

Official Title: The Emergence and Evolution of Social Self-Management of Parkinson's Disease

Date of Document: May 2, 2019

STUDY PROTOCOL and STATISTICAL ANALYSIS PLAN

This document reports the study protocol and statistical analysis plan approved by the Social, Behavioral & Educational Institutional Review Board of Tufts University Medford Campus (protocol # 1212038), and the Boston University Medical Campus (BUMC) Institutional Review Board (protocol # H-32114) on August 27, 2013 to initiate study implementation [1].

Background

This project proposes that *social self-management of chronic disease* is a valuable quality of life indicator. The investigators define social self-management as the practices and experiences that ensure personal social comfort while supporting mental and physical well-being. Articulating this model will guide research to identify social factors that are deleterious to or protective of quality of life when living with chronic disease. Parkinson's disease (PD) offers a model for studying the effect of physical disease on the social self-management of daily life when physical symptoms affect fundamental social capacities.

To better understand the social lives of people with PD, it is necessary to translate motor impairment in the face, body and voice into social participation outcomes. A social ecological analysis of facial, bodily and vocal behavior produces this translation [2]. Healthy engagement in social life occurs in relation to bodily capacities and resources in the social environment of informal and formal social networks [3]. A longitudinal study of the daily lives of individuals with PD and their care partners was designed to validate the construct of social self-management as an evolving ecological

system. The objective of this study is to understand the social self-management systems and trajectories of people living with PD. The specific aims are as follows:

1. Characterize social self-management trajectories of individuals with PD over a 3-year period by assessing: a) social participation and management of social activities, b) informal and formal social networks, and c) social comfort and overall health and well-being. Hypothesis: Over three years there will be a general decline in the facilitative components of social living that comprise social self-management.
2. Estimate the degree to which expressive nonverbal capacity predicts the social self-management trajectory. Hypothesis: People with PD with higher expressive capacity at baseline will have more positive social trajectories over time than people with less expressive capacity.
3. Determine the moderating effect of gender on the association between expressive capacity in PD and change in social self-management. Hypothesis: Gender will moderate the association. The social trajectories of women are expected to be more vulnerable to the influence of expressive disability than the trajectories of men.

Methods/design

Research design

This prospective cohort study design tracks general patterns of the sample as a whole as well as variation among individual trajectories in social self-management. The tracking creates evidence necessary to develop social life interventions that address the typical issues faced by people living with the disease as well as individual variations in needs. Over a 3-year period, the study plans to follow 120 individuals with PD and their

associated primary care partner. Individuals with PD are included whether or not they have an identified care partner.

There are seven full assessments of approximately two hours duration and in-person, one at baseline and one every six months thereafter, with six in a clinical research lab and one in the home. Between the 6-month full assessments, there is an additional brief telephone call (15 to 30 minutes), totaling seven phone calls over three years. This innovative design of 14 assessments over the three years aims at detecting social or health triggers that affect individual participant's trajectories [4]. Frequent points of contact, while also building statistical power, increases the possibility of capturing remembered details of daily life that send health patterns into non-linear trajectories, such as anniversaries, retirement, bad colds or significant family events [5,6].

Ethics review

Recruitment, consent and data collection protocol have been approved by Social, Behavioral & Educational Institutional Review Board of Tufts University Medford Campus (protocol # 1212038), and the Boston University Medical Campus (BUMC) Institutional Review Board (protocol # H-32114).

Participants

Recruitment

PD is documented to be more prevalent in men than women: 1.55 men for every woman [7]. To maximize the power of the hypothesis testing of gender differences (Aim #3) the plan is to oversample women, by targeting a gender distribution of 50% women (n = 60) and 50% men (n = 60) with the disease and their care partners, a maximum

combined total of 240 participants. Participants will be recruited through the BUMC Parkinson's Disease Movement Disorders Clinic, postings on PD and aging research and advocacy websites, and PD support groups in the urban, suburban and rural regions within driving distance of the Boston metropolitan area.

Eligibility screening

Individuals who respond to recruitment are screened in a 1-hour session by a movement disorders neurologist and movement disorders nurse specialist for eligibility and to collect demographic data and conduct a medical history protocol. Informed consent procedures are conducted prior to screening for eligibility and consenting participants sign the BUMC consent form. Before their baseline assessment, participants sign their Tufts University consent form. Screening and assessments take place at the BUMC Parkinson's Disease and Movement Disorders Center or at the Tufts University Health Quality of Life Lab in Medford.

