Evaluating the Cost-Effectiveness of an Early Detection of Parkinson's Disease through Innovative Technology

Abstract

Early detection of Parkinson's Disease (PD) is critically important as it can increase patient quality of life and save treatment cost. An innovative approach for early detection of PD is to use non-wearable sensors that are capable of capturing skeletal joint data. This paper evaluates the cost-effectiveness of this sensor-based intervention considering the quality-adjusted life years (QALYs) and the associated costs. The results indicate that the intervention would be cost-effective if devices were deployed for community health screening in public places such as health fairs and pharmacies.

Keywords

Cost-effectiveness analysis, quality-adjusted life years, healthcare intervention, Parkinson's Disease

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that typically affects the elderly population. In the U.S., almost one million people live with PD and approximately 60,000 new cases are diagnosed each year (Parkinson's Disease Foundation, 2015). PD has a tremendous impact on the populations' quality of life and levies a heavy economic burden. Kowal et al. (2013) estimate the total annual cost of PD in the U.S. to be $8.1 billion in medical expenses and $6.3 billion in indirect costs such as reduced employment, travel to see a physician, adult day care, and home modifications. There is currently no cure for PD. Therapies, such as medication, surgery, diet changes, physical therapy, support groups, occupational therapy, and speech therapy, focus on treating the symptoms that undermine the patient's quality of life (Giladi, Manor, Hilel, & Gurevich, 2014; Worth, 2013). PD is not homogeneous as~~with~~ patients have varying symptoms and different rates of progression, and early in the course of illness there are some disorders that may look like PD (e.g., multiple system atrophy, Lewy body dementia). A patient-centered approach that provides coordinated and interdisciplinary care offers the best outcome for PD. The National Parkinson's Foundation (2014) has estimated that 6,400 people with PD die each year due to insufficient and uncoordinated care. This is also supported by studies that have shown that nearly 60% of individuals suffering from PD do not get the expert care that they need (Landro, 2014).

Some of the key signs of PD include tremor, rigidity, bradykinesia, gait disturbances, and postural instability (Bakheit, 1995; Gelb, Oliver, & Gilman, 1999). A recent study showed that essentially all PD patients consulted a physician because of motor symptoms. Typically, primary care physicians refer patients to neurologists if they suspect PD motor symptoms. Neurology specialists then interview patients, screen medical records, and conduct a series of examinations and tests to determine if someone has PD~~ patient~~. It has been argued that standardized screening procedures focused on early motor symptoms could help detect individuals with high risk for PD (Gaenslen & Berg, 2010). In the pre-diagnosis phase (≤ 2 years) mild motor signs including asymmetric bradykinesia and rest tremor are significant in PD (Walter et al., 2013). Moreover, motor asymmetry has been found to have a high sensitivity (88%), specificity (54%), and positive predictive values (85%) for the diagnosis of PD (Busse et al., 2012). Although motor signs have been typically used to assess PD, the populations' access to current diagnosis methods is limited since the diagnosis of PD is costly and requires several visits to the specialist (Gaenslen & Berg, 2010; Pahwa & Lyons, 2010; Tucker et al., 2015).

Several studies have focused on the cost-effectiveness of the different types of treatments that exist to manage the symptoms of PD. These treatments include pharmacological regimens (levodopa being the

most important) and for later disease, neurosurgical approaches (e.g., deep brain stimulation) (Dams et al., 2011, 2013; Tomaszewski & Holloway, 2001). Interest in studying the economic burden of PD has been spurred by new reimbursement regulations, and the need for cost accounting when comparing different alternatives to improve health gains. Healthcare providers have been particularly interested in chronic diseases with high prevalence and high treatment costs such as various neurodegenerative diseases including PD.

One of the potential mechanisms to improve PD diagnosis and its coverage may be the use of telehealth solutions with innovative technology such as smartphones, sensing bracelets, and motion sensors (Dhillon, Ramos, Wünsche, & Lutteroth, 2012). There is still, however, a need for more research that demonstrates the efficacy of these technologies from a practical perspective. Quantitative metrics are needed that demonstrate the value of these innovations in providing substantial health gains, given their costs.

In this study, we present a cost-effectiveness analysis (CEA) to evaluate the implementation of a non-wearable sensor based telehealth technology for early detection of PD based on patients' motor patterns. Health gains in CEA were measured in terms of quality-adjusted life years (QALYs) and the costs associated with this intervention were estimated. The overall impact on society was calculated and a sensitivity analysis was conducted.

