:10 166:22 167:20</p> <p>dopamine-producing 116:20 117:7 169:11</p> <p>dosage 42:12 45:22 102:10 145:17 177:11</p> <p>dosages 155:8</p> <p>dose 60:8 98:6 108:10 148:4</p> <p>dosed 143:2</p> <p>doses 122:14 141:6 148:9</p> <p>dosing 98:4 111:7 112:7 131:2 141:8 177:12</p> <p>double 33:3</p> <p>downs 38:3 61:17 114:16</p> <p>downside 132:10</p> <p>downsides 27:12 136:8</p> <p>downstream 122:10</p> <p>dozen 99:17 119:16</p> <p>Dr 2:4,5,6,7,8,9,10,1 1,12,13,14,17 4:7 7:12,13,16,18,21 8:2,5,8,9,11,14,1 8 9:1,3,22 10:1,8 12:3 15:4,9 16:5</p>	<p>21:19 36:18 40:11 86:13 95:20 98:22 106:3,12,19,22 113:7 115:11,13,15,17 118:19 119:1 126:15 128:8 133:19 134:1,22 135:11,22 136:10 137:4,7,10,11,13, 22 139:1,10,20 140:7 141:18 142:14 144:1 146:1,4,10 147:6,21 148:11 150:1,4,8,17,22 151:7,15,18 152:2,15 153:15 154:19 155:21 156:8,12,15,17 158:17,22 159:6,10,14,18 160:14 162:12 172:16 173:22 174:2</p> <p>dramatic 36:6 38:15 59:20</p> <p>draw 61:20</p> <p>dreaded 110:16</p> <p>dream 48:7</p> <p>dreaming 23:18</p> <p>dreams 52:8 63:18</p> <p>dressed 57:18</p> <p>dressng 54:4 61:6</p> <p>drink 147:12</p> <p>drinking 54:12</p> <p>drinks 7:5</p> <p>drive 82:12,14 127:9 131:22 176:1</p>	<p>driven 102:12</p> <p>driving 42:5 52:6</p> <p>drooling 63:22</p> <p>drop 91:12 95:11 126:22 148:22</p> <p>drops 91:9,21,22</p> <p>drove 77:14 121:2</p> <p>drug 1:2,3,12 2:7 5:19 7:14 10:7,20 11:11 12:11,18 13:3,12,15,16 14:8 15:6 16:1,4 17:3,17 18:1 74:5,6 82:19 96:15 111:8,13 113:17 122:18 135:2 143:7,21 148:17,18 149:22 150:5,7 154:15 165:5 167:16 168:17 172:8 176:21 178:3</p> <p>drugs 8:13 10:10,11 14:14 24:16 25:4 44:5,11 47:18,19 48:9 73:5 108:17 109:14 110:3 111:3,10,11,12 113:2 133:1 136:15 137:2,8,11 168:12 174:5 176:17,21 177:21</p> <p>dry 130:1</p> <p>due 66:3</p> <p>Duke 56:21</p> <p>Dunn 2:4 3:5 7:16 9:22 10:1,8 16:5 40:11 86:13</p> <p>duopa 24:11</p>	<p>136:16 137:5 139:12 143:17</p> <p>durability 123:12</p> <p>during 10:14 51:5 52:4 85:4 98:6 127:13 130:1 131:18 145:18 155:17 163:1</p> <p>dying 81:12 116:15 168:19 169:10</p> <p>dysfunction 51:17 78:11 88:19 89:17 175:19</p> <p>dyskinesia 36:11 37:3 42:14 45:9 47:16 57:7 58:8,13,18 59:1 60:22 61:3 67:18 80:3 102:9 110:8,16 151:5 152:6,12 155:11 175:4</p> <p>dyskinesias 24:22 45:9</p> <p>dyskinetic 58:21</p> <p>dyspnea 80:14</p> <p>dystonia 45:3 58:3 90:12,14,16,17 91:2 95:12 107:16 108:19</p> <hr/> <p style="text-align: center;">E</p> <hr/> <p>eager 14:20 40:14</p> <p>earlier 13:21 62:7 71:15 81:2 117:2 124:22 125:20 137:16 140:9 166:12</p> <p>early 23:15 25:12 50:14 71:10,11 108:4,7 110:13</p>
---	---	---	---

<p>112:19 126:21 127:20 153:5 156:20 ease 41:10 50:1 107:19 112:3 easier 28:20 131:20 Eastern 69:16 71:2 easy 41:20 45:19 125:18 eat 36:12 43:7 45:18 54:13 eating 57:15 58:19 economic 111:15 edge 144:5 EDS 80:1,13 education 155:16 effect 88:2 98:2 110:8,17 111:15 125:5,21 128:9 130:15 140:14,15 153:1 effective 12:18 44:11 103:9,15 114:15 115:5,9 136:21 137:3 157:16 effectively 76:6 131:7 effectiveness 14:6 111:13 116:5 136:8 effects 42:2 44:6 47:15,16 48:5 110:21 112:3 116:6 117:14,16 123:11 125:10 130:14 133:1 152:1 155:14 164:9 167:11 172:13 177:6,9</p>	<p>efficacy 47:2 141:1 153:4 effort 15:5 18:7,18 41:8 Eggers 2:17 3:16 5:7 9:1 95:20 106:3,12,19,22 113:7 115:11,13,15,17 118:19 119:1 126:15 133:19 134:1,22 135:11,22 137:4,10,13,22 139:1,10,20 140:7 141:18 142:14 144:1 146:1,10 147:6,21 148:11 150:1,8,17,22 151:7,15 152:2,15 153:15 154:19 155:21 156:8,12,15,17 158:17,22 159:6,10,14,18 160:14 162:12 eight 36:7 75:15 113:13 either 30:10 35:10 107:22 109:2,8 111:5 112:4 145:18 elbow 85:14 elected 119:12 electrical 123:18 124:14 electronic 20:8 30:8 elements 130:21 elicit 19:11</p>	<p>eliminate 132:18 Elliot 72:16 Ellis 2:7 7:13 142:15 146:3 eloquent 154:10 else 41:22 66:8 67:8 87:17 142:11 152:3 171:2 embarrassed 54:7 embryonic 166:17 emerge 82:4 emergency 138:21 emotional 50:14,18 51:3 emotions 50:20 emphasis 125:15 emphasize 11:10 121:1 161:17 employed 131:19 179:9,12 employee 163:16 179:11 empty 111:11 enable 131:16 133:14 enabled 38:2 encounter 41:13 encounters 78:12 encourage 31:13 162:20 encouraged 78:15 173:3 encouraging 132:7 end-stage 125:19 endurance 82:13 energy 43:11 63:21</p>	<p>103:20 engage 10:20 81:17 engaged 14:9 61:15 Engagement 31:4 engaging 21:14 English 55:10,15 enjoy 132:1 172:18 enrolled 99:16 ensuing 119:8 ensure 12:10 16:8 102:18 ensuring 98:12 entire 58:4 85:17 168:9 entirely 129:6 entirety 10:15 environment 22:15,18 23:5 episodes 50:16 122:11 equally 14:22 25:12 125:1 equivalent 167:8 ER 148:6 Eric 2:8 4:7 7:19 173:22 174:3 especially 47:13 56:19 59:7 80:18 84:5 88:2 100:19 103:18 140:12 141:7 143:1 162:8 Esposito 3:14 79:13,15 et 80:15 143:21 168:15 eternal 105:5</p>
---	--	--	--

<p>ethnic 166:1</p> <p>evaluation 2:7 7:14 32:9 162:2 173:19</p> <p>evaluations 50:2</p> <p>event 170:16</p> <p>eventually 13:14 54:3</p> <p>everybody 113:9 119:2</p> <p>everyday 83:17</p> <p>everyone 7:12 82:5 97:16 136:13 162:13 173:16</p> <p>everything 31:9 61:14 94:14,18 135:12,13 149:2 170:13,14 177:19</p> <p>everywhere 15:16</p> <p>evidence 14:5 74:15 105:2 109:8</p> <p>evidenced 102:1</p> <p>evolved 27:2</p> <p>evolving 50:22 114:1</p> <p>exact 163:22</p> <p>exactly 44:16 79:22 106:18 119:6 123:15 135:21 166:19</p> <p>exam 127:19</p> <p>examination 36:16</p> <p>example 17:17 19:19 55:2 77:1 80:12 81:20</p> <p>excellent 25:6 38:1 40:5 43:9</p>	<p>except 36:1 37:3</p> <p>exception 103:2</p> <p>excess 80:2</p> <p>exchanges 98:22</p> <p>excited 142:19</p> <p>executive 49:15 88:19 89:17</p> <p>exercise 25:16 37:17,20 43:17 46:20 54:13 71:13 76:3 100:16,17,21 101:2 102:3 103:2 104:18,21 105:3,13,21 106:10 109:15,20 113:3 114:9 124:17 128:12 132:8 133:16 134:9 136:11 145:15 147:13 172:7,13,18 176:6,9</p> <p>exercises 38:7 131:10 172:20</p> <p>exercising 101:21 130:10 132:12 176:7</p> <p>exhausted 114:17</p> <p>exhausting 45:11</p> <p>exorbitant 111:19</p> <p>expand 69:5</p> <p>expect 45:19 129:22</p> <p>expected 140:6</p> <p>expending 58:15</p> <p>expensive 171:16</p> <p>experience 17:3 25:3 28:12 37:9</p>	<p>42:13,14 49:5 52:22 68:3 71:8 72:18 73:21 85:18 88:15 91:21 105:1 109:9 125:7,9 133:6 137:12 148:12 151:21 155:7 157:11 163:18 174:8,19 175:2 177:7</p> <p>experienced 45:1,6 51:6 62:21 63:2,10 81:4 122:20 126:21 127:2 132:5 155:10 175:10</p> <p>experiences 28:4,13 62:14,16 65:3 66:12,13 69:7 96:10 97:4 156:4 164:8,17</p> <p>experiencing 17:2 45:9 46:12 80:18 87:18 128:20 149:16 151:22 157:3</p> <p>experimenting 150:18</p> <p>experiments 128:9,11</p> <p>expertise 162:10</p> <p>experts 134:2</p> <p>expires 179:21</p> <p>explained 82:1</p> <p>exponentially 57:14 137:21</p> <p>expressed 32:6</p> <p>extent 57:4 61:10</p> <p>extra 58:20 145:17</p>	<p>extraordinary 62:8</p> <p>extreme 58:10 70:4 107:16</p> <p>extremely 19:6 21:13 25:17 30:14 36:17 103:12</p> <p>eye 172:12</p> <hr/> <p style="text-align: center;">F</p> <hr/> <p>face 42:9 145:4 170:4 171:6</p> <p>faced 12:18 13:18</p> <p>faces 10:4</p> <p>facilitate 96:1</p> <p>facilitating 5:8</p> <p>Facilitator 3:8,16 4:6</p> <p>facility 127:16</p> <p>fact 18:19 74:14 81:15 115:4 128:3 167:8</p> <p>factor 22:14 43:3</p> <p>factors 41:11,15,17,18 104:12,16</p> <p>fail 105:1</p> <p>faint 147:3</p> <p>fair 81:18</p> <p>fairly 35:21 36:1 85:4 126:19 131:9,17</p> <p>fall 39:10 44:10 77:16 138:9</p> <p>fallen 39:11</p> <p>falling 23:17 38:14 39:4 51:16 63:17 81:8 104:3</p>
---	---	---	--

<p>138:20 175:1 falls 101:18 familiar 11:17 12:6 23:8 86:16 family 19:12 25:19 50:17 54:18 56:19 61:13,18,21 82:11,15 89:13,15 103:17 104:6 115:19 118:1 122:21 132:2 family's 44:14 103:7 fan 122:4 fantastic 169:3 Farkas 1:20 179:2,17 fast 61:9 116:18 faster 53:22 fast-forward 119:11 fateful 105:16 fatigue 51:19 63:21 64:15 74:1,15 76:17 80:1,13 82:13 103:8 122:22 150:20 175:15 FDA 2:3 5:9,18 6:21 7:11 10:10 13:2,15 16:6 17:15 22:3 25:2 26:2,10 30:21,22 31:15 52:21 56:4 66:8 69:15 71:3,18 74:10 75:7,22 86:11 96:14 97:9 106:14 107:4</p>	<p>113:17 117:13 118:12 126:9 142:19 156:4 157:1,19 158:11 159:22 160:1,12 162:8 168:14,22 172:4 174:5 177:18 178:2 FDA's 5:6 12:9 15:10 20:18 74:2 82:18 fear 39:5 44:10 53:12 55:22 61:11 133:4 171:9 174:22 176:2 fearful 39:4 120:3 fears 56:4,17 feat 41:20 Fee 18:1 feed 54:4 feedback 137:1 143:15 177:17 feel 7:6 19:20 45:11 46:19 86:5 91:12 114:4 130:8,15 133:2,17 145:9,12,14 146:22 148:5 153:2 162:4 feelings 129:1 131:6 feels 59:11 85:10 86:5 feet 90:15 130:17 144:10,14 fell 39:12,13 94:18 fellow 97:11 felt 23:1 50:3 53:17,18 70:15</p>	<p>92:19 143:14 145:1 146:20 151:10 female 33:22 35:9 91:6 120:9,11,14 139:11 146:14 147:8 148:15 151:8 females 34:4 festination 45:3 80:18,20 fetal 116:15 167:9 fewer 44:11 112:2 177:9,12 fianchas 61:16 fiction 121:19 field 72:8 118:13 fight 76:5 94:19 117:21,22 145:6 fighters 157:12 fighting 118:1 figure 18:14 figured 147:8 file 117:12 fill 168:18 filled 114:21 final 38:22 106:3 finally 6:20 27:13 30:2 31:2 32:8 56:10 70:1 112:8 125:22 126:16 147:4 173:16 financial 162:21 financially 179:13 finding 49:10 53:20 125:13 137:2 145:19</p>	<p>finds 141:14 fine 121:12 129:15 finish 89:7 first 14:3 18:15,16,22 27:16 30:22 32:15,17 36:19 49:22 53:13 68:22 74:1 76:2,4 79:15 83:15 86:21 90:19 91:10 92:16 100:3 108:9 111:22 113:14 131:18 132:6,22 136:4,10 145:1 146:17,18 152:19 156:9 157:6 163:10,13 fit 144:12 fitness 105:1 five 17:22 18:10,15,16 28:5 33:12 34:17,18 35:1,2,10,11 39:12 59:9 97:3 128:2,17 129:3 five-and-a 130:6 five-and-a-half 132:4 five-year 19:2 flag 72:11 flexibility 41:9 54:14 flexible 14:10 floor 57:19 81:6 142:9 fluctuates 42:21 fluctuations 177:7</p>
---	--	--	--