Inclusion criteria for participants with PD ensure minimal capacity to participate in the study procedures:

1. Diagnosis of idiopathic PD utilizing the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria, as evaluated by the neurological team,
2. Modified Hoehn and Yahr stage 1 through 4,
3. Score \geq 26 on the Mini-Mental Status Exam,
4. Home setting within travel distance to study locations,
5. Able to communicate clearly and in English with research staff,
6. Interested in participating and willing and able to provide informed consent.

Inclusion criteria for care partners are very flexible since participation of a care partner, while desired, is not required:

1. Person with PD must consent for care partner to participate,
2. Score ≥ 26 on the Mini-Mental Status Exam,
3. Able to communicate clearly and in English with research staff,
4. Interested in participating and willing and able to provide informed consent.

Baseline and 6-month follow-up in-person assessment procedures

Each of the seven in-person assessment sessions is designed to take a maximum of two hours to complete. At each session, initially, participants with PD and care partners are interviewed separately with parallel questionnaires to assess each of their daily life activities, health and quality of life. After separate interviews, the two are interviewed together about their combined social self-management. Participants with PD are asked to take their medication approximately 45 minutes before their assessment session in order to be “on,” that is, moving and functioning at maximal capacity during their session. Upon arrival they are asked about the timing and effectiveness of their medication on that day as well as the severity of their movement symptoms. Updates on medication changes and background information are collected, such as: marital status, living arrangement, occupational status, and notable mental and physical health or life events in the recent past or since the previous visit.

Covariate measures

The diminished expressive capacity that occurs in PD is a motor problem that can be confounded with the motor symptoms of depression, apathy or cognitive impairment [8,9]. At initial screening for this study, individuals with dementia are screened from

participation (i.e., ≥ 26 on the MMSE) yet dementia may develop over the course of the study. Participants are monitored for dementia and basic cognitive functioning at every visit with the Montreal Cognitive Assessment [10]. The Geriatric Depression Scale [11] is administered to participants at every visit to monitor depression throughout the study period. These measures are used for covariate analysis and to group individuals for blocked analyses.

Primary interview measures

Unless noted as otherwise, assessments are administered to both the participant with PD and the care partner. Variables and assessment procedures are described below in order of priority to the study.

Social participation and management of social activities. Measures described here focus on assessing participants' experience and participation in social activities and their self-management of social life, which fall under the Activity & Participation construct of the World Health Organization's International Classification of Functioning, Disability & Health (ICF) [12], and its relationship to their motor and non-motor symptoms, which fall under the Body Function construct of the ICF. These measures are administered at every visit.

1. **Participation.** The Activity Card Sort (ACS) [13] provides a measure of social participation and activity continuity from the past into the present. It contains photographs of individuals performing activities in four activity domains: 20 photographs of instrumental activities, 35 of low-physical demand leisure activities, 17 of high physical demand leisure activities, and 17 of social activities. The participants sort the cards into the categories of *never done*, *do less than six months ago*, *do same as six*

months ago, do more than six months ago, and given up the activity. Scores are calculated for each domain and the total set of activities: 1) percentage of total retained activities, 2) percentage of retained activities that are performed less than six months ago, and 3) percentage of retained activities that are performed more than six months ago. The ACS demonstrates test-retest reliability in older adult community-living and clinical populations is responsive to change in activities over a 6-month period [14] and correlates with mental and physical health in older adults [15]. It demonstrates convergent validity with the Adelaide Activities Profile [16], the PD-specific quality of life measure (Parkinson's Disease Questionnaire-39) and the primary measure of PD symptoms (Movement Disorder Society Unified Parkinson's Disease Rating Scales) [17].

2. Management. An open-ended interview elicits participants' reflections about self-identified frustrating and satisfying recent events in daily life and how they manage these and similar events [18-19]. Probes include 1) *What do you normally do to be able to participate in this or similar activities?* and 2) *What routines or strategies help you participate in this or similar activities?* Next, participants describe an activity outside of the home and how they get ready for it and manage PD symptoms to do it. Finally, participants are asked – *How would you rate your overall ability to manage participating in your daily life activities?* They provide a response on a scale of 1 (not at all effective) to 5 (highly effective). Participants with PD are videotaped and care partners are audiotaped.

In a second management discussion, the person with PD and the caregiver are brought together and asked to think of an activity outside of the home that they recently

did together. Probes include: 1) *How do the two of you get ready for an activity like this?* 2) *Do you think about timing of medication?* 3) *Are there symptoms you have to control when you go out?* and 4) *How do you manage doing both physical health activities, like taking medication, and engaging in social activities out of the home?* The discussion is videotaped with the camera focused only on the participant with PD.