2. Telehealth Systems for Early Detection of Parkinson's Disease

2.1. Brief Description of Telehealth Diagnosis Systems

Technological advancements in mobile computing and networking infrastructure have spurred the availability of low-cost, commercially available telehealth diagnosis systems that have the potential to connect patients with their healthcare providers in a timely and efficient manner (Li, 2013). While there is a wide range of systems available for telehealth diagnosis (Fouquet, Franco, Vuillerme, & Demongeot, 2012; Gay & Leijdekkers, 2007; Lymberis, 2003; Suzuki, Tanaka, Minami, Yamada, & Miyata, 2013), several commonalities exist. A telehealth diagnosis system must be able to i) sense characteristics pertaining to a patient's health, ii) communicate data to a processing entity, iii) discover knowledge based on the patient's data, and iv) provide feedback to the patient and the healthcare provider. For example, wearable solutions such as armbands have been proposed to capture patient gait data for the modeling and prediction of Parkinson's Disease (Huang et al., 2012).

Non-wearable sensors, such as the Microsoft Kinect, are capable of capturing comparable patient gait data, without the need for contact with the patients' body, hereby expanding the environments and convenience of data capture (Mousavi Hondori & Khademi, 2014; Webster & Celik, 2014). The frequency of sensor data collection will depend on the objectives of the healthcare provider since non-wearable sensors, such as the Microsoft Kinect, can capture human gait patterns at a rate of 30 Hz or approximately one sample every 33 milliseconds. Machine learning techniques can be employed to discover patterns existing within the collected data that help predict anomalies in patients' health (Kumar, Nilsen, Abernethy, et al., 2013; Kumar, Nilsen, Pavel, & Srivastava, 2013).

2.2. Microsoft Kinect Based Early Detection System for PD

Tucker et al. (2015) have developed a Microsoft Kinect-based detection tool that can recognize gait abnormalities relevant to Parkinson's Disease. This tool can serve as the basis for a telehealth system that provides decision support for early-stage PD diagnosis. This telehealth system is anticipated to consist of three steps as outlined in Figure 1.

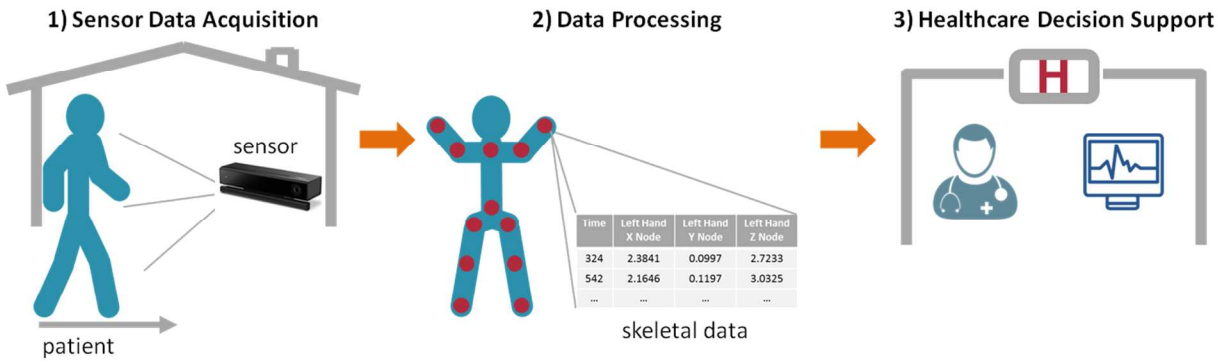

Figure 1: The overview of the sensor-based telehealth detection system

Step 1 Sensor Data Acquisition is the usage of Microsoft Kinect to capture skeletal joint data from individuals at home or in a public place. To collect gait data, the Kinect is configured at an elevation of 3 feet and 10 inches above the floor and the individual stands at a distance of 10 feet from the Kinect. A laptop or a tablet is connected to the Microsoft Kinect to save the collected data. A monitor is used to provide instructions (e.g., "Please start walking forward") and warnings (e.g., "The whole body is not observable") to the individual. Then, the individual comfortably walks towards the Kinect (forward) and walks away from the Kinect (backward) following the instructions in the monitor. During each walking, which may take 4-6 seconds depending on the individual, the Kinect collects 3D coordinates of the 20 skeletal joints (e.g., left elbow, right wrist, etc.) on the individual every 33 milliseconds. The Kinect is capable of tracking skeletal joints non-invasively and independent of the outfit. A nursing assistant will

guide the individual during data collection if the telehealth system is deployed in a public space such as malls or churches.

Step 2 Data Processing is data cleaning and processing. In this step, irrelevant/noisy data are removed from the initial data captured in Step 1 and then velocity and acceleration values of each skeletal joint~~s~~ ~~are~~is generated. In addition, the ratio in each dimension from each pair of joints in the position, velocity, and acceleration data are also generated to normalize variations in human characteristics (e.g., size, height, and weight). Therefore, by initially tracking 20 skeletal joints, a total of 630 features (i.e., 20 position features, 20 velocity features, 20 acceleration features, 190 position ratio features, 190 velocity ratio features, and 190 acceleration ratio features) are generated for each dimension (i.e., X, Y, and Z). These features are used as inputs for the machine learning algorithms that detects PD gait abnormalities in individuals.