<p>fluid 147:13 flutter 113:15 fly 39:3 flyer 171:1 focal 90:14 focus 18:10,14 31:20 75:22 76:1 96:13 102:18 137:5 156:1 173:6,7 focused 10:7 16:8 18:3 82:19 96:2,17 178:3 focusing 93:20 fog 59:11 folk 156:3 folks 10:22 30:4 86:14,15 156:3 161:12 food 1:2,12 45:17 83:22 111:10,11 foods 43:7 foot 58:21,22 59:2,5 90:21 107:16 108:19 126:22 127:9 128:22 132:1 forced 58:6,7 forces 41:22 fore 74:20 forecast 61:8 foregoing 179:3 forever 81:20 115:5 forewarning 41:16 forget 72:12 77:2 148:4 form 49:3 94:1 101:8 136:14</p>	<p>177:12 formal 109:11 format 5:22 26:13 formed 170:17 former 136:11 forming 84:13 forms 32:9 103:5 162:2 173:19 176:8 formulations 24:7 forth 7:5 70:20 fortunate 77:22 130:9 Forty 143:12 forum 164:12 173:13 forums 99:4 forward 15:7 20:22 21:14 31:14 45:8 49:19 81:8 116:18 145:11 153:10 fought 145:7 foundation 37:21 49:1,2 53:2 77:10,14 99:8 foundations 56:6 126:11 Fox 99:7 170:16 fractured 59:5 frame 102:2 Francisco 119:3 free 7:6 37:22 freezes 60:17 freezing 36:8 38:13 51:8 52:14 67:18 80:19 81:2</p>	<p>frequency 61:1 frequently 60:6 143:2 friend 55:13 friends 46:5,11 47:12 60:13 82:15 103:18 115:20 132:2 friendships 46:3,4 frightening 49:12 93:9 127:2 front 70:10 75:18 fruit 169:8 frustrated 103:19 114:18 frustrating 41:14 115:3 frustration 139:14 full 10:4 105:7 131:17,19 161:21 fully 11:12 58:19 123:4 fun 48:7 function 43:8 49:15 127:3 functional 25:17 functioning 103:17 functions 133:8 fundraising 168:4 funnel 105:7 furthering 118:12 fuse 75:18 future 26:7 32:12 48:8 56:7 61:15 65:10 66:14 68:5 111:20 116:7 118:2,5 133:5</p>	<p>169:6 <hr/> <p style="text-align: center;">G</p> <hr/> gain 17:3 18:4 99:15 137:1 gait 23:10 41:10 45:7 81:1 101:16 GAMBONE 3:8 gaps 124:3 Garrido-Revilla 65:6 67:4,5,7 90:10 148:1 Gary 3:18 107:1,2 113:7 gathering 54:18 gel 24:10 Gene 8:20 general 128:20 generally 68:14 81:14 82:6 100:9 130:7 generations 126:5 genes 94:20 genetic 93:6 genetics 22:14,16 23:4 173:9 gentleman 72:15 gentlemen 48:16 genuinely 5:12 Georgia 79:14 getting 44:17 54:13 57:16 71:10,14 73:12 74:6 81:11 96:14 107:21 157:2 173:8,11 Giambone 3:4 5:3,5 8:21 9:8 26:10 30:6 32:21</p>
--	---	---	--

<p>33:3,18 34:2,11,21 35:12 38:22 39:18 40:4,10,16 48:13 52:19 56:9 62:3,7 63:9 64:3,20 67:2,6,8 68:8 69:4 72:9,13 73:9 74:21 76:9 77:18 78:4,20 79:11 82:21 83:7 85:22 86:8 87:14 88:8 90:6 91:4,20 92:7,11 95:5</p> <p>GIAMGONE 2:3</p> <p>given 15:15 46:3 56:19 139:15 145:16 157:20 164:3 171:3,4</p> <p>gives 29:10</p> <p>giving 52:22</p> <p>glad 10:5 121:6 142:10</p> <p>glasses 36:13</p> <p>globe 61:22</p> <p>gloves 131:7</p> <p>glyphosate 160:7</p> <p>goal 11:22 177:2</p> <p>God 115:8,9</p> <p>gold 24:3 100:11 110:6</p> <p>Goldstein 2:9 3:7 8:2,3 12:3 21:16,19 98:22</p> <p>gone 122:11 144:16,22</p> <p>Google 20:16</p> <p>Googling 20:18</p> <p>gospel 100:20</p>	<p>Gould 142:16,17 163:11 166:5 167:22 168:1,2</p> <p>government 31:16 71:7 173:2</p> <p>gradual 51:6</p> <p>graduating 93:8</p> <p>Graham 2:15 9:5</p> <p>grail 126:1</p> <p>grandchildren 115:7 118:7</p> <p>grant 101:17</p> <p>grateful 15:12,13 43:13 132:16</p> <p>gratitude 50:19</p> <p>great 11:4 13:21 17:15 20:6 25:21 33:13 34:15 76:14 92:1 95:13 109:10 116:6 137:13 151:10 159:18 167:4 173:2</p> <p>greater 22:18 34:9 101:4 130:7</p> <p>greatest 45:11 51:16 55:22 169:9</p> <p>greatly 59:13 105:12</p> <p>Greetings 79:14</p> <p>Greg 43:10</p> <p>groceries 104:6</p> <p>ground 12:7 31:11 59:2</p> <p>group 6:8 31:6 37:7 53:3 88:15 97:11 157:2 168:5 169:5</p>	<p>170:3,18,22</p> <p>groups 25:21 34:15 56:5 98:15 128:6 132:14 166:2 176:11,12</p> <p>growing 105:2</p> <p>guess 15:1 77:15</p> <p>guide 26:7 109:12</p> <p>gut 24:12 70:11</p> <p>guys 134:2 173:5</p> <p>gym 109:18</p> <hr/> <p style="text-align: center;">H</p> <hr/> <p>habit 84:13</p> <p>Hagerbrant 138:2,3 163:11 169:17,18,19</p> <p>half 22:6 34:12 84:15 108:10 129:8 130:7 143:4</p> <p>half-a 144:13</p> <p>half-hour 6:9</p> <p>halfway 152:9</p> <p>hallmark 108:3</p> <p>hallucinations 23:20 111:1</p> <p>hallway 7:3</p> <p>hallways 51:11</p> <p>halted 103:17</p> <p>Hampshire 1:14</p> <p>hand 28:16 57:11 62:15 102:19 113:15 127:8</p> <p>handful 114:3</p> <p>handle 44:17</p> <p>hands 62:21 66:12</p>	<p>92:1 131:6 142:1</p> <p>handwriting 50:8,10 127:10</p> <p>hang 160:17</p> <p>happen 23:14 91:10,17,19 125:11 145:22 146:15 148:10</p> <p>happened 52:4 93:2,19 142:11 146:16,17,19</p> <p>happens 119:21 148:4</p> <p>happy 61:19 92:22 153:6 164:20 165:13,19</p> <p>hard 27:20 42:20 59:7 60:11 87:2 92:17 118:3 131:12 136:14 145:13 159:10</p> <p>hardened 51:9</p> <p>harder 84:5</p> <p>hardest 45:15 91:16</p> <p>hardly 144:11</p> <p>harm 17:3 39:13</p> <p>harmful 110:22</p> <p>harrowing 119:15</p> <p>haunting 77:15</p> <p>haven't 78:8 85:1 100:1 140:1 155:4</p> <p>having 19:3 33:15,20 49:18 58:14,18 70:16 94:7 100:3 101:22 104:14 159:10 175:1</p>
---	---	--	--

<p>177:13 head 62:15 63:3 91:12 95:11 146:20 148:22 170:8 headaches 58:5 head-drop 75:9 heads 72:6 83:1 86:1 health 8:16 30:22 104:20 130:20 healthier 43:7 130:15 hear 10:17 11:2 12:11 14:21 21:7,9 26:6 27:13 30:3 31:12 40:14 78:5 79:10,11 83:6,7 86:16,17 95:14 104:1 113:10 119:2 137:7 150:6 159:12,15,17 176:18,19 heard 10:14 28:10 62:13 73:10 76:16 78:8 84:9 85:1 95:10,11 96:7 114:18 140:9 141:10 143:2 146:4 152:2 155:5 162:5 165:14 172:16 173:3 174:17 175:14,19 176:7 177:11 hearing 21:14 27:16 29:21 31:14 35:6 86:21 140:19 141:13 157:2 159:11 174:10 176:10</p>	<p>heart 84:20 Hebb 3:11 48:15,17 52:18 heels 59:3 Heisler 101:1 held 59:9 104:11 Hello 8:2 35:18 92:7 107:2 142:16 156:11 162:13 help 12:14 19:18 24:21 25:21 26:6 33:6 37:2 38:13 43:17 44:15 47:11,12 54:11 61:5 65:15 67:1 69:2 75:8 100:2,14 101:14,17 103:20 108:20 109:10,11,22 126:8 130:22 134:16 135:2 153:11 154:16 173:7,12 helped 47:4 49:2 52:1 54:14 55:1 129:2 143:7 149:11 helpful 43:17 72:10 94:13 95:14 108:18 139:6,7 154:11 157:17 158:9,16 helping 58:20 95:22 139:7 158:13 helps 32:11 96:14 129:15 136:2 139:8 147:14,16 151:4</p>	<p>hemiparkinsonism 127:20 hereby 179:3 hereto 179:13 herself 12:4 53:15 54:5,11 He's 104:3,6 hesitant 141:20 hesitation 141:6,14 Hi 7:21 8:5,11 10:1 52:21 56:11 67:10 69:12 78:6 113:10 126:17 156:15 high 59:3 78:16 98:4 138:14 149:8 highlighted 64:9 95:8 highly 127:17 160:4 172:7 hiking 105:22 hindsight 15:13 hip 39:5,6 81:10 history 56:20 99:18 116:13 158:6 HIV 19:20 Hoehn 49:22 holding 54:12 holy 126:1 home 51:10 57:2 89:20 98:18 102:15 104:2 127:16 128:1 158:1 homebound 83:18 Hong 101:10</p>	<p>honor 27:18 honored 113:20 hoop 74:13,14 hoops 74:13 hope 56:4 61:21 109:2 131:15 168:7 169:4,5,6 172:4,7 177:3 hopeful 48:8 60:20 95:1 hopefully 108:15 153:12 157:3 hopes 117:12 hoping 167:18 Hopkins 75:16 hopping 81:1 horizon 126:4 horrendous 122:5 hospital 70:3 75:17 81:10 94:16 143:20 hospitalization 155:18 hot 147:10,11 Houde 3:13 56:11 151:3 152:5 hound 103:18 hour 60:1 80:9,10 143:5,9 176:19 177:14 hours 36:10 37:19,20 45:10,11 51:22 75:16 102:14 103:6,16 168:9 176:19 177:15 house 54:14 60:12,16 72:2</p>
--	--	--	---

<p>124:8 household 44:15 housekeeping 5:15 6:22 huge 46:15 89:17 147:12 human 49:16 humanity 53:18 humans 14:4 humorous 152:16 Huntington's 11:5 19:3 74:4 113:18 hurry 51:14 80:21 hurting 72:3 husband 71:19 118:6 170:9 husband's 138:4 Huskies 98:19 hygienist 130:2 hypertension 91:9 148:16 149:10 150:14 hypotension 146:5,8 147:2 148:3,13</p> <hr/> <p style="text-align: center;">I</p> <hr/> <p>ice 58:19 I'd 5:10,14 9:21 13:19 26:12 35:14 38:14 52:21 62:11,17 64:21 69:6,14 73:10 74:6 77:7 78:22 82:16,17 83:13 95:15 104:15 106:13 107:3 113:16 118:16 119:10,20</p>	<p>121:1 144:21 150:6 157:5 162:13 173:16 idea 67:20 93:9 ideal 27:14 97:1 105:14 106:5 132:17,20 Ideally 112:1 identical 166:17 identification 177:20 identified 18:8,12,21 19:16 64:4 79:2 130:21 161:11 identify 125:16 147:1 161:12 identifying 158:18 identity 41:22 175:22 idiopathic 79:19 94:2 I-do-not-do-that-anymore 81:21 I'll 5:21 21:16 24:2 115:15 120:3,18 135:6 136:17 163:6,8 165:13 illegible 50:12 illness 42:17,20,21 43:4 44:8,18 46:6 48:2 112:17 illustrated 11:12 13:5 I'm 5:5 7:13,16,18,19,21, 22 8:2,3,5,9,11,15,1 8,19 9:1 10:5,8 15:22 34:19</p>	<p>35:21 36:3,13 37:19 39:4 40:3,17,20,22 41:4 42:10 43:3,13 44:10 45:17 46:17 47:8,13 48:6,8 49:5 51:10,13,14 53:1,5 56:12 58:13,21 59:11 60:7 61:15 65:11,12,18 66:21 67:11 69:13,18 71:4,18 72:16 73:19 77:22 78:6 80:12,16,18 82:22 83:9,15,16,20 87:19 88:12,13,14 91:13 92:22 94:6,7,22 95:21 96:21 98:10,12 100:11,16 107:2 113:11,12 115:4,12,16 116:13,21 117:2,16 118:2,7,21 119:3,18 120:3,7 121:6,11,16 122:9 123:3 126:12 131:19 132:1,14,16 135:4,15 136:3 138:4,8 140:1 144:12 146:17 147:12,17 148:1,2 150:18 153:6,10 154:5 159:6,12 160:16 165:4,6 166:7,9,10 168:2,11</p>	<p>169:4,19 170:6 174:3 imagine 42:21 52:5 imaging 99:22 imbedded 160:9 immediate 89:14 impact 6:3 26:19 39:2 63:12 78:18 83:14 89:18 102:5 105:3 111:13 175:20,21,22 impacts 35:16 65:4 174:11 176:13 impaired 51:18 63:16 64:7,18 132:21 impairment 63:19 64:17 imperative 133:7 implant 36:19 implanted 151:20 importance 133:16 154:7,21 161:17 important 10:13 11:8,11 12:7 13:2 25:12,15,17,19 26:5 29:18 30:9,14 31:18 37:18 73:2,4 74:20 76:22 87:5 90:10 91:1 96:18 97:20 98:8 104:16 109:21 126:14 134:16,17 154:12 161:1,3 170:21,22 172:7 175:12 176:6,11 177:4 importantly 112:13</p>
--	--	--	---