Social networks. Measures described here assess participants' social environments, specifically informal and formal social network composition, contact frequency, social exchange of support, and the physical environments of social participation—which fall under the Environment construct of the ICF.

1. **Social network composition, contact and exchange.** At every visit, a set of items is used that discriminate cultural differences in social networks [20], including having a spouse or partner in the household, number and composition of individuals living in the household, total number of children and total number of grandchildren. Network contact is measured by frequency of contact with the most contacted child, with the most contacted friend, and with the care partner (if not the most frequently contacted child or friend). Social exchange is rated from 1 (very little) to 5 (a large amount) on 18 items. Nine of these items rate the amount of support received in three domains—help with daily activities, emotional support, and financial support—from each of three sources, if applicable: the other study participant (care partner or person with PD), other members of the household, and social network members outside of the household. The other nine items rate the amount of support given by the participant to the other care participant, other household members and others outside of the household, if applicable.

2. Social resources. At every visit, a modified version of the 22-item Chronic Illness Resource Survey (CIRS) assesses quality, composition and use of personal coping resources, informal social resources (e.g., family, friends, neighborhood, community) and formal social resources (health care team, work, organizations, and media/policy). There are nine sub-scores and a total score assessing resource support. For this study, wording is modified slightly to encompass resources commonly available to people with PD (e.g., Parkinson's support groups). The participant with PD and the care partner and respond to parallel forms that changed the wording of "chronic illness" to "health management" to make the questionnaire applicable for both. The original CIRS measure was validated on two large samples of community-living adults with a variety of illnesses and met all standards for psychometric soundness [21,22]. It is sensitive to change over a 1-year period and has provided findings useful for developing interventions.

3. Home visit. One assessment, scheduled approximately 1.5 years into the study, is in the home of each participant with PD. The modified CIRS was used by the interviewer to guide an audiotaped conversation about potential facilitators and barriers in the home and neighborhood environment that may affect social self-management.

Social comfort, health and well-being. These measures assess social self-management outcomes. The social comfort measures assess emotional well-being derived from one's social networks and are associated with the Environment construct of the ICF. The health and well-being measures assess health quality of life, disease severity and impairments and are associated with the Body Function construct of the ICF.

1. **Social Comfort.** At every visit, three measures assess social comfort: the Social Isolation Domain of the Nottingham Health Profile (NHP) [23], the Positive Social Interaction subscale items of the Medical Outcomes Study: Social Support Survey (MOS) [24], and the Stigma Scale for Chronic Illness (SSCI) [25].

- The Social Isolation Domain of the NHP is a 5-item measure of loneliness, difficulty with contacting people, difficulty getting along with others, and feeling like a burden [23]. The original dichotomous yes/no scale was converted to a more psychometrically sensitive and ecologically valid continuous measure. Participants rate their agreement with statements related to social isolation on a scale from 1 (extremely disagree) to 5 (highly agree). The domain score has been found to be responsive to change in PD over time [26]. It provides a measure of loneliness, which can predict motor decline and risk of death over one year in an older adult population including people with PD [27].
- The three Positive Social Interaction items in the MOS Social Support Survey were modified to identify positive interaction frequency with the care partner or the person with PD, rather than a non-specific “someone.” The revised wording is: “How often is each of the following kinds of support available to you *from your partner* if you need it?” The original subscales were developed and validated on 2,987 patients and have high internal consistency and stability over time [24]. These items measure mutuality in the care relationship [28].
- The 24-item SSCI was developed based on focus groups with people experiencing chronic neurological disorders including PD and has two domains: felt stigma and enacted stigma [25]. Felt stigma items assess the emotional

experience of stigmatization such as worry, embarrassment and self-blaming.

Enacted stigma items assess the perception that people act differently toward the respondent: acting uncomfortable, being unkind, avoiding contact, and unfair treatment. The total score and subscores demonstrate psychometric soundness in cross-sectional validation studies. For the current study, the original scale is used with the participant with PD. A modified form is used with care partners to identify how being with the person with PD affects their own felt and enacted stigma. For example, the modified wording (italicized) is "Because of *my partner's* illness, I have felt left out of things."

2. Health and well-being. The measures to assess health and well-being are the SF-12 (version 2) [29,30], the Parkinson's Disease Questionnaire-39 (PDQ-39) [31] or the shorter form PDQ-8 [32], and the Movement Disorder Society Unified Parkinson's Disease Rating Scales (MDS-UPDRS) [33]. The SF-12 (version 2) is the only one of these measures that is given to the care partner in addition to the person with PD.