Step 3 Healthcare Decision Support employs machine learning methods on the generated set of features to reveal the gait abnormalities related to PD. According to Tucker et al. (2015) the most reliable machine learning method is J48 decision tree model with an accuracy of almost 75%. The telehealth system notifies the neurology specialist of the individual's motor symptoms and the output of J48 decision tree model. This step can integrate the screening data with patient's EHR and serve as a decision support system. Based on the neurology specialist's final decision, the individual may be scheduled for a visit in the clinic.

This intervention demonstrates the feasibility of telehealth system in enhancing patients' health as a means of delivering remote screening outside of the traditional healthcare facility. Hence, this intervention might help to advance the early-stage diagnosis of PD whose main symptoms are manifested through motor signs. In this study, we investigate the cost-effectiveness of this sensor-based telehealth intervention.

3. Cost-Effectiveness Analysis

Cost-effectiveness analysis (CEA) evaluates the health benefits over the costs involved to obtain such benefits (Jamison et al., 2006). Although costs might not be the only criterion for guiding the allocation of resources, CEA provides a fair and comprehensive way to compare different interventions based on their potential to increase people's health relative to the costs. Hence, CEA has been used in practice to inform different health policy making levels as it integrates life expectancy, treatment cost and the change in health-related quality of life due to an intervention (Lubowitz & Appleby, 2011). The integration of these

elements provides an appropriate baseline for comparisons in the resource allocation process in healthcare (Weinstein, Siegel, Gold, Kamlet, & Russell, 1996).

Typically, health gains in CEA are measured in terms of quality-adjusted life years (QALYs). This metric has been used consistently for over four decades. Zeckhauser & Shepard (1976) used the term QALY for the first time to propose a metric that combines duration and quality of life. Pliskin et al. (1980) demonstrated that QALY maximization based on the utility theory is justifiable under two conditions; utility independence between health status and life of years, and risk neutrality with respect to life of years. The estimation of QALY incorporates a measure of quality of life (Q) also known as health-related quality of life status (HRQoL). This value typically ranges from 0 to 1 where 0 represents the worst possible health state and 1 represents a maximum or perfect health status.

Currently, QALYs are used in most economic assessments conducted by agencies that encourage the cost-effectiveness factors as fundamental component of their decision-making processes (Sassi, 2006). Mathematically, the number of QALYs lived by a person can be expressed as follows:

$$QALY\ in\ one\ year = 1 * Q, \qquad 0 \leq Q \leq 1. \tag{1}$$

The expected quality-adjusted life or quality-adjusted life expectancy (*QALE*) at a certain age a of disease is formulated as:

$$QALE = \sum_{t=a}^{a+L} Q_t, \tag{2}$$

where L is the residual life expectancy of the individual at age a, and t is the number of years that the individual is expected to be attached to the corresponding Q. Typically, discounting factors are used to calibrate the utility of QALY. In other words, discounting translates~~ing~~ future QALYs into a present value. The *discounted QALE* can be calculated as follows:

$$Discounted\ QALE = \sum_{t=a}^{a+L} \frac{Q_t}{(1+r)^{t-a}}\ , \tag{3}$$

where r is the discount rate or normalization factor to evaluate health using present value. Typically, a discount rate of 3-5% is in line with the Global Burden of Disease (GBD) and practical guidelines

(Brouwer, Hout, & Rutten, 2000). In order to compare the impact of health interventions, the pre-intervention QALY and post-intervention QALY must be compared. This metric gives an estimate of the QALYs gained as a result of the health intervention. Thus:

$$QALYs \text{ gained} = \sum_{t=a}^{a+L^i} \frac{Q_t^i}{(1+r)^{t-a}} - \sum_{t=a}^{a+L} \frac{Q_t}{(1+r)^{t-a}} \ , \tag{4}$$

where Q^i is the vector related to the health status quality of life weights predicted after the health intervention for each time step *t*.

The cost-effectiveness of two interventions is compared by incremental cost-effectiveness ratio (ICER), estimated as:

$$ICER = \frac{C_i - C_j}{QALYs_i - QALYs_j}, \tag{5}$$

where C_i and C_j are the costs of interventions i and j wheraes $QALYs_i$ and $QALYs_j$ are the $QALYs\ gained$ by interventions i and j. ICER represents the additional cost per extra QALY gained by an intervention compared with another.