<p>131:21 133:9 impossible 46:9 improperly 151:9 improve 32:12 45:8 123:7 143:7 157:3 167:18 improved 46:18 93:4 122:7 167:11,13 improvement 46:15 150:21 improves 43:8 impulsive 144:7,15 inability 51:8 53:14 inaudible 46:13 64:16 83:18 140:1 incidents 155:18 include 23:13 98:8 99:12 110:22 included 95:9 includes 57:15 including 10:12 51:17 60:4 108:17 132:8 160:5 incontinence 51:3 incorporate 10:19 30:16 125:3 161:16 incorporated 30:1 increase 24:17 47:14 61:2 100:6 102:8 139:16 147:15 increased 37:14 57:14 137:19,20 142:13 152:11</p>	<p>increases 81:8,9,10,11 82:13 86:4,9 increasing 122:14 incredible 29:16 incredibly 27:21 61:9 independence 56:1 176:2 independent 53:16 India 144:9 indicated 74:7,12 individual 35:22 164:16 166:18 individuality 112:9 individuals 17:8 induced 116:9 industry 14:16,20 31:16 71:5,6 106:15 125:17 inevitable 82:9 infection 85:14 inflammation 85:2,12,16,18 86:4,5 inform 12:17,22 information 18:5 20:12,17,21 21:11 31:1,7 98:21 158:20 164:11 171:4 174:14,17 informative 10:18 infused 24:12 infusion 24:11 ingredient 160:8 inhalant 48:4</p>	<p>inhibitors 24:20 initial 56:15 124:3 initially 51:20 57:10 122:12 151:9 153:2 initiate 13:10 initiative 3:6 5:20 16:2 19:2 inner 94:6 innervating 152:19 innovation 153:11 input 11:2 19:7 20:9 33:6 96:14 161:15 inside 94:5 120:10 insidious 49:7 88:1,5 insight 17:15 19:6 insightful 134:12 insights 164:2 insomnia 53:11 instability 23:11 80:15 115:2 install 49:20 instances 148:20 instantly 151:13 instead 93:15 95:3 123:19 130:3 Institute 160:6 166:8 instructor 101:17 insurance 47:18 84:11,13 103:12 105:20 intake 147:16 Integrative 70:2</p>	<p>intended 14:5 18:4 intense 100:21 101:2 105:21 intense-interval 100:17 intensity 172:20 intention 52:15 interact 84:21 interacted 31:6 interactions 27:3 interest 15:3 interested 80:17 140:1 179:13 interesting 152:22 interests 162:21 interfere 37:4 Internet 66:5 128:6 130:19 144:8 170:1,9 interrelationships 131:11 interrupt 159:7 interventional 109:4 112:15 113:1 intestinal 70:5 intimacy 95:10 intravenous 112:5 intricate 41:20 introduce 7:11 169:18 introduced 12:3 128:18 introduction 3:4 14:3 introductions</p>
--	---	--	---

<p>10:14 invaluable 177:18 invasive 44:5 112:5 143:17 investigators 99:18 invitation 82:18 invite 28:8 64:21 69:6 inviting 107:4 involved 13:8,9 77:11 94:10 111:15 123:16 126:12 153:7 156:21 ironically 138:16 irregular 103:4 ish 121:20 isn't 88:17 isolated 129:18 issue 68:7 78:17 83:20 108:13 133:5 139:9 140:4 166:2 issues 19:9 25:16 45:2,4 63:17 64:8,17 67:17 69:8 76:21 88:16 107:12 111:5,10 125:13 140:8 171:10 ITEM 3:2 4:2 items 5:15 6:22 112:12 it's 12:9 13:2,6,7 16:22 17:11 21:13 22:21 23:1 24:6 26:5 29:8 30:9 35:20 39:9,14 41:20</p>	<p>42:19 52:5 68:15 72:10 74:7,8,12 81:5 83:18 84:5,13 85:2 86:16,20 88:1 89:2,22 90:17 91:14,15,17 93:15 94:2 95:1 97:20 98:8 101:16 102:4 103:12 111:17 113:8 117:11 120:12 121:1,4,6 122:17 123:12 132:14 133:7 134:2 135:11 136:1 141:3,9 143:18 145:16 147:9,10,11 151:3 152:13,16 158:2 159:15 165:9,11 166:2 170:21,22 175:12 176:19 177:13 I've 27:17 40:21 46:5 47:7 51:5,19 58:11 71:11 72:17 73:17 77:4 83:11 84:9 91:10 92:15 98:9 99:3,16 100:4,5 103:9 114:7 115:6 116:1 117:17 122:4,11 123:8,11,16 130:4,12,16 132:2 138:3,4 141:10 147:11 148:15 152:11 165:7 170:20 172:16 173:3,13 174:17</p> <hr/> <p style="text-align: center;">J</p> <hr/>	<p>jam 120:3 Japanese 55:9,12,14 Jay 128:8 Jeanne 163:12 166:7 167:21 Jefferson 70:3 Jenifer 3:19 113:10 118:20 166:12 Jennifer 113:8 jeopardize 42:5 jerk 148:22 Jersey 107:3 jet 172:1 job 59:8 jobs 171:8 Johns 75:16 joined 9:15 49:1 joining 9:15,18 29:15,17 79:1 Jolla 142:18 166:8 173:4 jolted 50:6 journey 107:4 joy 50:18 118:6 judge 36:16 judgment 50:13 Judy 3:15 79:6 83:4,6,9 85:22 jump 74:13 justified 104:21 justify 58:19</p> <hr/> <p style="text-align: center;">K</p> <hr/> <p>Kapcala 8:8,9 150:4</p>	<p>Karen 67:12 Karl 3:10 39:20 40:4,20 48:13 62:22 77:19 84:2 115:20 141:11 Karl's 88:12 141:1 Kathy 138:1 keen 11:2 140:21 keenly 26:3 Ken 8:5 KENNETH 2:10 Kevin 4:4 68:10 69:4 119:1,3 124:5 126:15 152:2,3 key 174:16 keys 102:16 killed 70:8 killer 77:8 Kim 3:12 52:21 53:1 67:10 68:8 kinds 172:20 kiosk 7:4 knew 69:19 70:18 127:6 170:7 knock 36:12 knowledge 133:8,10,13 179:7 known 22:14 23:15 100:12 Kong 101:10 Korean 53:3 55:9,13,15 Kwok 4:4 68:10 119:2,3 120:1,6,12,18 121:8 150:18</p>
--	---	--	--

<p>152:16</p> <hr/> <p style="text-align: center;">L</p> <hr/> <p>La 39:11 142:18 166:8 173:4</p> <p>label 12:21</p> <p>lack 109:6</p> <p>ladies 48:16</p> <p>lamotrigine 151:3</p> <p>landed 148:6</p> <p>Langston 160:5</p> <p>lap 142:7</p> <p>laptop 142:7,9</p> <p>large 35:1 37:11 51:15 70:6 176:17</p> <p>larger 22:16 136:19</p> <p>large-scale 14:4</p> <p>last 6:9 27:19 36:19 39:11 45:10 51:5 60:14 85:13 101:7 123:11,22 130:6 145:7 168:11 171:21</p> <p>lastly 43:17 99:15 173:22</p> <p>late 68:15 119:5</p> <p>later 22:18 24:4 40:22 56:20 70:17 79:18 93:18 128:17 158:4,5 173:21</p> <p>lateral 94:2</p> <p>latest 99:5</p> <p>Latin 80:21</p> <p>laugh 118:3</p> <p>laughed 50:9</p> <p>Laughter 71:21</p>	<p>98:20 101:13 106:21 115:14 118:4 119:22 121:7</p> <p>law 56:21 57:1</p> <p>lawyer 36:13</p> <p>laxative 100:13</p> <p>lazy 104:2</p> <p>Lazzarini 73:16,17</p> <p>L-dopa 73:5</p> <p>leader 7:22 88:16</p> <p>leading 58:4</p> <p>leads 84:22 103:7 152:18,20</p> <p>leap 168:16</p> <p>learn 25:22 43:16 125:18 128:5 133:7</p> <p>learned 18:17 20:6 42:18 51:2 128:10</p> <p>least 74:18 101:3,7 119:16 122:6 135:12 164:2 172:5</p> <p>leave 20:8 59:8 102:15 173:17,18,19</p> <p>leaves 84:15 172:4</p> <p>Leaving 60:16</p> <p>lecture 142:8</p> <p>lecturer 41:1</p> <p>led 98:9 101:1 126:19 128:8 160:3</p> <p>leeches 123:14</p> <p>Lee's 101:12</p> <p>leg 51:21 127:9</p>	<p>128:21 132:1 139:7</p> <p>legislation 38:18</p> <p>legs 51:8 72:3 139:8 145:9,13 149:14</p> <p>Lei 8:18</p> <p>Len 8:9</p> <p>length 34:16 36:2 60:9</p> <p>Leonard 2:11 150:3</p> <p>less 22:11 34:17 35:1,10 44:13,14 101:6 129:12 137:12</p> <p>less-frequent 177:8</p> <p>lethargic 103:19</p> <p>let's 5:3 32:14 69:5 72:15 76:15 78:5 87:15 88:10 90:7 92:2 124:11,12 141:18 159:15 172:19 173:6,7</p> <p>letting 85:19</p> <p>LEU 2:13</p> <p>levadopa 24:3,5 51:12 85:6 108:10 110:13,18 129:9 142:21</p> <p>levadopa-induced 80:3</p> <p>level 44:20,21 103:20</p> <p>levels 102:11 111:7 173:9</p> <p>Lewis 3:9 35:18 39:1 76:2,20</p> <p>Lewy 122:10</p>	<p>LID 80:2,13</p> <p>lie 127:12 145:5 147:19</p> <p>lieu 105:11</p> <p>life 6:4 12:13 17:12 26:19 28:11 44:22 59:21 61:19 63:13 65:4 75:13 77:4 92:20 93:3,14 100:3 104:14 110:7 112:18 115:18 116:4 118:1 119:13 121:21 124:18 126:19 131:17 143:8 153:12 157:7 164:8 170:20 172:22 173:7 174:11 175:22</p> <p>life-altering 112:20</p> <p>life's 114:12</p> <p>lifestyle 112:22</p> <p>lightheaded 147:3</p> <p>likewise 100:8</p> <p>Lilliputian 50:10</p> <p>limitations 73:3 125:6</p> <p>limited 55:10 104:15 110:7 112:7 118:9,10</p> <p>limp 57:13</p> <p>limping 127:7</p> <p>Linderman 75:2 144:2 163:12 171:21 172:1,4</p> <p>line 92:5,8,13 156:10 159:3 172:15</p>
---	---	--	---

<p>link 157:18 158:11 linked 50:17 linking 158:19 list 18:22 81:21 91:18 135:5 listed 123:8 listen 31:15 99:5 106:14 listened 48:20 listening 26:17 27:6 31:19 85:21 118:17 little 22:20 28:20 29:6 32:22 38:17 44:12 54:11 64:12 68:6 73:6 85:20 93:12 104:7 106:1 132:3 134:18 141:1 143:17 148:18 152:16 159:14 163:17 live 17:11 32:18 56:3 60:11 75:12 83:11 112:18 113:4 120:19 124:18 134:3 143:9 157:8 lived 47:9 67:12 119:7 170:17 lives 26:1 44:19 59:19 113:5 176:14 living 41:18 46:8 56:13 63:2 64:6 89:15 lobby 7:1,2 local 33:12 100:22 locally 156:21</p>	<p>location 152:8 locked 121:6 long 45:22 47:7,8 53:12 54:21 57:2 110:15 115:1,8 119:8 123:12 147:1 157:9 172:18 long-acting 24:8,9 142:20 longer 41:7 53:17 112:6 172:22 long-term 46:17 172:14 long-time 43:5 Lord 81:22 Loring 163:12 166:6,7 lose 138:14 loses 43:22 losing 55:22 56:2 171:8 176:2 loss 23:2 49:10 53:11 63:21 64:16 76:22 175:10 lost 46:5 54:3 58:16 59:3 77:4 89:3,4 107:11 122:4 130:4,16 142:9 lot 10:3 13:6 16:15 18:17 24:1 37:8 47:12 58:12,19 63:3 70:15,22 72:20 77:9 86:15 87:6 88:6,17,20 89:14 90:2,3 93:1 94:9,22 100:18 102:12,18 121:14 124:16</p>	<p>125:6,8,15 137:7 138:12 141:11 155:10,12 167:8 168:21 171:10,17 174:14 175:7 176:12 lots 54:17 94:8 141:22 loud 55:18 love 61:11 125:22 143:12 loved 28:12 59:9 65:3 loving 53:9 low 38:17 46:1 95:11 146:11 149:8 lowest-hanging 169:7 luckily 39:13 lucky 37:12 lying 57:19 lying-down 148:21 149:12 Lynn 138:3 163:11 169:17,19,22 171:20 <hr style="width: 20%; margin: 10px auto;"/> <p style="text-align: center;">M</p> <hr style="width: 20%; margin: 10px auto;"/> ma'am 55:6 machine 130:6 machinery 52:6 machines 130:13 magic 71:9 105:10 magnesium 130:22 mail 138:11 main 23:6 38:17 110:5 111:2</p>	<p>139:13 160:8 169:9 mainly 24:2 maintain 47:1 99:21 maintaining 25:17 maintenance 47:19 major 36:6 43:3 53:13 110:4 139:13 141:16 majority 64:4 120:20 malarkey 172:15 male 33:21 34:5 35:9 106:18 120:16 150:12 172:6 Man 66:18 manage 91:16 97:19 114:12 managed 148:18 149:21 management 96:5,19 155:1 158:19 Manager 165:6 managing 11:20 105:3 132:13 148:13 mandatory 112:22 MAOB 24:20 marital 115:20 marker 68:14 markers 123:19,20 market 16:11 marketing 17:20 married 61:16</p>
--	--	---	--