- The 12-item SF-12 (version 2) is a highly used and cross-culturally validated survey of functional health and well-being that is a short form of the SF-36 [29,30]. It provides a norm-based score that can be used to compare the respondent against population level health. The SF-12 has been shown to be responsive to longitudinal changes in health. This measure is administered at every visit.
- The PDQ-39 assesses life concerns of individuals with PD [31]. It is composed of a summary index and eight domain scores—mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication, and

bodily discomfort. A higher score indicates a higher self-perceived frequency of quality of life and health problems in the past month that are due to the disease, with 0 indicating *never a problem* and 100 *always a problem*. The index and domain scores have adequate internal consistency, convergent validity with health status and quality of life measures, test-retest reliability, and responsiveness to intervention. The exception is the social support scale which has weak psychometric properties [34]. The PDQ-8 summary index is a short form of the PDQ-39 that is administered in place of the PDQ-39 for approximately half of the in-person assessments to allow for time to administer the MDS-UPDRS once per year. The PDQ-8 provides adequate psychometrics for detecting minimally important differences in change in health status of PD over a 1-year period [32].

- The MDS-UPDRS is a widely-used clinical assessment and research tool for assessing motor and non-motor symptom severity [33]. Parts I and II assess self-reported non-motor and motor aspects of daily living. Parts III and IV assess observed motor capacity and extent of abnormal movement and are the primary measures for this project. This assessment is administered once per year.

Brief telephone assessments

Calls are scheduled to interview the participant with PD and the care partner separately. The primary objective of these calls is to help inform findings relative to shifts in social trajectories. Participants have the opportunity to elect an alternate means of assessment, such as a mailed questionnaire, if a telephone assessment is perceived as burdensome. It has been found that telephone assessments that occur between

scheduled in-clinic visits are welcomed by people with PD [35], who typically do not find them burdensome, and experience them as comforting, positive attention. The 15- to 30-min audiotaped protocol involves the following assessments:

1. Recent important life events, changes in physical and mental health, and medication changes since the previous assessment,
2. PDQ-8 (administered only to the participant with PD),
3. Social Isolation domain-NHP,
4. Three simple 5-point scale questions (1= low, 5 = high), followed by open ended probes: 1) *How satisfying is your social life right now?* (probes: stressful or exciting changes in networks, finances, activities); 2) *How satisfied are you with managing the effects of PD on your life right now?* (probes: physical, social, emotional effects); and 3) *How satisfied are you with your health right now?* (probes: physical, social, emotional health), and
5. SF-12 (version 2).

Measure of expressive nonverbal capacity

The Interpersonal Communication Rating Protocol: Individual Expressive Behavior (Parkinson's Disease Version) (ICRP-IEB) [36] is used as the primary measure of the expressive capacity of participants with PD in videotaped discussions about management of social activities at baseline and 6-month follow-ups. This rating protocol employs a "thin slice" method, which links discrete behaviors (e.g., an upturned lip, a movement of the limb) into socially meaningful units (e.g., smiling, happiness, dominance) that are closely aligned with individuals' social life outcomes (e.g. health or work success) [37-39]. The primary method is to extract short segments (thin slices)

from a video or audiotaped social interaction, and have raters draw behavioral or social conclusions from the segments. For this project, 60-second clips are extracted from the videotapes at two standardized time points during the interview: first when the participant is asked to describe a frustrating activity, and again when asked to describe an enjoyable activity [40]. Sixty-second clips have been found to yield optimal accuracy-to-slice length ratio for making judgments of behavior [41]. Using the methods described in the ICRP-IEB manual, trained research assistants view the clips separately and rate the quality, intensity and frequency of expressive behavior on 20 discrete actions (e.g., smiling, gesturing, bodily movement, vocal tone) and PD symptoms (tremors and postural slouch) that observers use as cues to form judgments about a target individual's emotions, thoughts, social motives and personality. Previous studies provide evidence that expressive capacity in PD can be measured reliably and validly at this social level of analysis [40,42]. Expressive behavior composite scores are formed based on principal component analyses.

Power Calculation

The data analysis assumes 120 participants with PD and seven full assessment time points over three years; dropout per year at 15%; intra-class correlation (ICC) at 0.82, based on prior data [43]; and type I error at $\alpha=0.05$. These metrics predict 80% power to detect a mean change over time of 0.40 of a standard deviation in the PDQ-39 outcome per year; 80% power to detect a correlation between continuous variables of 0.23; and 80% power to detect a difference of 0.50 standard deviations in the outcome scale between genders (Aim 3). Previous studies of similar outcomes have found a

sample size of 120 to be adequate for demonstrating statistically significant effects [43, 44].