Although these calculations are straightforward, the main challenge is to accurately obtain an estimate of the parameter *Q* (Rowen & Brazier, 2011). There are mainly two different ways to obtain *Q*: direct and indirect valuation. In direct valuation, such as the time trade-off (TTO) and the standard gamble (SG), individuals are asked to imagine themselves in different health states and think about the trade-off of sacrificing years of life or what risk in death (percentage) they would be willing to take in order to achieve a full health state. Since measuring patients' preferences using this type of methods is difficult and time-consuming, indirect valuation methods (also called generic preference based methods) are generally preferred. Such methods involve using pre-scored generic preference-based measures in which health states are described using standardized utility questionnaires (Dolan, 2008; Thorrington & Eames, 2015; Whitehead & Ali, 2010).

In practice, a range of generic preference-based instruments to approximate *Q* for different health states are used. Valuation instruments such as the EQ-5D (Dolan, Gudex, Kind, Williams, & others, 1995; Williams, 1995), SF-36 (Brazier, Roberts, & Deverill, 2002; Ware Jr & Sherbourne, 1992), SF-12 (Lundberg, Johannesson, Isacson, & Borgquist, 1999; Ware Jr & Sherbourne, 1992), SF-6D (Brazier et

al., 2002), and QWB-SA (Kaplan, Anderson, & Ganiats, 1993; Kaplan, Bush, & Berry, 1976) have been found to provide a good estimate of quality of life for different health states. These instruments typically consider different dimensions, such as physical, social, mental, pain, and depression, to account for the factors affecting health as a whole.

Willingness-to-pay threshold represents the maximum amount that society is willing to pay to gain on additional QALY. Generally, an intervention is considered as cost-effective if its ICER (cost per QALY) is below the willingness-to-pay threshold (King, Tsevat, Lave, & Roberts, 2005; Ryen & Svensson, 2015; Shiroiwa et al., 2010; Torrance et al., 1996). Even though the concept of thresholds is used by healthcare decision makers in practice, explicitly setting them is politically sensitive (Zwart-van Rijkom, Leufkens, Busschbach, Broekmans, & Rutten, 2000). Moreover, not using explicit thresholds can be considered attractive by decision makers as it gives them room for other considerations rather than tangible value per cost (Eichler, Kong, Gerth, Mavros, & Jönsson, 2004). Nevertheless, the thresholds can be inferred from past allocation decisions. In the United Kingdom, for instance, an incremental cost-effectiveness of £20,000 – 30,000 per QALY (approximately US$30,000 – 50,000) is typically used (Devlin & Parkin, 2004; McCabe, Claxton, & Culyer, 2008), whereas in the United States the threshold is US$50,000 – 100,000 per QALY. A justification for these thresholds can be found in Shiroiwa et al. (2010). In practice, most decision makers in the U.S. agree that interventions that cost less than US$50,000 – 60,000 per QALY provide good value for society.

In summary, CEAs enhance consistency, comparability, and coherence of impact assessment among different health studies. Therefore, a more informed health policy discussion can improve people's health and reduce existing disparities while accounting for cost-effectiveness factors. Finally, it must be understood that CEAs should not be used as strict guidelines for resource allocation. There may be other ethical considerations to implement interventions that do not achieve the typically used cost-effectiveness thresholds (Owens, Qaseem, Chou, & Shekelle, 2011). In this study, we used CEA to assess a healthcare intervention that uses telehealth technology to support early detection of Parkinson's Disease.

3.1. Potential QALYs Gained from Early Detection of PD

Due to the progressive nature of PD, the symptoms and their severity worsen over time. There are different rating scale tools to describe the symptom progression of PD. Most of these tools combine the severity of movement symptoms and the impact of the disease on the individual's daily activities. The Hoehn and Yahr scale (Hoehn & Yahr, 1998) has been widely used to classify PD patients into five

different stages depending on the severity of dysfunction based on the deterioration in gait and balance. Some of the main characteristics of the Hoehn and Yahr stages are presented in Table 1.

Table 1: Hoehn and Yahr stages and characteristics

HY Stages	Characteristics
Stage 1	Unilateral involvement only; no functional disability
Stage 2	Bilateral involvement without impairment of balance; minimal functional disability
Stage 3	Mild to moderate bilateral disease; some postural instability; physically independent
Stage 4	Severe disabling disease; still able to walk or stand unassisted
Stage 5	Wheelchair-bound or bedridden unless assisted

Zhao et al. (2010) estimated the progression in PD by analyzing the transit time from one stage to another using the Hoehn and Yahr (HY) scale. They obtained medical records of almost 700 patients from the movement disorder database of the National Neuroscience Institute in Singapore. Using Kaplan-Meier survival analysis, they investigated the time taken for patients to progress from one HY stage to the next one. The results of the study indicated that the median times to transit from Stage 1 to 2 and 2 to 3 are 20 and 87 months, respectively. Additionally, the transit times in more advanced stages were 24 and 26 months to move from Stage 3 to 4 and 4 to 5, respectively (Table 2). Therefore, the overall mean time from disease onset to Stage 5 was about 13 years (based on life expectancy of 79 and onset at age 64.9). This value is similar to that found in other studies. According to Hoehn & Yahr (1998) the median delays before reaching Stages 4 and 5 are 9 and 14 years, respectively.