<p>martial 101:8 Maryland 1:15 172:17 179:18 masks 153:4 Massachusetts 56:12,16 massage 43:15 176:14 massively 41:20 master 46:14 match 141:4 matter 26:16 maturing 50:22 maximum 98:5 125:21 may 9:19 12:6,19 14:19 20:9 25:7 30:21 71:14 86:19 102:22 109:12 111:17 112:10,11 125:4 126:3 133:13 139:15,17 155:13 156:2 162:21 maybe 21:10 68:5 73:12 84:5 103:22 109:4 137:1,12 143:4 156:3 157:20 176:19 mcclary 67:10 McCleary 67:11 MDS 105:17 mean 48:1 meaning 80:21 means 48:2 58:18 82:1 94:3 meant 57:11</p>	<p>measurement 68:20 measures 99:21 130:10 meat 46:19 84:4 mechanism 23:1 141:9 med 85:5 medical 2:9,11 8:3,6,9,15,19 16:7 26:3 54:19 72:8 75:8 98:13 107:10 117:4 127:15,17 155:17 medically 38:12 medication 55:20 58:11 59:22 60:3,8 66:15,20 71:12 74:17 83:20 84:10,12,14,18,2 1 98:10 100:8 102:17 103:9,11 106:1 109:19 128:15 129:7 138:19,22 139:15 141:5,17 143:19 147:22 148:2 149:9 medications 52:1 58:9 65:19,20 80:4 90:3 100:2,11 101:5 102:8,9,13 106:9 115:1,9 116:4,5 117:15 120:7 136:20 140:21 147:7 157:14 medicine 2:12 8:17 37:17 56:7 69:16 70:2 71:2,8 72:6 113:12 118:14</p>	<p>143:4 medicines 115:5 Medieval 123:14 Meditation 43:15 176:14 meds 42:1,3,10,12 43:19 45:13,16 47:22 84:7 102:15 meet 14:13 meeting 1:4 2:2 5:8 9:10,11,12,13,16 10:6,13 11:12 14:17 15:14 16:3,4 19:5,19 20:13 29:19 30:8,9 31:8,17 32:10,11 82:19 161:5 164:22 178:2 meetings 17:22 18:6,20 19:3,8 20:7 21:8,9 26:5 32:13 162:4 Meghana 2:14 9:3 melatonin 100:13 member 41:2 members 14:20 82:11 103:17 170:18 171:14 memories 158:8 memory 23:14 49:14 76:22 77:4 158:7 175:10 men 171:8,9 mental 46:16 110:15 mention 11:22 73:11 76:17 100:2 102:11</p>	<p>139:5 140:18 mentioned 26:14 27:8 50:7 62:7 64:1,11 81:2,12 84:2 85:1 86:9 95:9 103:3 109:21 110:2 135:13 150:6 166:11 175:7 mere 131:14 merit 70:22 message 172:5 176:3,6 messaging 36:20 met 170:14,16 metro 32:18,19 33:10 Michael 1:20 99:7 121:19 170:16 179:2,17 Michelle 101:1 micro 173:9 microcosms 173:8 micrographia 50:13 62:19 126:22 microlesion 153:1 microphone 28:17 73:17 88:11 mid 119:5 mid-30s 148:17 middle 145:20,21 mid-term 112:19 midwife 146:17 migraine 66:1 mild 54:2 111:4 mildly 108:19</p>
--	--	---	---

<p>miles 109:17 127:16</p> <p>milk 104:4</p> <p>milligram 129:8 144:5,14</p> <p>milligrams 128:18 129:9,11</p> <p>million 22:5 113:20 169:2</p> <p>mimic 24:15</p> <p>mind 30:12 32:5 39:10 43:10 44:8 47:10,11 48:3 52:3 54:20 55:5 114:13 157:9 161:2 162:16 169:19</p> <p>minded 14:11</p> <p>mindfulness 43:12</p> <p>mine 36:1 94:5</p> <p>minimized 81:17</p> <p>minus 48:5</p> <p>minute 15:22 60:15</p> <p>minutes 12:6 28:5 60:1 79:5 87:16 95:17 130:8 143:5 149:5 154:1 163:3,4,5 174:16</p> <p>miracle 45:6</p> <p>Mirapex 110:20 142:5 144:3,14 148:5</p> <p>misdiagnosed 79:18</p> <p>miserable 80:16</p> <p>miss 148:4</p> <p>missing 69:1 116:21,22 168:19</p>	<p>169:10</p> <p>mission 170:12</p> <p>mix 34:14 35:4</p> <p>mixed 167:10</p> <p>mixing 45:16</p> <p>moaning 55:18</p> <p>mobile 38:2 42:10</p> <p>mobility 45:2,8 66:7</p> <p>mode 31:19</p> <p>model 117:9 167:6</p> <p>moderate 46:20 78:10 111:18</p> <p>moderately 110:4</p> <p>modifying 105:9 109:5</p> <p>molecules 14:1</p> <p>Mom 53:15 55:4</p> <p>moment 12:4 42:22 43:1 97:21,22</p> <p>moments 52:2</p> <p>momentum 49:19</p> <p>money 49:3 77:13 93:16 144:9 168:6 169:1</p> <p>month 57:1 91:3</p> <p>monthly 84:12,19 169:1</p> <p>months 30:7 38:3,8 74:17 93:8 117:13 130:3 136:15 152:19 158:4,5</p> <p>mood 27:3 54:15 151:4</p> <p>moon 66:18,19</p> <p>morning 9:16</p>	<p>10:3,5 11:4,8 13:4,19 15:2,11 19:4 74:3 96:4,7 114:3 144:22 149:13</p> <p>mother 53:5,7 55:9 56:3 67:12</p> <p>mother's 55:22</p> <p>motor 23:8 24:3 25:9 26:4 49:8 50:2 51:6 63:15 64:5,15 65:4,7 67:16,20 68:13,21 70:19 76:17 107:11 119:19 120:8,22 121:3 127:3 129:15 132:19 175:6</p> <p>motorcycling 81:20</p> <p>mountains 79:14</p> <p>mourn 59:4</p> <p>mouse 127:8 131:22</p> <p>mouth 58:5,7 130:1</p> <p>mouthwash 129:22 130:2</p> <p>move 11:7 15:20 21:10 51:8 53:14,17 71:17 97:5 102:7 106:22 118:1 151:16 163:9</p> <p>moved 55:19 56:20 57:11</p> <p>movement 23:9 41:5,9 47:2 52:12 63:15 85:15 99:3 100:6 117:11 128:7,14</p> <p>movements</p>	<p>128:20,21</p> <p>moves 101:11</p> <p>movies 50:19 101:12</p> <p>moving 45:8 55:20 57:7,8,11,14 80:17 145:11 162:15 175:1</p> <p>MRI's 107:22</p> <p>Mullin 2:5 3:6 8:11 15:4,9 134:1</p> <p>multiple 107:20</p> <p>multi-task 59:12</p> <p>multitude 97:19</p> <p>muscle 23:9</p> <p>muscles 57:21</p> <p>museums 39:3</p> <p>music 50:20</p> <p>myriad 68:19</p> <p>Myrna 70:1,13</p> <p>myself 20:18 36:15 38:10 39:13 60:12,13 70:21 98:15 99:2 130:18 131:2 149:4 169:19 170:6 171:3</p> <p>mystery 44:18</p> <hr/> <p style="text-align: center;">N</p> <hr/> <p>name's 113:10</p> <p>Nancy 69:12 150:1</p> <p>nap 54:21</p> <p>narcolepsy 74:8</p> <p>nasal 112:4</p> <p>National 37:22</p> <p>nationally 156:22</p>
--	--	--	--

<p>natural 43:7 116:15</p> <p>nausea 111:4 128:22</p> <p>nearly 33:9 42:12 50:8 122:8</p> <p>necessarily 22:3 88:6 91:9 123:9 126:4</p> <p>necessary 57:5 100:5 102:8</p> <p>neck 58:5 75:19,20 108:21</p> <p>negative 111:13</p> <p>neglected 76:20</p> <p>neighbors 33:12</p> <p>neither 179:8</p> <p>Network 41:3 99:7</p> <p>Neupro 110:20 114:2 138:3,7,12,20</p> <p>neuro 23:1</p> <p>neuroleptic 25:4</p> <p>neurological 2:12 8:17 10:11 108:6 127:19 172:11</p> <p>neurologist 36:4 49:22 50:5 74:13 94:13 124:4 127:4,18 138:22 141:4 145:2 150:19 169:21</p> <p>neurologists 133:10</p> <p>neurologist's 127:21 145:17 171:2</p> <p>neurology 2:4,6,8,9,10,11</p>	<p>7:15,17,20 8:1,4,7,10 10:9 174:4</p> <p>neuron 116:21 169:12</p> <p>neurons 117:8 166:22 167:2,20</p> <p>neuroprotective 128:12 131:16 150:15</p> <p>neurotransmitters 153:8</p> <p>newer 137:10,12 164:12,13</p> <p>news 70:9 82:5 86:22 87:9 99:5</p> <p>night 72:1 84:16,22 85:9,17 103:5 114:4 127:12 130:2</p> <p>nights 85:10,15</p> <p>nighttime 60:5</p> <p>nigra 167:3</p> <p>NIH-funded 167:9</p> <p>nine 57:13 74:7</p> <p>Nintendo 46:21</p> <p>nobody 69:22</p> <p>nod 62:15</p> <p>nodding 83:1 86:1</p> <p>nods 63:4</p> <p>noises 54:17</p> <p>nomenclature 75:5</p> <p>nondrug 176:5,10</p> <p>none 37:12 103:2</p> <p>nonembryonic 116:11</p> <p>nonmedicative</p>	<p>98:9</p> <p>nonmotor 26:4 54:6 88:18 124:21 125:1,5 175:7</p> <p>non-motor 25:1 121:1</p> <p>Nonmotor 23:12</p> <p>Nonpharmacologic al 25:11</p> <p>nonprescribed 109:12</p> <p>nonprofit 49:3</p> <p>nor 179:9,13</p> <p>normal 44:22 50:11 77:3 80:22 103:16 112:18 115:19</p> <p>normally 121:5 150:13</p> <p>North 79:14</p> <p>Northern 122:3</p> <p>Notary 179:1,17,22</p> <p>note 9:21 31:15 32:7 35:5 58:18 62:17 86:3 95:15 162:20</p> <p>noted 150:5</p> <p>notes 67:14 142:8</p> <p>nothing 25:2 44:21 75:7,8 168:10</p> <p>notice 16:2 138:9</p> <p>noticeable 107:14 140:13</p> <p>noticed 71:14 100:4 132:2</p> <p>not-so 102:1</p> <p>nouns 77:6</p>	<p>November 48:19 138:5,6 169:21</p> <p>nudge 115:15</p> <p>numerous 56:16</p> <p>nurse 138:8 146:17 168:2 170:6,7</p> <p>nursing 128:1</p> <p>nutritionist 99:14</p> <hr/> <p style="text-align: center;">O</p> <hr/> <p>Oak 1:13</p> <p>obnoxious 122:4</p> <p>observation 44:17</p> <p>observations 99:19</p> <p>obviously 11:17 103:6 139:9 157:10 158:6,7</p> <p>occasional 83:16</p> <p>occasionally 52:8 123:1 155:19</p> <p>occasions 59:5</p> <p>occupational 25:14 99:13</p> <p>occur 37:11 81:1 87:13</p> <p>occurs 51:10,13</p> <p>off-and-on 60:10</p> <p>offer 20:10 87:8</p> <p>office 2:3,5,7,14,15,16, 17 5:6 7:14 8:12,20 9:2,4,6,7 10:10 30:22 31:3 95:21 101:10 157:18 171:2 174:4</p> <p>officer 2:11 8:3,6,9,19 179:2</p>
---	--	---	---

<p>off-label 74:5,19 off-time 38:9 174:22 175:2 off-times 46:2 61:1 oftentimes 78:14 123:13 oh 91:4 93:15 115:8 141:22 148:13 171:13,22 oil 129:14 okay 31:10 33:9,18 34:7,11,16,21 35:5,12 40:3,10,15 62:16 63:3,5,9 64:3,20 76:10,13 79:13 83:4,8 86:8,10 87:15 88:9,10 90:9 91:4,20,22 92:1,3,11 106:12 113:10 135:11,22 139:10,20 140:7 141:18 142:1,14 144:1 146:10,12 147:21 148:14 150:3,8,10,17,22 151:7,15 154:19 158:17 159:14,19 160:18 Okun 78:6,7 163:10,13,15 old 22:7 36:3 40:21 48:17 49:9 56:13 57:3 113:13 119:4 143:14 older 167:14 170:6 olfactory 70:19 Olson 69:12 71:22 72:10 onboard 138:22</p>	<p>once-a-day 48:4 ones 13:10,13 17:1 20:14 137:10 143:1 one's 44:1 73:1 one-sided 152:17 one-third 150:4 ongoing 110:11 164:6 online 92:17 165:16 on-off 47:16 48:6 onset 22:19 108:3 170:19 171:11,18 on-time 101:5 onto 115:16 open 6:10,12,16 14:11 20:8 30:7 32:3 58:6 77:14 92:6,9,13 97:5 124:8,9 153:17,18,19,20 156:10 159:3 162:15 opening 3:5 5:17 operating 52:6 operation 36:22 Operator 79:7 92:3,5,8,13 156:6,8,10 159:3 opinion 127:15 opinions 10:17 32:7 opportunities 18:19 opportunity 19:17 35:19 40:20 52:22 160:21</p>	<p>164:18 168:14 optimist 105:5 option 106:11 141:22 145:16 176:7 177:4 options 5:21 44:3 65:22 176:15 oral 112:4 order 83:21 organic 44:7 organization 49:3 original 82:2 originally 79:17 82:4 129:12 152:6,17 orthopedic 49:21 orthostatic 146:5,7 147:1 148:3,13 others 14:16 18:19 21:2 42:6 61:5 62:19 66:6 72:22 86:5,6 91:7,21 99:14 109:21 112:12 114:15,19 122:17 146:6 150:22 otherwise 179:13 outcome 179:14 outcomes 165:18 outdoor 160:9 outside 6:15 32:2,19 33:10 58:22 89:20 101:10 109:19 147:10,11 168:17 173:20 outspoken 126:7 outweigh 12:11</p>	<p>16:9 overall 45:7 46:18 133:15 overemphasize 133:16 overgrowth 70:4,14 overly 59:20 oversees 7:15 over-the 108:22 overused 85:11 overview 3:6 5:19,22 26:13 overviews 163:21 overwhelming 71:16 131:11</p> <hr/> <p style="text-align: center;">P</p> <hr/> <p>p.m 95:18,19 pack 172:2 padykinesia 45:3 PAGE 3:2 4:2 pages 164:14 pain 54:9 55:20,21 58:5 108:21 114:22 painful 58:6,14 111:17 152:13 pair 144:11 PAN 38:18 panacea 38:7 panel 6:7 27:17 28:3,10 35:15 39:17 59:18 62:13 80:10 86:11 119:18 panelist 3:9,10,11,12,13,1</p>
---	--	--	---