Data analysis

Aim 1: Social self-management trajectories

Descriptive analyses

Descriptive statistical analyses will be performed on the total sample and on demographic subgroups that are relevant to the progression of Parkinson's disease (e.g., current age, age of onset, disease severity at baseline, gender). Mean trajectories over time will be plotted for all repeated measures by the same demographic subgroups. Scales will be checked for floor and ceiling effects. Associations between the scales, which represent the different components of social self-management, will be examined through scatter plots and relational statistics.

Audiotaped open-ended discussions during in-person and telephone assessment sessions will be transcribed. Quantitative content analysis will be performed on the transcriptions using Linguistic Inquiry Word Count (LIWC) to describe proportions of verbal content meaningfully related to the three ICF social self-management categories in the study's model [45]. LIWC contains word dictionaries that measure 80 language dimensions including psychological constructs (e.g. affect, cognition), biological processes (e.g. body, health), personal concerns (e.g., social, home, work, leisure) and linguistic indicators of socio-emotional experience and interpersonal interaction. The dimensions have been validated in over 120 published studies as indicative of a variety of life preferences and health outcomes [46] and in previous work on motivation indicators (e.g., helplessness, hopefulness, apathy) in PD [40]. Verbal content

proportions from the LIWC analysis will be included with quantitative questionnaire results that are entered into quantitative descriptive and longitudinal analyses.

In addition to quantitative content analysis, qualitative content analysis will be performed on the transcribed open-ended narratives using standard methods [47]. Each transcribed interview will be searched for phrases meaningfully related to the three ICF social self-management categories in this study's model. These phrases will be coded to identify themes across participants that can be abstracted to social self-management categories and the relationships between these categories (e.g. phrases that link a social activity to motor symptoms). If the data reveal new dimensions to social self-management, new codes, themes or categories will be developed to accommodate these data. To assess and assure coding reliability and dependability, two independent coders will assess a sub-set of data (approximately 40 transcripts of the same type) in an iterative process until coding agreement is achieved. Data will be summarized with coding categories and illustrated with participant quotations. Qualitative and quantitative data will be compared and contrasted to elaborate the construct of social self-management.

Models for longitudinal trajectories

Longitudinal data will be analyzed using the multilevel model for change (also called random coefficient, mixed, or hierarchical model) [48]. Primary outcomes measured at baseline and the semi-annual fixed time points are: 1) retained activities (ACS), 2) proportions of quantitatively content coded words during open-ended responses of social self-management discussions (LIWC), 3) network composition, structure and exchange scores, 4) social network resource utilization scores (modified CIRS), 5)

social isolation score, 6) positive interaction with partner score, 7) felt stigma and enacted stigma scores (SSCI), 8) physical and mental health scores (SF-12), 9) health quality of life with PD scores (PDQ-39 or PDQ-8), and 10) motor capacity scores (MDS-UPDRS, Parts III and IV). Outcomes measured at all 14 time points are: 1) physical and mental health scores (SF-12), 2) health quality of life with PD score (PDQ-8), and 3) loneliness score (Social Isolation, NHP). Temporal dynamics of these outcomes will be explored in order to better understand the similarities, differences and factors governing such dynamics. By including random effects, the population trajectory and the degree of variations of individual trajectories will be explored. Outcomes reported by both the person with PD and the care partner will depict both perspectives, which enable an assessment of the synchronicity between the two sources. Statistical tests of interaction terms will evaluate whether particular factors affect the ratings of one source more than another.

The multilevel models can accommodate subjects with and without care partners, as well as incomplete data collection, as long as data are missing at random [49]. For sensitivity analyses pattern mixture models are used to account for the possibility of informative missingness. The models will stratify by pattern of and reason for missing data [50].

Effects of triggers on trajectories: Exploratory analysis

For exploratory purposes, the general multilevel modeling approach is expanded to consider potential effects of unanticipated triggers assessed at the individually identified time points [4]. The timing of measurements will be calibrated as “time elapsed since an event” or “time preceding an event”. Recalibration enables synchronization of triggering

events across the cohort, allowing determination of synchronized changes in one of the outcomes of interest after occurrence of an unanticipated event. For example, there may be an increase in loneliness following hospitalization of a spouse or a decline in social activity following an episode of physical illness.

Non-linearities with non-parametric fitting will be explored if a sufficient number of subjects have experienced a similar event. For example, some social triggers may have a temporary U-shaped trajectory. This description of potential rapid or unexpected changes in the trajectories is highly innovative for research in the social aspects of PD and other chronic degenerative conditions. Adding trigger event monitoring to the research design builds power for repeated measures, and it may illuminate the understanding of disease progression as a social ecological phenomenon.