To estimate the quality of life of (Q) for different HY stages, we used the EQ-5D instrument, which is a feasible and valid tool for such purpose in PD (Schrag, Selai, Jahanshahi, & Quinn, 2000). This instrument includes questions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression with three response options for each (1: no problem, 2: moderate problem, and 3: severe problem). A final score is derived from these five questions where the maximum score of 1 indicates the best health state. Schrag et al. (2000) provided the average EQ-5D scores for each HY stages based on a survey of ninety-seven PD patients under treatment (Table 2). We estimated the EQ-5D scores of untreated PD patients based on the symptoms. Since typically treatments are not offered in Stage 1, EQ-5D scores are not expected to differ between treated and untreated patients in this stage. Table 2 summarizes the transition time and quality of life of (Q) treated versus untreated PD patients.

Table 2: *Q* of treated vs. untreated PD patients by HY stage

HY Stage	**Median duration (months)** (Zhao et al., 2010)	**Cumulative duration (months)**	**Treated *Q* based on the EQ-5D** (Schrag et al., 2000)	**Untreated *Q* based on the EQ-5D[2]**
Stage 1	20	20	0.90	0.90
Stage 2	87	107	0.60	0.40
Stage 3	24	131	0.30	0.25
Stage 4	26	157	0.20	0.20
Stage 5	8[3]	165	0[1]	0

[1]at the end of the stage, [2]estimated based on symptoms, [3]estimated based on life expectancy of 79 years and onset at age 64.9

Some patients may not be diagnosed by a neurologist based on standard clinical criteria (Gelb et al., 1999) until they reach Stages 2 or 3 (Muslimović, Post, Speelman, & Schmand, 2007; Post, Speelman, Haan, & CARPA-Study Group, 2008; Velseboer et al., 2013). The telehealth intervention explained in Section 2.2 is expected to detect PD patients in Stage 1. The potential QALYs gained due to early detection of such patients, who would be otherwise diagnosed in Stages 2 or 3, are shown in Figure 2. Since PD treatment typically does not occur in Stage 1, we would expect a QALY gain only in Stages 2 and 3.

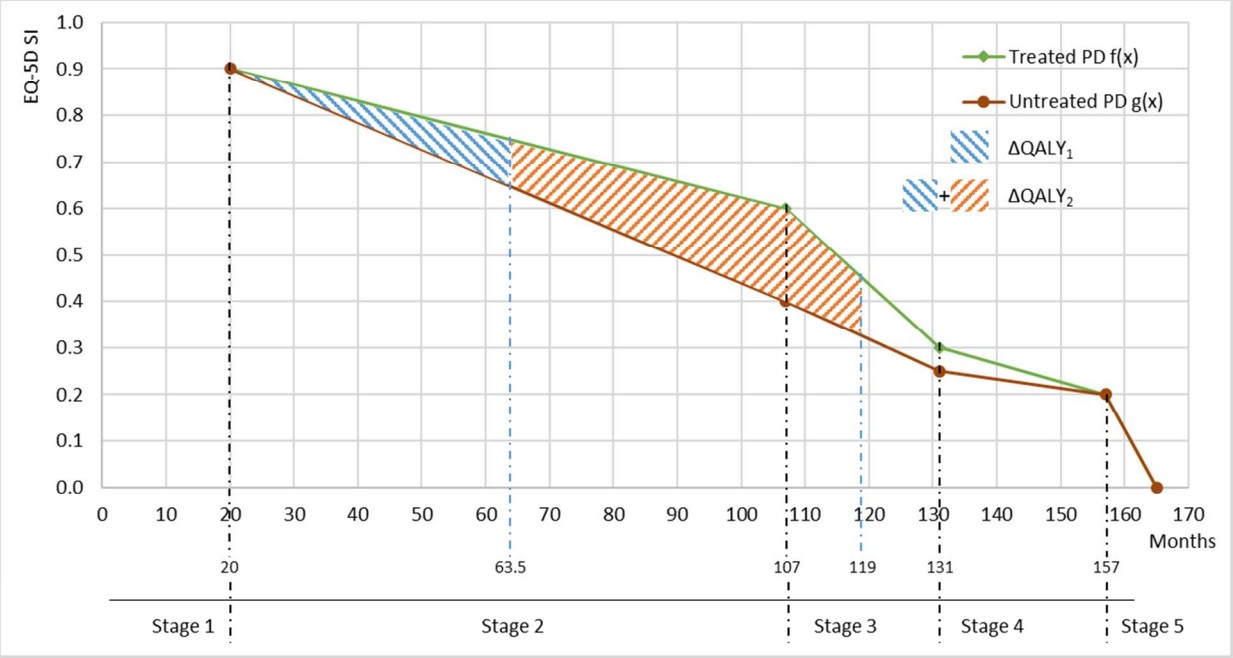

Figure 2: QALYs gained by early-diagnosed PD patients

The mathematical formulation to estimate the impact of the intervention is based on the area analysis and can be expressed as follows:

$$\int_a^b [f(x) - g(x)]dx, \tag{6}$$

where *f(x)* is the function of health representing the *Q* of a PD patient under treatment and *g(x)* represents the *Q* of an untreated PD patient. For the purpose of this study, we assumed a linear change in *Q* between two consecutive HY stages, thereby *f(x)* and *g(x)* are linear fit functions of EQ-5D values in Table 2. In this case, *a* represents the initial period and *b* represents the end period of evaluation. Thus, $f(x) = -0.003448x + 0.968966$ and $g(x) = -0.005747\text{x} + 1.014943$ for Stage 2. Similarly, $f(x) = -0.0125\text{x} + 1.9375$ and $g(x) = -0.00625\text{x} + 1.06875$ for Stage 3.

A typical Stage 2 diagnosis is expected to be obtained at 63.5 months $(20 + 87/2)$ on average (Table 2). Similarly, a Stage 3 diagnosis is expected to occur at 119 months $(107 + 24/2)$ on average. The following calculations show the QALYs lost by such patients.

To estimate the average QALYs lost by a PD patient that is diagnosed in Stage 2, the area analysis should consider for 43.5 months, starting from *a*=20 till *b*=63.5. From the area analysis, the QALYs lost by a patient that is diagnosed in Stage 2 ($\Delta QALY_1$) is computed as:

$$\frac{\int_{20}^{63.5}[-0.003448\text{x} + 0.968966 - (-0.005747\text{x} + 1.014943)]dx}{12} = \frac{2.175}{12} = 0.1813.$$

Similarly, the average QALYs lost by a Stage 3 diagnosed patient ($\Delta QALY_2$) is computed for 99 months, starting from *a*=20 until *b*=119, as follows:

$$\frac{\int_{20}^{107}[-0.003448x + 0.968966 - (-0.005747x + 1.014943)]dx}{12}$$
$$+ \frac{\int_{107}^{119}[-0.0125\text{x} + 1.9375 - (-0.00625\text{x} + 1.06875)]dx}{12} = \frac{8.7}{12} + \frac{1.95}{12}$$
$$= 0.7250 + 0.1625 = 0.8875.$$

According to the results, PD patients diagnosed in Stages 2 and 3 could gain 0.1813 and 0.8875 QALYs, respectively, if they were detected in Stage 1.

To estimate the average QALY gain of an early-stage diagnosed PD patient, we needed the prevalence of HY stages when patients are first diagnosed by a neurologist. We have identified three studies that survey the HY stages in which the patients are first diagnosed with PD (Muslimović et al., 2007; Post et al., 2008; Velseboer et al., 2013). Although the exact percentage of patients diagnosed within each HY stage varies across these studies, they all are consistent in reporting that the diagnosis occurs most frequently in Stage 2, followed by Stages 1 and 3. Thus, to get a single estimate of such distribution, we obtained the average of the results reported in these studies (Table 3).

Table 3: The HY stages of newly diagnosed PD patients

HY Stage	**Muslimović et al., 2007**	**Velseboer et al., 2013**	**Post et al., 2008**	**Average Prevalence**
Stage 1	34.7%	40.3%	41.0%	38.7%
Stage 2	50.5%	48.1%	47.0%	48.5%
Stage 3	14.7%	11.6%	12.0%	12.8%
Cohort size	95 patients	129 patients	131 patients	-

By using a weighted average based on the prevalence, we estimated that early-stage diagnosis by the proposed telehealth intervention is expected to add 0.3285 QALYs to a PD patient, on average:

$$\frac{(0.485 \times 0.1813 + 0.128 \times 0.8875)}{(0.485 + 0.128)} = 0.3285.$$

3.2. Overall Impact on the Society

People over 60 were selected as the target population because the prevalence of PD rapidly increases after the age of 60 (Eeden et al., 2003; Kowal et al., 2013). In order to estimate the proposed health intervention's overall impact on the society, data with respect to the target population and diagnosis parameters were needed (Table 4).