<p>4,15,17,18,19 4:4,5 28:5 97:10</p> <p>panelists 27:19 35:15 62:4 65:1 79:3 84:2 97:3 133:21 140:12 151:19 161:12,13</p> <p>panic 60:16</p> <p>pants 58:2</p> <p>par 90:3</p> <p>paramount 32:8</p> <p>parent 65:16</p> <p>Parkinsonian 82:8 87:6 114:16 117:8 129:6</p> <p>Parkinsonians 79:17,20</p> <p>Parkinson's 3:3 4:3 5:20 6:3,6 10:7,12,16,21 11:1,13,15 12:1,5,16,20 14:18 16:3 19:5 20:21 21:17 22:1,4,9,12,17 23:3,7,19 24:13 26:18 27:5 28:4,12,13 32:1 33:15,20 37:20,21 38:16,19,20 39:22 40:21 41:2 42:3 44:13,16,18,19 46:7,10 48:17 49:1,7,13 51:4 53:2,4,6,10 54:1 56:5,6,13,19,22 58:9 59:19 60:3 62:1 63:1,11 65:9 67:13,17 70:10,11,12,17</p>	<p>72:17 73:18,20 74:8,12,16 75:9 77:10,21 78:2 83:10 85:5,20 88:22 89:15 90:18 91:19 92:15 93:6 94:1,3,21 96:3 97:12,14,15 98:16,17 99:7,8,9 105:2,16 107:5,11 108:2 109:22 110:6 112:17 113:11,12,19,22 114:6,16 115:6,19,21,22 116:8,13 117:3,19,22 118:10,15 119:4,12 126:20 135:3 136:22 138:5,17 154:16 156:19,20 157:8,11 159:5,19 160:5,6,11 164:6 166:14 167:1 168:5,7,10,20 169:7,11 170:1,5,15 171:7,11,15,18 174:9,19 175:8,11,17,21 177:21</p> <p>participant 81:3 91:6 106:18 120:9,11,14,16 139:11 146:14 147:8 148:15 150:12 151:8</p> <p>participants 79:1 80:10 157:1 161:8</p>	<p>participate 66:10 82:18</p> <p>participated 48:22</p> <p>participating 19:21 20:4 174:7</p> <p>participation 99:16</p> <p>particular 16:6 19:9 59:17 68:6 136:21 142:13 156:5 174:21 175:8</p> <p>particularly 11:19 25:9,12 86:18 88:18 128:4 137:5</p> <p>parties 54:17 179:10,12</p> <p>partner 47:14 82:8 88:16</p> <p>partners 106:15 170:15</p> <p>partway 142:5</p> <p>PASE 31:5</p> <p>pass 83:22 148:6 149:1,3,6</p> <p>passed 53:7 100:3</p> <p>passing 32:9 100:20</p> <p>past 59:9 65:9 66:13 68:5 73:7</p> <p>patch 48:4 138:20 151:10,11</p> <p>pathological 51:1</p> <p>pathos-defiant 48:15</p> <p>patience 43:16</p> <p>patient 10:6 13:13 17:7 20:16 25:18 29:2,9 32:16 33:4</p>	<p>68:18 69:13,14 73:18 82:18 87:20 95:2 109:22 113:11 117:2 119:4 126:11 156:19 158:14 165:5 178:3</p> <p>Patient-Focused 1:3 5:19 11:10 15:6 16:1,4 113:16</p> <p>patient-led 98:15</p> <p>patients 6:13 11:2,19,20 16:17,21 17:1 19:20 20:9 22:10,17 25:7,21 27:17 28:8 29:2,9 30:19 31:12 32:16 35:19 43:13 44:11,16 49:11 54:1 62:12 64:22 66:4,5 78:9 93:14,20 96:18 108:14 112:17 117:6 124:7 125:14,17,20 126:2,7,10 129:15 142:22 143:3,11,17 163:21 164:2,7,16 165:1,10,17 166:14 167:6,11 168:5</p> <p>patient's 6:4 19:11 92:20</p> <p>Patients 98:21 143:19</p> <p>PatientsLikeMe 78:7 163:17</p> <p>patient-specific</p>
--	--	--	--

<p>116:10 117:5 167:19 patterns 52:13 103:4 123:18 Patterson 4:5 126:17,18 142:3,4 Paul 87:19 139:22 163:11 165:3,4 166:4 Pause 21:18 30:5 32:20 33:2,17 34:1,10,20 39:21 40:2 41:6 63:8 64:2 65:5 69:11 75:1 79:9 86:7 92:10 115:10 118:22 120:5 134:21 135:10 154:18 159:9 pay 87:6,11 104:19 PCP 79:16 PD 43:12 48:15,21 49:6,18 50:13 79:19 80:4 81:15,22 82:12 100:22 102:7 108:14 110:12 128:5,10 129:20 132:6,12 133:14 148:19 PD-certified 104:17 PDUFA 18:2 peace 42:17 peers 56:2 people 6:18 20:10 22:5,8 23:8 25:15 27:22 29:15 34:22 35:10 37:10 38:16</p>	<p>48:22 53:10 54:17 61:11 64:10 67:21 69:2,18 77:9 82:22 83:3 84:9 88:22 89:14,19,20 90:11,12,13 91:15 94:4 97:12 117:17 120:17 125:9 136:9,18 137:2 139:19 140:19 154:3 155:13,19,22 163:2 165:19 166:18 168:7,10,20 169:5,10 172:6,19 175:9,11 people's 93:13 per 84:14 127:5 129:10 163:5 percent 22:6,8,10 33:10,12,20 35:8,10 37:2 64:14,15,16,17,1 8 77:21 78:9 139:16 143:11,12 175:11 perfect 48:3 177:1 perform 109:16 performances 81:18 performing 50:1 perhaps 70:10 96:19 106:5 period 19:2 112:20 periodically 28:14 29:20 periods 38:3 112:6</p>	<p>177:8 permanently 39:14 permethrin 160:8 Perry 92:14,15 person 53:9 72:1 89:15 93:4 145:1 155:7,11,15 163:5 166:19 personal 32:6 72:22 73:21 76:5 99:21 130:12 158:15 174:8 persons 174:18 person's 35:21 perspective 16:21,22 17:10,18 perspectives 5:13 6:5 19:12 27:14 29:11 34:5 162:5 pervasive 52:13 Peter 2:12 8:14 151:2,15 pharmaceutical 71:4 96:20 106:5,8 134:8 154:8 pharmacologic 124:16 pharmacological 39:15 pharmacologist 123:9 phase 13:22 phenol-converted 125:15 Philadelphia 70:3 76:8</p>	<p>philanthropy 169:3 Phoenix 156:18 phone 30:3 79:1,2,7 90:8 92:3 95:12 102:16 154:3 155:22 156:1 phonetic 36:5 43:11 83:9 photo 90:21 photography 119:11 phrase 97:15 physical 2:12 8:17 25:14 44:21 46:16 52:12 99:13 104:22 110:14 114:8 136:11 144:18 physician 138:4 physicians 78:12 pick 104:4,5,6 173:18,21 piece 72:12 pill 46:18 48:4 103:1 105:10 pills 37:18 45:13 60:4 100:9,10 102:16 104:5 pilot 117:7 pins-and-needles 131:5 placebo-like 153:2 places 77:5 plan 98:3,7,10 99:2 101:22 103:14 105:19 planned 15:14</p>
---	---	--	--

<p>plans 54:8 60:13 plates 75:19 play 22:15,16 23:5 playing 46:20 plays 22:18 please 7:6,11 28:16,19 29:3 30:12 32:3 62:4 65:1 67:1 92:4 156:6 162:3,16 163:14 173:17,22 pleasure 27:18 plethora 87:12 114:7 pluripotent 116:9,19 166:16,21 167:20 plus 46:19 129:9 pneumonia 81:11,15 pockets 85:12 Podskalny 2:6 7:21 136:10 137:7,11 point 12:9 45:10 65:14 69:5 94:6,15 97:20 105:14 112:21 127:11 139:18 140:7 141:21 142:6 144:11,13 149:1 154:20 170:12 points 11:8 95:13 134:6 139:18 poll 136:19 polling 28:22 29:5,7 32:15 63:6 134:19 154:5 poor 41:9 45:1</p>	<p>101:15 population 12:22 17:5 22:6 portion 9:16 34:5 35:1 76:1 position 58:6 59:9 147:18 148:21 149:12 positive 52:15 58:17 105:3 140:13 153:2 possibility 50:21 possible 20:2 109:16 110:16 150:15 165:19 possibly 110:1 128:2 150:20 post 148:19 posted 31:9 post-marketing 14:7 Postow 72:16 posts 164:14 postural 23:11 80:15 posture 45:2 potassium 131:1 potency 45:13 potentially 81:7 140:5 pounds 58:16,17 power 124:5 powerless 53:18 practice 130:11 practiced 46:13 practitioner 168:2 pre 107:11</p>	<p>preaching 136:12 precise 50:9 167:2 preclinical 167:5 predictable 44:22 91:15 preparation 59:18 prescribe 84:10 143:19 prescribed 109:19 110:3 129:12 prescribes 168:11 prescription 18:1 27:7 105:13,17 129:7 157:20,22 prescriptions 99:11 132:13 present 28:5 66:5,14 70:5 79:5 97:10,18 105:17 167:2 presentations 5:17 9:19 presenting 74:1 133:11 presents 51:16 press 32:21 pressure 91:8,11,21,22 95:11 146:11 147:4 148:5,22 149:7 pretty 39:11 46:8 70:20 76:6 80:16 prevalence 22:7 prevent 70:16 101:18 104:13 preventing 90:1 prevention 124:13</p>	<p>125:12 160:2 previous 110:2 primary 23:1 68:13,22 110:18 123:9 135:14 Princeton 56:12 prior 107:7 108:3 122:12 148:19 priority 132:22 probably 15:18 22:15 25:3,7,12 42:14 47:16 67:22 72:21 88:1 112:20 132:18 133:4 153:18 154:1 probe 152:8 problem 40:10 77:11 81:7 85:18 110:9 111:2 127:6 147:14 175:3,9 problematic 68:1 problems 37:11,14,15 38:11 42:13 45:2 52:7 53:20 57:15 88:19 94:8 95:10 107:10 111:9 procedure 75:16 proceeding 179:3 proceedings 179:4,6 process 13:3,17 162:19 processes 134:15 prodromal 125:14 produce 20:20 produced 165:8</p>
---	---	---	--

<p>production 145:10 productive 42:10 43:2 113:5 products 2:4,6,8 7:15,17,20 8:1,10 10:9 16:7,9,10 174:4 Product's 8:4 Professional 31:4 professor 166:7 profile 35:22 prognosis 127:21 program 23:3 101:1,2 165:6 166:10,11 programmer 126:19 programs 2:3,5,14,15,16,17 5:6 8:12 9:2 17:6,7 95:21 100:18 104:18,21 progress 61:10 73:7 125:20 128:13 progressed 49:7 55:11 57:4 68:16 progresses 82:12 progression 61:8 82:6,7 99:21 108:16 110:1 112:16 124:14,19 132:3,5,9 progressive 81:22 112:17 113:22 115:6 124:10 progressively 127:1 prohibitive 103:13</p>	<p>project 89:6,7 prolong 153:12,13 promise 116:7 prompting 21:8 pronounce 135:5,15 proper 77:5 109:20 112:19 113:3 168:15 properly 79:19 102:19 108:1,8 pros 141:5 protect 171:17 protein 46:19 111:12 protein-sensitive 45:17 protocol 172:10 prove 74:14 proven 121:20 provide 5:18,22 12:4 18:18 26:13 28:18 33:6 101:15 103:3 112:2 137:18 172:20 provided 19:6 provider 103:12 providers 172:11 provides 17:15 99:10 101:3 providing 19:7 Provigil 103:10,11 proximal 81:14 psychiatrist 99:13 psychological 37:11</p>	<p>psychologically 144:6 public 1:4 4:6 6:10,12,16 16:3 18:9,12 30:6,12,15,19 32:3,4 153:17,18,19,21 162:15,18 163:20 164:21 178:2 179:1,17 Pujita 2:16 4:6 9:7 pull 155:5 pulling 58:2 purchase 7:6 purpose 52:16 89:19 168:6 purposely 89:21 push 60:13 pushing 38:17 putting 72:6 113:17 165:16 PWD's 98:5 PWP 49:4 <hr/> <p style="text-align: center;">Q</p> <hr/> Qigong 109:17 qualification 140:2 quality 92:19 93:3,14 104:14 143:8 quantities 70:7 quantum 168:16 quarter 143:5 quarters 51:11 question 13:18 32:15,17 33:14,21</p>	<p>47:5,7,10 50:5 63:6 86:14 92:19 134:19 135:1 139:2 142:15 146:3 150:3 151:2,16 154:5 159:21 160:12,15,16,20 questionnaire 165:8 questions 13:4 19:10,14,15,16 28:15,22 29:5,7 31:21 55:13 59:11 62:18 67:15 86:12 87:21 96:22 124:22 136:7 160:22 161:2 163:22 164:4 quick 171:6 quickening 80:22 quickly 148:21 149:12 163:9 quit 77:14 quite 16:13,15 46:1 96:8 122:8 140:3 152:13 157:12 <hr/> <p style="text-align: center;">R</p> <hr/> Radiologic 8:16 Rafaloff 3:18 107:2,3 raise 28:16 49:3 62:14 66:11 72:11 168:6 raised 53:15 62:21 92:1 96:7 134:6 169:2 raising 77:13 140:7 142:1 169:1</p>
--	--	---	---