Aim 2: Expressive nonverbal capacity as predictor

Analysis will start with a simple linear model, considering a random intercept and slope for each individual. The assumption is that, the variation among individuals in the intercept and slope of their trajectories can be explained by subject characteristics, including expressive capacity at baseline. For example, it may be found that the rate of change in the study outcomes may vary and depends on expressive capacity at baseline. This preliminary step will guide the further model building.

Multivariate models are built by first adding demographic factors, then clinical factors, and then other variables of interest including masking, life stage, and access to support. The number of variables are reduced in each group before adding the group to the model, and the number of variables are reduced further as groups are added. Since expressive masking will be measured at follow-up times as well, repeated measures

analyses are performed to estimate the relation between change in expressive masking and change in social self-management.

Aim 3: Moderating effect of gender

Models developed for Aim 1 and 2 are applied to explore in detail the effect of gender on the modeling results. For example, it may be found that rates of change in the study outcomes depend on both, expressive capacity at baseline and gender. The test of the moderating effect of gender on the relationship between expressive masking and social self-management in PD is conducted by stratifying the analysis and by including an interaction term between gender and potential predictors. For all models, non-linearities in predictors are tested, and variables are transformed when necessary to obtain good model fit. Models will be examined with respects to over-fitting and fine-tuned to improve their performance.

Problems and Alternative Strategies

Attrition can be a problem in longitudinal studies of a disease like PD, due to morbidity, mortality or other uncontrollable factors. The investigators' previous research, which enrolled similar numbers of people with PD, had a relatively low attrition rate despite significant time burden [43], and a similarly low rate is expected in the proposed study. Data are collected on reasons for any attrition, rigorous strategies are implemented to counteract controllable sources of attrition and these strategies are tested for their effectiveness. Retention strategies, such as activities that develop strong rapport with participants, may create unintentional "social intervention" effects on study outcomes [51]. Strategies are applied with the intent of maximizing retention while minimizing and monitoring unintentional effects on everyday social life.

Although existing research is supportive of the hypothesis that gender moderates the effects of expressive capacity on life trajectories, there are many parameters of living with PD that cannot be controlled. Expressive masking may create vulnerability in women, but in general aging women are more likely than aging men to have strong social support networks, which is a possible confound for the current study [52]. Recent literature suggests that PD presents and progresses differently in men and women, for example, that women may have a more benign disease than men [53]. Gender research into quality of life domains is in its infancy, thus the current study is unusual and does not have precedents to follow. Gender is evaluated at all steps of the project.

References

1. Tickle-Degnen L, Saint-Hilaire M, Thomas CA, et al. Emergence and evolution of social self-management of Parkinson's disease: study protocol for a 3-year prospective cohort study. *BMC Neurol*. 2014;14(1):95.
2. Tickle-Degnen L: **Nonverbal behavior and its functions in the ecosystem of rapport**. In *Handbook of Nonverbal Communication*. Edited by Patterson ML, Manusov, V. Thousand Oaks, CA: Sage. 2006: 381-399.
3. Stokols D, Grzywacz JG, McMahan S, Phillips K: **Increasing the health promotive capacity of human environments**. *Am J Health Promot* 2003, **18**(1):4-13.
4. Naumova EN, Must A, Laird NM: **Tutorial in biostatistics: Evaluating the impact of 'critical periods' in longitudinal studies of growth using piecewise mixed effects models**. *Int J Epidemiol* 2001, **30**(6):1332-1341.
5. Harezlak J, Naumova E, Laird NM: **LongCriSP: A test for bump hunting in longitudinal data**. *Stat Med* 2007, **26**(6):1383-1397.

6. Sarkar R, Ajjampur S, Ward H, Kang G, Naumova E: **Analysis of human immune responses in quasi-experimental settings: Tutorial in biostatistics.** *BMC Med Res Methodol* 2012, **12**:1.
7. Dahodwala N, Xie M, Noll E, Siderowf A, Mandell DS: **Treatment disparities in Parkinson's disease.** *Ann Neurol* 2009, **66**(2):142-145.
8. Tickle-Degnen L, Lyons KD: **Practitioners' impressions of patients with Parkinson's disease: The social ecology of the expressive mask.** *Soc Sci Med* 2004, **58**:603-614.
9. Bogart KR: **Is apathy a valid and meaningful symptom or syndrome in Parkinson's disease? A critical review.** *Health Psychol* 2011, **30**(4):386-400.
10. Nazem S, Siderowf AD, Duda JE, Have TT, Colcher A, Horn SS, Moberg PJ, Wilkinson JR, Hurtig HI, Stern MB, Weintraub D: **Montreal Cognitive Assessment performance in patients with Parkinson's disease with "normal" global cognitive according to Mini-Mental State Examination score.** *J Am Geriatr Soc* 2009, **57**(2):304-308.
11. Sheikh J, Yesavage J: **Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version.** In *Clinical Gerontology: A Guide to Assessment and Intervention* Edited by Brink TL. New York: Haworth Press; 1986:165-173.
12. World Health Organization: **International Classification of Functioning, Disability and Health (ICF).** Geneva; 2001.
13. Baum CM, Edwards D: **Activity Card Sort, 2nd edition.** Bethesda, MD: AOTA Press; 2008.