Table 4: Data for estimating overall impact on society

Parameters	Value and Source
Population parameters	
Population of people 60+	67,018,905 (U.S. Census Bureau, 2015)
Households with one or more people 60+	44,964,354 (U.S. Census Bureau, 2015)
Annual PD diagnoses	60,000 (Parkinson's Disease Foundation, 2015)
% of 60+ PD diagnoses	95% (Eeden et al., 2003; Kowal et al., 2013)
Diagnosis mechanism parameters	
Coverage (reachability)	80% (estimation)
Accuracy of detection	75% (Tucker et al., 2015)

Approximately 60,000 people are diagnosed with PD each year in the U.S. (Parkinson's Disease Foundation, 2015), with only about 5% of the cases being under the age of 60 (Eeden et al., 2003; Kowal et al., 2013). Thus, it is estimated that 57,000 of the diagnoses are within our target population (i.e. population of people 60 or older). Aiming to reach 80% of the target population with 75% detection accuracy, it can be estimated that about 34,200 out of the 57,000 cases will be detected in Stage 1 by the proposed telehealth intervention. Currently diagnosis may be delayed and less than four out of ten are obtained in Stage 1 (Table 3). Based on the prevalence rates in Table 3, the numbers of early-stage diagnosed patients who would otherwise be detected in Stages 2 and 3 are 16,597 ($34{,}200 \times 0.484$) and 4,374 ($34{,}200 \times 0.128$), respectively. Thus, the total number of early-stage diagnoses by the telehealth is 20,971. In terms of QALYs, the early-stage diagnosis of patients creates 6,890 QALYs ($16{,}597 \times 0.1813 + 4{,}374 \times 0.8875$) for society.

3.3. Cost per QALY

In the previous sections, the incremental difference in QALYs due to early-stage diagnosis of a patient by the telehealth intervention and the overall impact on the society were estimated. In this section, the cost-effectiveness of the intervention is~~was~~ determined. The cost of this telehealth diagnosis intervention will mostly depend on the implementation setting to make the diagnosis available for the target population. We considered two alternative implementation settings: household-level and community-level. At the most granular level, the proposed telehealth system could be available at the household-level; the number of households with one or more people 60 years and over is 44,964,354 (U.S. Census Bureau, 2015). A more realistic implementation setting may be to install the telehealth systems in public places that reach larger groups of people (e.g., pharmacies, malls, churches, and other religious locations, etc.). In such cases, the number of telehealth systems needed to reach the target population decreases substantially.

Costs related to telehealth intervention include telehealth device costs, annual operating costs, and personnel cost. The telehealth device costs include the costs of Microsoft Kinect, adapter for Windows PC, monitor, and laptop. Annual operating costs represent yearly data transmission and maintenance costs. The personnel costs represent annual salary paid to a nursing assistant who is responsible for~~of~~ administrating the data collection in public spaces (note: the personnel cost is excluded in household-level implementation). We relied on U.S. market prices, publicly available sources, and previous telehealth studies to estimate the costs associated with the proposed telehealth intervention (Table 5). The detailed calculations regarding to costs and screening capacity are given in the Appendix.

Table 5: Data related to the cost of telehealth intervention

Parameters	Value and Source
Telehealth device costs	
Microsoft Kinect	$100 (market price)
Adapter for Windows PC	$40 (market price)
Monitor	$200 (market price)
Laptop	$800 (market price)
Annual operating costs	
Data transmission and maintenance costs	$200 (Kilinc & Milburn, 2016; Milburn, Hewitt, Griffin, & Savelsbergh, 2014)
Personnel Cost	
Nursing assistant salary	$26,820 (Bureau of Labor Statistics, 2015)

For household-level implementation, it was estimated that the cost of one early-stage diagnosis is $2,298,536. This estimation leads to a cost-effectiveness of $6,996,136 per QALY ($2{,}298{,}536/0.3285$), substantially above the typically used cost-effectiveness thresholds. Thus, the household-level implementation is not attractive from a cost-effectiveness perspective and was not furthered analyzed. On the other hand, the cost per early-stage diagnosis was calculated as $10,285 for community-level implementation. Thus, the telehealth intervention costs $31,305 per QALY ($10{,}285/0.3285$) and becomes cost-effective if implemented in public spaces. Community-level implementation with moderate reachability (80% of the target population) and detection accuracy levels (75%) was considered as the base case in the sensitivity analysis.

3.4. Sensitivity Analysis

One of the main drawbacks of using high-level estimations is that some of the parameters used are subject to significant uncertainty. In this regard, sensitivity analysis on those parameters provides a clearer vision of how robust the results are in terms of cost-effectiveness ~~are~~. While economic models are useful to approximate the estimation of impact under given conditions, uncertainty cannot be removed. One-way

sensitivity analysis is intended to provide an assessment of the impact of changes in the parameters and how those changes can have an impact on the model's conclusions. Additionally, sensitivity analysis can help the researcher to identify what are the key drivers of the model's results.