<p>ramped 128:15 random 128:21 range 28:3 34:13 35:9 41:8 rarely 43:1 rat 167:6 rate 73:4 129:11 rather 112:5 117:18 167:7 172:19 173:8 rating 50:1 124:1 125:4 Raub 3:19 113:9,10 115:12,16,18 118:5,21 react 60:7 reaction 36:19 51:19 reactions 58:10 readers 47:12 real 38:18 78:12 117:11 133:5 149:4 realist 48:6 realize 14:19 15:21 54:22 56:3 88:2 112:8 realized 16:19 101:19 really 13:5 15:7 16:20 17:8 21:3,5 22:13 31:11 32:11 38:20 39:19 41:15 42:15 69:8 77:8 84:4 85:17 93:19 94:4 95:13 96:14 120:21 121:2 123:6,12</p>	<p>134:12,16 138:14,18 140:13,20 141:14 142:10 153:20 154:9 156:1 157:12 158:19 161:6 162:9 163:8,21 164:3 168:13 169:6 170:11 171:7 174:9 176:13 177:13 reason 65:11 94:11 reasons 66:7 72:22 113:20 reassure 40:11 86:15,20 reassured 50:3 Rebecca 137:22 recall 77:5 receive 99:5 111:18 received 144:21 receiving 155:19 recent 136:15 recently 22:22 24:10 59:7 70:9 74:5 100:22 105:6 136:20 151:5 recess 36:14 95:18 recliner 80:17 recognize 154:6 recognized 80:4 recognizing 23:13 recommended 49:21 98:13 reconvene 95:19 record 30:15 157:21 158:1</p>	<p>162:18 179:7 recorded 9:10 179:4 recording 9:11 recover 75:17 recovery 39:7 redefined 115:19,21 reduce 135:2 154:16 172:13 reduced 37:1 129:20 152:12 179:5 reduces 82:13 reduction 43:15 127:3 refer 22:11 reference 21:2 refill 74:6 84:12 refilled 84:19 reflect 22:3 96:20 reflected 162:6 reflecting 21:6 reflection 154:12 reflects 14:11 28:3 reflex 50:2 reflexology 43:16 refocus 124:21 reformulated 24:5 refreshing 35:20 regained 117:10 regarded 81:14 regarding 159:22 160:1 regardless 98:3</p>	<p>regatta 76:7 regenerative 113:12 117:4 118:13 regimen 27:7 37:19 47:6 100:8 113:3 131:9 140:20 141:2,15 142:13 143:14 registered 100:22 registration 163:2 173:20 179:22 regular 101:22 143:9 164:9 regularly 39:11 109:17 130:13 rehab 155:18 REI 160:10 reiterate 11:7 77:20 reiterated 96:4 154:20 reiteration 86:17 related 19:9 20:5 60:3 78:19 102:9 129:18 132:12 162:21 175:17 179:9 relation 12:15 relationship 78:18 relationships 46:4 78:18 103:22 115:20 175:20 relative 179:11 relatively 50:11 relentless 82:9 relief 97:21 98:6 101:3,15 103:3 108:18 111:19</p>
--	---	--	---

<p>112:2 172:21 rely 61:5 REM 103:7 107:13 remain 81:20 remainder 116:4 remarks 3:5 4:7 6:21 9:22 22:2 26:11 28:6 104:1 remember 13:2 88:20 89:10 101:9 104:6 113:14 127:19 133:10 148:8 remembered 104:5 remembering 94:7,12 reminded 16:5 115:4 renovated 124:8 repeated 111:4 repeatedly 97:17 repetitive 9:19 replace 168:19 replies 165:10 report 20:13,17,20 30:1,17 78:8,9 153:6 161:16 reported 1:20 79:15 174:20 reporting 1:21 78:10 reports 21:1 represent 97:13 representation 166:1 representative 17:7 representatives</p>	<p>14:15 29:3,9 32:16 represented 136:5 representing 14:18 73:19 164:15 reprogramming 166:15 repurposed 74:19 repurposing 74:5 reputed 127:17 requests 144:8 Requip 45:22 47:3 100:13 110:20 139:6 require 111:11,12 112:7,11 required 132:11 requirement 167:15 requirements 140:3 requires 52:16 102:18 111:8 research 19:21 22:15,22 26:7 49:1 53:1 92:18 100:19 105:7 109:7,8,11 117:4 126:6 128:8 132:17 150:14 160:3 166:1,8 168:6 177:20 researched 14:2 researcher 83:12 researchers 13:13 61:22 68:18 105:13 resembled 101:12</p>	<p>reserved 6:10 resonate 62:14 86:6 resonated 83:2 resource 56:6 165:17 resources 30:21 66:17 respect 32:7 56:2 66:3 respected 160:4 respond 29:9,14 44:2 69:7 146:13 responded 64:4 respondents 150:5 responding 33:4 34:12 144:8 162:16 response 33:7 101:4 156:7 responses 139:2 responsibilities 77:11 responsibility 12:10 77:13 responsible 10:16 80:5 responsive 54:10 rest 64:18 75:13 resting 23:10 restless 51:21 139:7 restorative 51:20 restroom 57:20 restrooms 7:3 result 58:9 59:2,15 109:3 129:20 173:11 175:16 results 35:8 99:20</p>	<p>135:19,20 139:15 167:7,19 172:21 resume 103:21 129:22 retired 83:11 126:18 131:19 132:14 retiree 71:4 retrospect 73:22 return 103:20 revealed 134:14 reverb 159:15 reverberates 160:17 reversing 48:2,11 review 13:15 16:9 17:20 19:15 reviewed 161:15 reviewer 2:9,10 8:6,15 reviewers 21:2 reviewing 10:16 26:15 reviews 10:11 revolutionary 118:13 revolves 59:22 rheumatoid 99:12 rich 36:4,18 134:6 Ridmal 84:20 rigidity 41:8 67:18 80:14 rigmarole 74:9 rigorously 114:9 rising 149:11 risk 16:13 17:1</p>
---	---	--	--

<p>42:6 51:16 59:20 81:8,9,11,12 117:17,18,21 risks 12:11,15,19 16:9,18 117:14,15 river 145:21 RN 138:4 road 15:15 roads 15:17 roadwork 102:22 Robb 3:10 39:22 40:3,8,17,20 41:7 77:20 88:12 140:17 166:12 robs 41:21 175:22 rodent 117:9 rodents 117:10 rods 75:19 role 22:15,16,18 23:5 96:15 134:8,9,10 roles 67:11 room 11:16 28:18 29:12 33:19 34:4,6 61:22 67:21 83:3 114:19 117:1 126:2 136:6 143:3 154:11,12 156:3 165:15,22 ropinirole 100:12 139:6 Rosa 3:12 52:20 53:1 56:9 ROSTER 2:2 ROUDE 137:15 roughly 28:5 33:19</p>	<p>163:3 round 62:4 106:2 133:20 162:8 Round-Up 160:8 routine 49:8 111:7 114:1 176:20 rowing 76:7 145:21 RPM 130:8 rules 31:11 run 37:7,21 163:8 runners 28:17 running 65:22 rush 36:6 rushed 43:21 Rytary 24:8 136:15 137:5,15 141:7 142:19 143:10 155:6</p> <hr style="width: 20%; margin: 10px auto;"/> <p style="text-align: center;">S</p> <hr style="width: 20%; margin: 10px auto;"/> <p>safety 74:9 saliva 129:20 Sally 78:6,7,21 163:10,13 165:2 salt 147:15 San 119:3 sand 170:8 sandwiches 7:5 Sara 2:17 3:16 5:7 9:1 95:20 SAUJANYA 2:3 savings 101:19 saw 45:7 86:1 127:17 140:16 scale 50:1 124:2 scales 125:4</p>	<p>scans 107:22 scared 127:21 scary 61:9 scenario 128:1 schedule 45:20 59:22 127:11 128:15 schedules 111:7 scheduling 111:9 scheme 49:9 school 56:21 57:1 127:17 schools 71:7 72:6 schoolteacher 53:8 science 121:18 scientific 29:8 160:6 scientist 165:6 scope 6:15 32:2 scopolamine 151:10,11 scoured 128:5 scrawl 50:13 screaming 103:5 screws 75:20 Scripps 142:18 166:8 168:2 search 44:3 second 33:14 40:9 41:5 84:8 102:7 112:13 124:20 159:7 seconds 121:9 149:5 sedentary 126:19 seeing 47:10</p>	<p>101:19 128:7 136:5 140:5 168:9 seek 44:3 99:17 141:22 seem 54:19 88:5 143:19 173:6,10 seemed 19:22 54:18 128:12 seems 43:8 72:18 73:6 78:2 85:17 88:3 104:2 114:10 141:7 143:17 144:16 149:10,21 153:3 seen 46:14 seizure 58:14 selegiline 128:17 129:10 self 98:4 send 20:11 seniority 49:12 seniors 101:18 sensation 81:5 sense 107:11 122:4,22 sensitive 58:8 78:11 sensitivity 50:15 sent 161:10 sentence 50:12 55:15 157:7,8 September 1:8 91:2 serious 11:13 81:7 110:21 127:6 serves 7:5 service 161:13</p>
---	--	--	--

<p>services 49:4</p> <p>session 1:6 3:3 4:3 5:2 13:5 162:15 163:10</p> <p>settings 155:18</p> <p>seven 48:20 51:5 60:1 72:17 112:21 113:13 143:5</p> <p>several 9:14 34:22 38:3,8 46:3 59:5 62:21 64:10 82:22 83:3,19 84:6,9 85:14 91:22 107:9,18 108:2,16 109:17,18 130:21 148:7 155:8</p> <p>severe 16:15 58:4,13 78:10</p> <p>severely 51:14 85:11</p> <p>severity 60:9 61:1</p> <p>sexual 78:10 95:10 175:19</p> <p>shaking 49:9 118:21</p> <p>shape 138:18</p> <p>share 5:13 6:14 27:22 28:10 30:10,20 39:6 49:5 65:1 67:9 76:18 85:19 87:17 98:7 110:12 165:13 177:3</p> <p>shared 161:22 174:15</p> <p>shares 82:5</p> <p>sharing 21:20 62:9</p>	<p>63:4 91:5 95:6 97:4 174:8</p> <p>sheer 41:15</p> <p>Sherrie 142:17 163:11 166:5,6 167:22 168:1</p> <p>Sherry 169:16</p> <p>she's 54:12</p> <p>shifted 68:3</p> <p>shoes 144:12</p> <p>shoot 36:15</p> <p>short 24:9 93:8</p> <p>shortcomings 137:8</p> <p>shortening 80:22</p> <p>Shortly 51:2 105:15</p> <p>short-term 77:4</p> <p>shoulder 85:11,13 107:12</p> <p>show-and-tell 120:13</p> <p>showed 90:20</p> <p>showering 57:15</p> <p>shown 160:7,10 167:5</p> <p>shuffling 81:1</p> <p>Shulman 172:16</p> <p>sides 124:9</p> <p>sign 6:16 32:3 105:8</p> <p>signed 6:18 163:3</p> <p>significant 26:18 27:10 35:16 47:21 57:6 63:12 64:5 99:1 111:16 126:3 132:14</p>	<p>170:19</p> <p>significantly 83:14 127:10</p> <p>sign-in 163:1</p> <p>signs 15:16</p> <p>Silver 1:15</p> <p>similar 28:11 35:7,9 62:16 108:7</p> <p>similarities 79:21</p> <p>similarly 145:14</p> <p>simple 50:2 59:11 108:10 116:19 118:6</p> <p>simply 71:12 173:10</p> <p>sincerely 161:9</p> <p>Sinemet 24:7 36:9,10 37:1 45:5,22 47:1 60:1,2 66:1 108:17 122:13 141:10,11 142:4,13 145:18,19 155:12,14</p> <p>sir 40:11 76:9 92:14</p> <p>sister 93:7</p> <p>sisters 65:8</p> <p>sit 39:3 149:13,14,18 168:8 169:20</p> <p>sitting 148:21</p> <p>situation 39:2 55:8 65:17 89:13</p> <p>six 40:22 53:6 93:7 100:9 130:3 158:4 163:2</p>	<p>size 165:9</p> <p>skepticism 101:9</p> <p>skills 179:8</p> <p>skin 46:18 116:19 138:15 166:14 169:12</p> <p>slam 59:1</p> <p>sleep 25:5 38:13 43:12,13 51:17,20 52:2,7 63:17 64:7,17 72:4 73:12 84:20 85:8 88:4 98:1 100:14 103:4,7 107:13 110:22 122:7,8 127:11,13 139:8 142:8 147:19 175:8</p> <p>sleepiness 51:18</p> <p>sleeping 23:17 84:8,22 85:15,16 86:4,9</p> <p>slide 22:21</p> <p>slides 31:9</p> <p>slight 37:4 57:12 69:18</p> <p>slow 24:16 36:5 39:7 51:6,18 82:7 104:7 108:16 110:1 112:15 128:13</p> <p>slowed 63:15 132:9</p> <p>slower 57:12</p> <p>slowing 48:10 49:9 52:13</p> <p>slowly 41:11 42:20 46:2</p> <p>slowness 23:9</p>
--	---	---	---