14. Lyons KD, Hull JG, Root LD, Kimtis E, Schaal AD, Stearns DM, Williams IC, Meehan KR, Ahles TA: **A pilot study of activity engagement in the first six months after stem cell transplantation.** *Oncol Nurs Forum* 2011, **38**(1):75-83.
15. Everard KM, Lach HW, Fisher EB, Baum CM: **Relationship of activity and social support to the functional health of older adults.** *J Gerontol B Psychol Sci Soc Sci* 2000, **55**:S208-S212.
16. Doney RM, Packer TL: **Measuring changes in activity participation of older Australians: Validation of the Activity Card Sort-Australia.** *Australas J Ageing* 2008, **27**:33-37.
17. Duncan RP, Earhart GM: **Measuring participation in individuals with Parkinson disease: Relationships with disease severity, quality of life, and mobility.** *Disabil Rehabil* 2011, **33**(15-16):1440-1446.
18. Tickle-Degnen L, Zebrowitz LA, Ma H: **Culture, gender, and health care stigma: Practitioner's response to facial masking experienced by people with Parkinson's disease.** *Soc Sci Med* 2011, **73**:95-102.
19. Tickle-Degnen L, Thomas C, Saint-Hilaire M, Naumova E, Ambady N, Ellis T, Wagenaar R: **The social self-management of Parkinson's disease in daily life [abstract].** *Movement Disord* 2012, **27**:(S1), S313-S314.
20. Litwin H: **Social networks and well-being: A comparison of older people in Mediterranean and non-Mediterranean countries.** *J Gerontol B Psychol Sci Soc Sci* 2009, **65B**(5):599-608.

21. Glasgow RE, Strycker LA, Toobert DJ, Eakin E: **The Chronic Illness Resources Survey: A social-ecologic approach to assessing support for disease self-management.** *J Behav Med* 2000, **23**(6):559-583.
22. Glasgow RE, Toobert DJ, Barrera M, Strycker LA: **Cross-validation and sensitivity to intervention: The chronic illness resources survey.** *Health Educ Res* 2005, **20**(4):402-409.
23. Hunt SM, McEwan J: **The development of a subjective health indicator.** *Sociol Health Ill* 1980, **2**(3):231-246.
24. Sherbourne CD, Stewart AL: **The MOS social support survey.** *Soc Sci Med* 1991, **32**(6):705-714.
25. Rao D, Choi SW, Victorson D, Bode R, Peterman A, Heinemann A, Cella D: **Measuring stigma across neurological conditions: The development of the Stigma Scale for Chronic Illness (SSCI).** *Qual Life Res* 2009, **18**(5):585-595.
26. Karlsen KH, Tandberg E, Årslund D, Larsen JP: **Health related quality of life in Parkinson's disease: A prospective longitudinal study.** *J Neurol, Neurosurg Psychiatry* 2000, **69**(5):584-589.
27. Buchman AS, Boyle PA, Wilson RS, James BD, Leurgans SE, Arnold SE, Bennett DA: **Loneliness and the rate of motor decline in old age: The rush memory and aging project, a community-based cohort study.** *BMC Geriatr* 2010, **10**:77.
doi:10.1186/1471-2318-10-77.
28. Tanji H, Anderson KE, Gruber-Baldini AL, Fishman PS, Reich SG, Weiner WJ, Shulman, LM: **Mutuality of the marital relationship in Parkinson's disease.** *Movement Disord* 2008, **23**:1843-1849.

29. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Leplege A, Prieto L, Sullivan M, Thunedborg K: **Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: Results from the IQOLA Project. International Quality of Life Assessment.** *J Clin Epidemiol* 1998, **51**(11):1171-1178.
30. Ware J, Kosinski M, Keller SD: A 12-item short-form health survey: **Construction of scales and preliminary tests of reliability and validity.** *Med Care* 1996, **34**:220-233.
31. Peto V, Jenkinson C, Fitzpatrick R: **PDQ-39: A review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures.** *J Neurol* 1998, **245**(Suppl 1):S10-S14.
32. Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N: **The PDQ-8: Development and validation of a short-form Parkinson's disease questionnaire.** *Psychol Health* 1997, **12**:805-814.
33. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stern MB, Dodel R, et al: **Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results.** *Movement Disord* 2008, **23**(15):2129-2170.
34. McComb M, Tickle-Degnen L: **Developing the construct of social support in Parkinson's disease.** *Phys Occup Ther Geriatr* 2005, **24**(1):45-60.

35. Worth A, Tierney A: **Conducting research interviews with elderly people by telephone.** *J Adv Nurs* 1993, **18**(7):1077-1084.
36. Tickle-Degnen L: **Interpersonal Communication Rating Protocol: A manual for measuring individual expressive behavior (ICRP-IEB) (Parkinson's disease version)** [<http://ase.tufts.edu/hgl/projects.asp>.]
37. Ambady N, Rosenthal R: **Thin slices of expressive behavior as predictors of interpersonal consequences: A meta-analysis.** *Psychol Bull* 1992, **111**:256-74.
38. Ambady N, Koo J, Rosenthal R, Winograd C: **Physical therapists' nonverbal communication predicts geriatric patients' health outcomes.** *Psychol Aging* 2002, **17**(3):443-452.
39. Ambady N, LaPlante D, Nguyen T, Rosenthal R, Chaumeton N, Levinson W: **Surgeon's tone of voice: A clue to malpractice history.** *Surgery* 2002, **132**(1):5-9.
40. Takahashi K, Tickle-Degnen L, Coster W, Latham N: **Expressive behavior in Parkinson's disease as a function of interview context.** *Am J Occup Ther* 2010, **64**(3):484-495.
41. Carney DR, Colvin CR, Hall JA: **A thin slice perspective on the accuracy of first impressions.** *J Res Pers* 2007, **41**:1054-1072.
42. Lyons K, Tickle-Degnen L: **Reliability and validity of a videotape method to describe expressive behavior in Parkinson's disease.** *Am J Occup Ther* 2005, **59**:41-49.

43. Tickle-Degnen L, Ellis T, Saint-Hilaire M, Thomas CA, Wagenaar RC: **Self-management rehabilitation and health-related quality of life in Parkinson's disease: A randomized controlled trial.** *Movement Disord* 2010, **25**(2):194-204.
44. Post B, Muslimovic D, van Geloven N, Speelman JD, Schmand B, de Haan RJ: **Progression and prognostic factors of motor impairment, disability and quality of life in newly diagnosed Parkinson's disease.** *Movement Disord* 2011, **26**(3):449-456.
45. Pennebaker JW, Booth RJ, Francis ME: **Linguistic Inquiry and Word Count (LIWC).** [Computer software]. Austin, TX: LIWC.net; 2007.
46. Tausczik Y, Pennebaker JW: **The psychological meaning of words: LIWC and computerized text analysis methods.** *J Lang Soc Psychol* 2010, **29**:24-54.
47. Graneheim UH, Lundman B: **Qualitative content analysis in nursing research: Concepts, procedures and measures to achieve trustworthiness.** *Nurs Educ Today* 2004, **24**:105-112.
48. Singer JD, Willet JB: *Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence.* New York, NY: Oxford University Press; 2003.
49. Horton NJ, Laird NM, Murphy JM, Monson RR, Sobol AM, Leighton AH: **Multiple informants: Mortality associated with psychiatric disorders in the Stirling County Study.** *Am J Epidemiol* 2001, **154**(7):649-656.
50. Hedeker D, Gibbons RB: *Longitudinal data analysis.* Hoboken, NJ: Wiley; 2006.
51. Davis LL, Weaver M, Habermann B: **Differential attrition in a caregiver skill training trial.** *Res Nurs Health* 2006, **29**(5):498-506.

52. Netuveli G, Wiggins RD, Montgomery SM, Hildon Z, Blane D: **Mental health and resilience at older ages: Bouncing back after adversity in the British**

Household Panel Survey. *J Epidemiol Commun Health* 2008, **62**(11):987-91.

53. Haaxma CA, Bloem BR, Borm GF, Oyen WJG, Leenders KL, Eshuis S, Booij J,

Dluzen DE, Horstink MWIM: **Gender differences in Parkinson's disease.** *J Neurol Neurosurg Ps* 2007, **78**(8):819-824.