<p>25:10 41:4 52:10 small 127:10 smaller 50:8 smart 153:9 smell 53:11 107:12 122:5 smile 55:6 smooth 155:9 snack 7:7 sneak 170:10 snowflakes 79:21 so-called 110:6 social 27:3 44:20 87:21 88:4,8 societal 72:22 sold 160:10,13 sole 168:5 solutions 44:3,5 somebody 65:2 73:13 138:17 141:14 144:7 170:5 171:2 172:11 someone 41:22 42:8 45:21 118:9 121:10 141:19 sometime 176:17,19 somewhat 55:5 144:15 somewhere 142:11 175:2 somnolence 80:2 Sophie 92:5,8 sorry 40:18 115:9 116:14 136:1 148:1</p>	<p>sort 52:3 108:4 123:13 147:9 149:2 153:10 sought 128:6 Soujanya 3:4,8 5:5 Soujanya's 95:22 sound 62:15 sounding 59:20 sounds 83:2 south 56:20 speak 55:12,14 66:12 87:4 107:4 113:6,20 speaker 6:19 88:16 speakerphone 159:8,11,13 speakers 163:8 speaking 29:14 83:1 86:2 88:13 155:16 specialist 99:4 100:7 128:7,14 specialists 99:12 specialized 10:22 130:20 specialties 107:21 specific 22:13 86:13 105:1 130:10 172:19 specifically 12:5 23:10 49:6 101:18 116:9 spectacular 167:7 speech 25:15 38:13 42:13 45:3 53:20 speed 129:17 spend 15:22 154:1</p>	<p>168:9 spent 66:17 107:20 spiking 149:8 spirit 44:9 spiritual 46:16 splicing 173:10 split 34:3 35:8 spoke 55:9 68:4 98:22 spoken 72:21 172:6 sponsors 10:21 14:14 87:7 96:16 spotlight 113:18 Spring 1:15 stabilize 38:10 151:4 staff 155:17 stage 97:3 125:20 stages 44:19 staging 121:16 stake 142:12 Stakeholder 31:4 stand 45:12 57:17 91:10 114:22 123:1 145:6 147:10 149:15,18 174:1 standard 24:4 100:11 110:6 141:9 standing 51:15 58:1 91:11 146:16,18 stand-out 87:12 standpoint 119:20 124:15 125:17 Stanford 124:4</p>	<p>start 5:16 19:14 27:16 32:14 35:17 50:11 65:2 79:8 89:3,6 97:2,6 110:13 124:12 125:19 137:14 142:1,5 146:13 150:10 started 5:4,16 18:7 54:3 55:14 69:17 76:2 96:6 100:1 119:6 122:14,15 128:14 131:3 147:5 151:5 157:21 168:3 starting 132:4 starts 70:11 state 28:19 98:18 101:16 103:19 179:18 stated 117:2 states 22:5 60:10 stating 56:18 stationary 130:5 stave 114:11 stay 16:11 30:7 31:19 94:14 130:8 143:20 153:20 staying 23:18 63:18 stem 116:9,11,12,20 117:5,12,16 166:9,11,16,17,2 1 168:4 stem-cell 116:7 stem-cell-derived 167:20 step 14:8 15:4 66:11 89:1,10</p>
--	--	--	--

<p>steps 98:9</p> <p>Steve 3:17 36:4 97:6 106:4,19</p> <p>Steven 106:20</p> <p>stick 141:15 163:5</p> <p>stiff 58:4</p> <p>stiffness 23:9 25:10 49:9 53:14 71:16 101:4,15 108:21 114:12</p> <p>stimulation 25:8 57:5 121:8 152:1</p> <p>stitches 39:12</p> <p>stomach 54:9 57:21 111:11</p> <p>stood 61:16</p> <p>stop 15:3 49:21 66:1 107:19 147:11</p> <p>stopped 142:12</p> <p>stopping 48:10</p> <p>stored 138:13</p> <p>stores 160:10</p> <p>stories 28:1 48:21 62:9</p> <p>story 85:20 161:21</p> <p>Strategic 2:3,14,15,16,17 5:6 8:12 9:2 95:21</p> <p>strategies 129:4</p> <p>Strategy 2:5</p> <p>strength 61:21 117:10 130:13</p> <p>stress 40:1,13 43:3,15,20 73:11 77:8,21 89:12 94:17 144:17</p>	<p>stressed 54:19</p> <p>stressors 114:12</p> <p>stretch 7:7 114:11 130:13</p> <p>stride 80:22</p> <p>stringent 140:3</p> <p>strong 11:18</p> <p>strongly 116:6</p> <p>strong-willed 53:8</p> <p>struck 67:13</p> <p>struggle 45:12 114:15</p> <p>stuck 58:7 81:6 175:2</p> <p>studies 93:13 99:17,20 167:9 168:15</p> <p>studying 62:1</p> <p>stuff 20:19</p> <p>subject 106:9</p> <p>sublingual 112:5</p> <p>submit 13:14 30:13 32:3 33:7</p> <p>submitted 161:14 165:7</p> <p>submitting 163:20</p> <p>substances 131:10</p> <p>substantia 167:3</p> <p>substitute 174:9</p> <p>success 60:22 169:9</p> <p>successful 36:22 37:5 111:21</p> <p>sudden 51:8</p> <p>suddenly 81:5</p> <p>Sue 159:4,6,10,12,17,</p>	<p>19 160:16,17,18</p> <p>suffer 58:3 59:16 76:22 78:1</p> <p>suffered 53:6 108:11</p> <p>sufferers 110:12</p> <p>suffering 25:16 50:3 80:13</p> <p>sugar 58:12</p> <p>suggest 39:16 70:10 157:5 163:4</p> <p>suggested 22:16 75:15 132:7</p> <p>suggesting 155:12</p> <p>suggestion 177:11</p> <p>summarize 29:20 41:19 174:16</p> <p>summary 4:7 30:1,17 154:2 155:3 165:8</p> <p>summer 79:16 138:13</p> <p>Summit 117:4,12 166:11 168:4</p> <p>Sunday 67:14</p> <p>Sunnyvale 160:7</p> <p>supervised 37:20</p> <p>supplement 100:14</p> <p>supplementing 130:21</p> <p>supplements 109:1,9,12,15 111:3 114:3</p> <p>supply 164:21</p> <p>support 25:20 37:7 46:12 53:3 56:5 88:15 98:15</p>	<p>126:6 128:6 132:13 158:18 164:20 166:2 170:2,18,22 176:11 177:20</p> <p>supporting 118:12</p> <p>supports 132:17</p> <p>supposed 65:12 92:18</p> <p>sure 34:19 42:6 64:11 79:4 82:22 102:20 119:6 136:10 151:18 161:21 176:21</p> <p>surgeon 49:21</p> <p>surgery 25:8 61:17 75:15 151:21 152:7,9,10</p> <p>surgical 134:9</p> <p>surprise 41:17 156:2,4</p> <p>surprising 135:11</p> <p>surrogate 123:19</p> <p>surveillance 14:7</p> <p>survey 38:19 163:20</p> <p>surveyed 163:22</p> <p>Susanne 2:9 3:7 8:2 12:3 21:16 27:8</p> <p>suspect 97:15</p> <p>sustained 24:19</p> <p>swallowing 25:15 63:22 94:11</p> <p>sweat 46:21</p> <p>sweats 94:10 95:12</p> <p>swell 144:11</p> <p>swing 149:14</p> <p>switched 52:3</p>
---	--	--	--

<p>152:18 switching 166:7 swollen 144:15 symposiums 99:4 symptom 23:6 50:14 51:3 69:8 72:20 74:1 78:8 84:8 85:1 89:22 90:11,19 91:7 97:21 98:6 110:9 113:14 131:14 symptomatic 108:18 112:1,2 113:2 symptoms 6:2 12:13 22:8,11,19 23:8,12 24:3 25:1,9 26:4,15,18,22 27:1,10 31:20 35:16 41:12,16 42:2 43:21 47:17 48:5 49:6,10 51:7 53:11,13 54:6,7 56:15,17 57:6,9 60:6,19,21 63:10,15 64:1,5,6,9,10,15 65:4,7,20 67:16,20 68:13,16,19,22 69:17 70:19 71:11 72:19 73:13,14 75:4 76:18 77:9,12,16 79:16 80:1,7 81:17 82:2,3 83:13 87:6,12,13,18,22 88:18 91:1,8 94:3 95:8,9 96:8 97:19 98:2 99:11 102:12 107:7,11</p>	<p>108:4,7,11,15 110:1,5 114:17 117:22 119:7,19 120:7,8,22 121:2,3,12 122:2,19 123:2 124:1,21 125:1,5 128:10 131:9,10 132:3,18,19 133:12 135:2 138:10 146:7,9,14 151:12 154:16 155:13 164:8 167:17 174:18,19 175:7,8,14,17 177:6 synapses 52:14 syndrome 23:16 139:8 system 41:19 94:17 systematic 21:11 systematically 16:21 systematize 164:19 systems 49:15 94:9 151:19 <hr style="width: 20%; margin: 10px auto;"/> <p style="text-align: center;">T</p> <hr style="width: 20%; margin: 10px auto;"/> <p>table 14:13 29:4 36:13 97:8 162:3 173:19,20 tables 173:17 tablet 129:9 144:5 tablets 84:15 85:6 128:16 129:8 tackled 132:20 Tai 101:7,17 106:1 109:16 130:11 tailor 19:15</p> </p>	<p>tailored 19:8 take-home 154:20 taking 26:9 36:9 37:2 73:5 74:6 83:21 106:14 109:19 111:16 112:18 135:13 142:7 147:7,22 148:2 150:10 155:14 157:15 166:13 talk 17:8 35:15,19 38:4 68:19 84:9 87:2,4 145:2 154:6 161:19 171:1 173:4 talked 78:15 98:1 102:11 134:7,13 talking 55:1 83:16,17 139:12 155:11,13 163:17 164:16 target 175:12 targeted 174:13 task 18:13 59:13,17 89:2,6 tasks 41:7 61:5 63:20 team 2:9,11 7:22 10:16 87:4 99:10 136:14 177:19 teams 8:4 160:3 tearful 50:16 tease 96:22 technique 166:15 technology 158:10 tedious 102:17 143:18 teenagers 65:14</p>	<p>teeth 130:4 temperament 52:9 temperature 97:22 temperatures 138:14 temporarily 81:6 ten 34:18 35:2,3,10 112:21 tennis 141:4 Terminal-Man-like 121:19 terms 17:16 21:2 25:1 96:16 144:17 172:13 174:18 176:4,16 177:1 terrible 36:11 terrifying 52:5 test 29:5 testament 10:15 tested 49:22 testing 99:22 tests 117:9 Texas 83:12 thank 5:4,10 8:21 9:8,17 14:15 15:7,9 21:20 26:8,10 28:1 29:16 33:11 35:12,18 39:18,19 40:19 48:11,13 52:18,19,21 56:7,9 57:2 62:3,10 63:4 64:20 65:6 67:2,6,7 68:8 69:2,4 72:9,13,14 73:9 74:21</p>
---	--	---	---

<p>76:9,10 77:18 78:4,19,20 82:19,21 85:19,22 86:14 87:14 88:9 90:5,6 91:5,20 92:1,14 95:5,12 97:7,9 106:13,19 107:3 113:6,7,16 118:16,19 120:6 126:12,14,15 133:17,19 135:22 137:13,15,22 139:1,10,20 142:16 146:1 147:21 148:11 150:1 151:7 152:15 153:15 158:17,22 160:14,15,18 161:5,9 162:12,14 163:15 164:22 165:2 166:4 167:21 169:13,16 171:19,20 173:13,15 174:6 177:16,21</p> <p>thankful 40:13 121:17</p> <p>thanks 126:5</p> <p>that's 12:1 15:1 22:14,22 25:2 26:5 29:16 32:1 42:8 44:7 47:6 52:17 65:10,15,18 69:5,19 70:5 75:14 78:2 86:22 90:1,19 93:20 94:18,20 96:21 104:17 105:19 116:22 121:4 122:6 125:18</p>	<p>131:6 134:15 139:9 140:4 143:21 145:22 148:9 149:16 155:4 159:18 160:19 164:13 165:11 171:11 176:7</p> <p>theme 124:20 177:13</p> <p>themes 29:21 123:7</p> <p>themselves 10:17 88:5 102:13</p> <p>theoretically 14:3</p> <p>therapeutics 114:7,14</p> <p>therapies 11:18,21 27:7,8 48:9 90:4 118:14 134:10 135:2 150:6,7 154:7,15,21 172:9 175:13 176:5</p> <p>therapist 99:13 105:18 136:11</p> <p>therapists 104:17,22</p> <p>therapy 8:20 25:14 104:22 114:8 116:7,12 117:6,16 121:20 122:15 123:7 148:17 167:16 168:17 169:8</p> <p>thereafter 179:5</p> <p>Therefore 12:11 53:16 97:18 98:3</p> <p>there's 11:17 22:13 25:1 70:9,22 72:5 74:14 76:13 87:3 88:17,20 90:2,3</p>	<p>93:1,22 94:1,9,15 102:21 103:15 111:14 113:19 123:1,22 124:16 125:12 136:4 141:16 150:14 154:9 164:18 171:9,10,17</p> <p>Theresa 2:5 3:6 8:11 15:4 134:1</p> <p>They'll 5:18 28:18</p> <p>they're 30:13,14 37:22 38:1,7 65:14,15 85:4 87:2 90:15 94:13 124:2 130:22 133:2 136:21 140:21 143:1 171:3,4</p> <p>they've 27:20 28:10 149:9</p> <p>thief 48:11</p> <p>third 81:5 85:1</p> <p>Thomas 70:2</p> <p>Thompson 2:15 9:5 35:7 64:14 135:20 155:6</p> <p>Thorazine 150:12</p> <p>thorough 127:18</p> <p>thoughtfulness 162:9</p> <p>thoughts 6:15 21:21 26:6 27:21 28:19 30:11 32:5 38:22 65:2 71:7 79:5 95:6 106:4 161:10,22 164:3</p> <p>thread 164:12</p> <p>three-times-a-day 144:4</p>	<p>throughout 13:16 17:16 25:13 38:6 45:15 60:4 114:11 140:9</p> <p>throw 136:17</p> <p>tie 157:19 158:12</p> <p>tight 153:16</p> <p>time-elapsed 119:11</p> <p>tiny 58:10</p> <p>tissue 8:20 167:10</p> <p>titanium 75:19</p> <p>titrated 143:20 149:9</p> <p>today 5:8,12 6:1 11:3 12:12 15:8,14 17:9 19:2 21:4,15,20 26:6 29:16 30:11 31:11 32:6,11 49:5 66:4 72:8 79:2,3 96:14 104:2,7 107:4 113:6,21 115:1,22 116:14,18 118:16 124:18 129:6 144:12 157:1 160:21 161:4,20 162:14 164:1,22 165:1,15 172:6 177:17</p> <p>Todd 3:11 48:14,17 52:18,19 62:18 81:3</p> <p>tolerated 24:6</p> <p>tomorrow 15:15,19 114:20</p> <p>tongue 58:7</p> <p>Tonight 97:10</p>
---	--	--	---

<p>tools 21:11 68:20</p> <p>top 89:12</p> <p>topic 3:8,9,10,11,12,13 ,14,15,16,17,18,1 9 4:4,5 6:2,4,8,9,15,16 26:15,16 27:4 31:21 32:2 78:12 96:1,2 140:9 151:17 161:7</p> <p>topics 6:1 26:14 73:1</p> <p>total 38:7 103:14</p> <p>totally 112:16</p> <p>touch 22:21 23:22 64:11 140:12</p> <p>touched 62:22 95:7</p> <p>tough 97:7 161:11</p> <p>toward 32:9</p> <p>towards 21:10 30:3 68:13 117:5 126:8</p> <p>toxic 160:13</p> <p>track 87:11 130:9 157:15 163:6</p> <p>tract 70:6</p> <p>traditional 69:16</p> <p>trainer 76:5 105:18 144:18</p> <p>trainers 99:14 105:1 130:12 144:18</p> <p>training 11:1 100:17 101:2</p> <p>transcribed 9:10 162:17</p> <p>transcript 9:11</p>	<p>20:12 28:21</p> <p>transformation 45:6</p> <p>transmitters 153:9</p> <p>transparent 13:6,8 99:19 162:20</p> <p>travel 33:11 66:6</p> <p>traveling 45:18</p> <p>treat 11:15 80:4 90:4 108:8 124:20</p> <p>treated 131:6 133:3 148:15</p> <p>treating 6:5 27:5,9 47:6 70:12 97:14 110:10 136:21 147:6</p> <p>treatment 5:21 12:14 19:13 20:3 27:6,15 48:3 96:3,10 97:1 98:3,7 99:1,10 101:22 103:14 105:9,14,19 110:5,13,19 116:8 118:14 122:11 125:7 129:13 131:8,14 132:4,16,17,20 133:14 134:11,17 151:6 160:1 171:16 176:4,10,16 177:1,4,13,21</p> <p>treatments 11:14 12:15 16:16 17:13 19:22 20:2 23:21 24:1 25:11 26:8 27:9,12 31:21 96:10,20 97:18 100:16 103:3 105:6</p>	<p>106:5 108:15 111:17,21 112:1,10,15,19 113:2 116:1 131:15 132:8,10 133:17 134:3,9 135:5,18 136:6,9 140:11 156:5 164:9,12,13 174:12 175:5 177:9</p> <p>treats 131:9</p> <p>tremor 23:10 24:22 25:9 63:15 67:18 86:8,10 108:20</p> <p>tremors 23:9 45:1 80:13 85:3,9 101:6 155:10</p> <p>trend 72:7</p> <p>trial 123:17</p> <p>trials 13:11,14 14:4 20:4 21:12 66:10 99:16 153:7</p> <p>trickling 105:7</p> <p>tricky 47:6</p> <p>tried 54:11 114:7 129:4 135:8 137:15 143:22</p> <p>trigger 73:12 141:20</p> <p>triggers 60:16 73:14 147:9</p> <p>trip 101:9</p> <p>trouble 74:6 126:22</p> <p>true 179:6</p> <p>truly 42:3 44:7 93:11 113:3</p> <p>trust 99:9 145:1</p>	<p>try 19:11 20:2 21:3 43:2 96:22 109:15,18 114:12 120:18 135:15 159:15 174:15</p> <p>trying 16:8 18:14 42:19 43:16 46:7 51:13 54:12 87:11 94:13 96:13 123:7 156:21</p> <p>Tuesday 1:8</p> <p>tune 69:19</p> <p>turn 9:21 21:16 35:14 101:5 119:21 120:2 136:3 166:16,22</p> <p>turned 170:13</p> <p>turning 57:16</p> <p>turns 18:3 58:21</p> <p>TV 52:5</p> <p>twenty 33:12 34:18,19 35:3</p> <p>twice 83:21 114:10</p> <p>twitching 90:13</p> <p>two-thirds 33:18</p> <p>type 127:7 131:22 142:20 157:17 169:8,10</p> <p>types 60:3 78:14</p> <p>typewriting 179:5</p> <p>typical 35:21 36:1</p> <p>typing 129:16,17</p> <hr/> <p style="text-align: center;">U</p> <hr/> <p>Uh-oh 120:11</p> <p>UK 99:9</p> <p>ultimate 11:22</p>
--	---	---	---

<p>105:9 ultimately 12:1 Um-hm 72:13 88:8 unable 20:10 26:21 81:6 127:7,8 uncertainty 60:9 unchecked 85:16 uncommon 51:3 86:18 undependable 116:5 undergoing 58:15 underrated 72:19 understand 11:12 12:14 19:18 31:22 46:7,11 89:16,22 96:15 134:16 148:2 152:20 153:17 understanding 29:11 59:10 137:1 155:17 understood 38:5 44:12 93:11 undiagnosed 127:2 132:6 undivided 52:16 unforeseen 102:21 unfortunately 37:16 56:3 84:19 108:1 110:20 140:17 Unger 2:7 7:12,13 142:15 146:4 uniqueness 112:9 United 22:5 University 70:3 75:16 100:19</p>	<p>172:17 unless 104:21 unmet 26:3 96:16 158:18 unpredictability 41:15 63:1,3 114:21 174:21 unpredictably 60:7 unusual 49:12 upcoming 98:6 UPD 139:14 UPDRS 124:1 139:17 UPDS 121:12 upon 32:12 49:13 62:22 64:11 69:6 95:7 140:12 167:18 upped 36:9 upper 58:4 145:12 ups 38:3 61:17 114:16 upset 137:18 uptake 46:19 140:5 urge 38:14 urgent 147:15 urging 68:17 useful 21:1 161:15 165:17 176:9 usefulness 110:8 User 18:1 usual 15:19 130:3 usually 20:17 50:15 51:11 112:18 120:2 133:2 141:15 170:5</p>	<p style="text-align: center;">————— V —————</p> <p>Vaidya 2:16 4:6 9:7 162:13 165:2 166:4 167:21 169:16 171:20 172:3 173:15 valuable 14:22 21:13 104:18 value 12:13 72:5 100:17 101:21 Variables 97:22 variance 42:22 129:19 varied 67:21 111:7 varies 97:21 129:17 variety 24:6 87:3 108:14,22 174:19 various 60:10 99:11 107:21 175:5,6 176:8,21 vary 80:9 vegetarian 43:6 45:18 46:17 84:4 velocity 52:12 versed 98:12 versus 157:7 via 29:14 viable 116:17 vibration 131:7 Vicky 92:13,15 view 12:14 82:5,6 viewed 123:13 views 32:6 97:10 vigilant 125:10 vigorous 128:11 visit 82:15 130:2</p>	<p>visitations 100:6 visiting 127:4 Vitamin 151:5 vitamins 109:1 vivid 52:7 voice 20:16 21:6 162:4 voluntary 29:8</p> <p style="text-align: center;">————— W —————</p> <p>wait 103:20 waiting 66:22 117:8 walk 38:4 39:2 51:22 53:17 54:5 58:22 72:1 75:6 81:7 107:18 108:12 109:17 149:17,18 walked 57:12 walker 38:4,10 39:2 walking 36:8 41:10 46:20 49:18 57:15 149:15 wall 71:15 wallet 102:16 walls 124:8 warehouse 138:13 warn 148:8 warned 84:11 warning 50:16 warnings 102:9 Washington 15:17 wasn't 42:6 152:20 watch 84:1,4 102:16 115:17</p>
--	---	---	---

<p>watches 84:3</p> <p>watching 52:5 101:10 115:12</p> <p>ways 12:12 46:16 167:8 173:6</p> <p>wear 45:13 59:3 145:19</p> <p>weather 102:21</p> <p>Web 29:13,15,17,21,2 2 35:6 64:13 67:22 76:12 90:8 135:19,20 136:6,18 154:2 155:3</p> <p>webcast 29:14,16</p> <p>Webinars 99:5</p> <p>website 9:12 20:15,18 31:8</p> <p>we'd 27:13 31:10 63:5 125:22 158:11 164:19</p> <p>week 39:11 83:19 101:3 109:19 123:22</p> <p>week-and-a-half 27:19</p> <p>weeks 9:13 117:10 128:17</p> <p>weeping 50:17</p> <p>weigh 17:19</p> <p>weighing 16:12,14</p> <p>weight 58:17 130:12,16</p> <p>weird 129:1 146:19</p> <p>welcome 5:11 10:2,3,6 15:10 21:19 30:18 35:20 78:15</p>	<p>welcoming 9:22</p> <p>we'll 5:16 6:7,17,20 9:11 11:5 15:3 20:20 26:15 27:16 28:7,8,14,17,22 29:5,19,20 30:2,15 32:1 35:16 64:11 90:9 95:17 97:8 137:14 139:3 142:1,2 146:12 150:10 151:1 152:3 153:19 156:1 163:9 173:18,20</p> <p>welling 50:18</p> <p>we're 5:16 6:1 10:4 13:9 14:7,9,12 15:11,13 17:9 18:2 19:3,4 21:6,14 26:2,17 27:5 29:21 32:8 35:6 40:13 65:21 66:3,8,9,10,11,13 68:14 69:1 79:7 86:17,21 87:10 96:12 106:16 126:13 134:22 135:17 139:12 140:22 151:16 153:16 154:4 157:2,15,20,21 158:1,7 159:10 162:3,14 165:19 166:13,15 167:1,18 168:22</p> <p>Western 71:3</p> <p>we've 6:10 18:17 20:6,19 21:7 24:10 37:9 38:17 73:6 75:20 76:16 98:1 102:11 105:6 140:8</p>	<p>143:16,22 163:1 165:8,14 167:4,5,6 169:2</p> <p>whatever 7:7 14:1 66:9 143:6 158:5 169:22</p> <p>what-not 157:13</p> <p>Wheaton 3:15 83:8,9</p> <p>wheelchair-bound 54:2</p> <p>whenever 59:16 148:4</p> <p>whereas 22:17</p> <p>Whereupon 95:18 178:2</p> <p>whether 16:10 48:2 71:18 109:9</p> <p>white 1:13 120:1</p> <p>whole 38:6 43:8 60:17 87:3,12 93:4 95:2</p> <p>whom 179:2</p> <p>who's 45:21</p> <p>whose 130:21</p> <p>wide 10:11 87:3</p> <p>widely 17:4</p> <p>widespread 38:20</p> <p>wife 88:13 144:21 171:14</p> <p>Wii 46:21</p> <p>William 2:4 3:5 160:5</p> <p>willing 20:1 117:17 143:1</p> <p>willingness 16:16,17</p>	<p>window 46:1 72:2</p> <p>wine 122:4</p> <p>wire 124:9</p> <p>wish 65:16 97:12,18</p> <p>withdrawal 87:22 88:4,9</p> <p>withdrawn 53:21</p> <p>woke 54:21</p> <p>woman 53:16 68:3</p> <p>women 171:9</p> <p>wonder 44:3 115:8 122:9</p> <p>wondered 146:6</p> <p>wonderful 170:15</p> <p>wondering 62:19</p> <p>work 10:20 12:17 13:6,16 54:19 77:10 87:7 110:3 114:10 122:1,2 137:16 143:13 165:19,22 167:5 168:3,21 171:17</p> <p>workday 168:9</p> <p>worked 27:20 42:19 71:5 100:18 121:6,17 123:15 136:14</p> <p>workers 101:10</p> <p>working 13:12 17:14 18:8 19:22 27:11,18 42:11 66:1 94:5 105:11 115:1 117:5 120:1 121:4 123:4 141:7 145:13 147:11 152:21 168:22 172:9</p>
--	--	---	---

<p>workload 47:15</p> <p>workout 145:9,13,18,20</p> <p>workplace 88:22 89:13</p> <p>works 122:17 123:15 140:20 157:16 177:15</p> <p>world 61:11</p> <p>worried 44:10 47:13 171:8</p> <p>worries 44:4,13 122:6</p> <p>worry 50:17 61:15 122:9</p> <p>worse 54:6 77:12 88:7 111:18 133:3 147:9 151:13 167:17</p> <p>worsen 43:22 82:2</p> <p>worsening 51:6</p> <p>worsens 77:8</p> <p>worst 41:12 42:12 47:17 132:19</p> <p>worst-case 127:22</p> <p>wrap 6:20 106:4 161:7</p> <p>wrapped 67:19</p> <p>write 12:21 46:21</p> <p>writhing 128:21</p> <p>writing 74:4</p> <p>written 30:13</p> <p>wrong 70:1,18 152:19</p> <hr/> <p style="text-align: center;">X</p> <hr/> <p>XL 100:13</p>	<p>X-rays 107:21</p> <p>Xu 2:13 8:18</p> <hr/> <p style="text-align: center;">Y</p> <hr/> <p>Yahr 50:1</p> <p>ya'll 10:1</p> <p>yellow 149:3</p> <p>yet 69:14 85:2 107:6 108:4 121:11 125:14 140:1 173:7</p> <p>yoga 43:9 114:9 130:11 176:11</p> <p>York 170:16</p> <p>you'll 7:3,4 20:14 29:4 93:16 168:16</p> <p>young 42:16 56:18 170:18 171:11,18</p> <p>younger 34:7</p> <p>young-ish 118:2</p> <p>young-onset 22:12,17</p> <p>yours 85:21</p> <p>yourselves 7:11</p> <p>you've 62:20 67:17 134:7 143:2</p>		
---	---	--	--