In Section 3.1 we found that, on average, an early-stage diagnosed PD individual could gain 0.3285 QALYs if properly treated. A sensitivity analysis was conducted to account for the uncertainty that could be present when estimating QALYs (Figure 3). The base case considered a cost per early-stage diagnosis of $10,285, which under the current estimations is translated to $31,305 per QALY. This value is just over the threshold for interventions considered to be very cost-effective ($25,000). For this case study, an intervention with a cost per early-stage diagnosis of $10,285 is very cost-effective for values of QALYs gained of 0.4 and above, reaches the typical cost-effectiveness for ranges of QALYs gained between 0.2 and 0.4, and becomes ineffective for values of QALYs gained of 0.1 or below. According to these results, the intervention is robustly cost-effective under the uncertainty or errors of estimation of QALYs gained. The same figure includes the sensitivity of the cost per early-stage diagnosis.

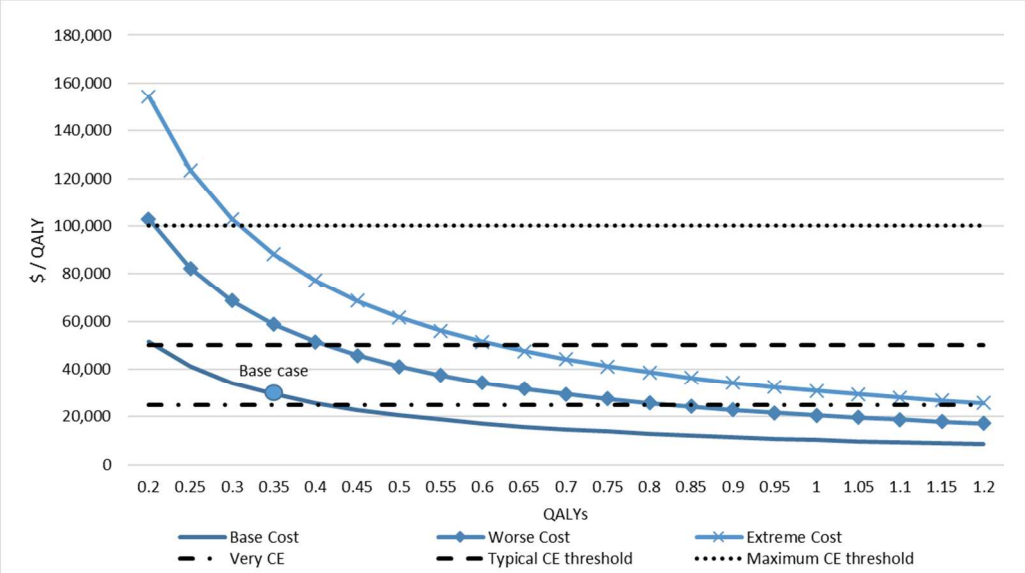

Figure 3: Cost-effectiveness sensitivity

In addition to the base cost ($10,285 per early-stage diagnosis), we define two more levels of cost per early-stage diagnosis: worse cost ($20,570 per early-stage diagnosis); and extreme cost ($30,855 per early-stage diagnosis). If the cost per early-stage diagnosis were double the initial estimate (i.e., $20,570 per early-stage diagnosis), then in order for the intervention to be very cost-effective, the QALYs gained must be 0.8 or above. To be cost-effective under the typical threshold, the QALYs gained must be

between 0.4 and 0.8. Finally, the intervention is ineffective if the QALYs gained are 0.2 or below. For an extreme cost per early-stage diagnosis of $30,855, the intervention will be very cost-effective if the QALYs gained are 1.2 or above, typically cost-effective for a range of QALYs gained between 0.6 and 1.2, and ineffective for values of QALYs gained below 0.3. These results also show that the intervention is robust in terms of cost-effectiveness. Even though the cost per early-stage diagnosis is three times the initial estimate, the intervention will still be cost-effective under the base case estimate of QALYs gained (0.3285). Under the estimates for the QALYs gained, the cost per early-stage diagnosis could increase up to $32,850 to maintain the cost per QALY below the maximum cost-effectiveness threshold of 100,000 $/QALY.

A tornado diagram is presented in Figure 4 to show how sensitive the cost-effectiveness of the intervention is given a ±20% change on various relevant parameters including cost per early-stage diagnosis, cost per telehealth system, data collection duration, QALYs gained, and accuracy of the diagnosis tool. The parameters cost per early-stage diagnosis, cost per telehealth system, and data collection duration have the same impact. If one of these parameters decreases by 20%, the cost per QALY decreases to 25,044. On the other hand, if one of these parameters increases by 20%, the cost per QALY increases to 37,566. A sensitivity for the parameters QALYs gained and accuracy shows that if one of these increases by 20%, the cost-effectiveness becomes 26.088 $/QALY. Additionally, if the QALYs gained or accuracy is decreased by 20%, the cost-effectiveness becomes 39,132 $/QALY. Under a ±20% one-way sensitivity for the parameters shown, the intervention remains to be cost effective (< 50,000 $/QALY). Thus, the intervention is fairly robust.

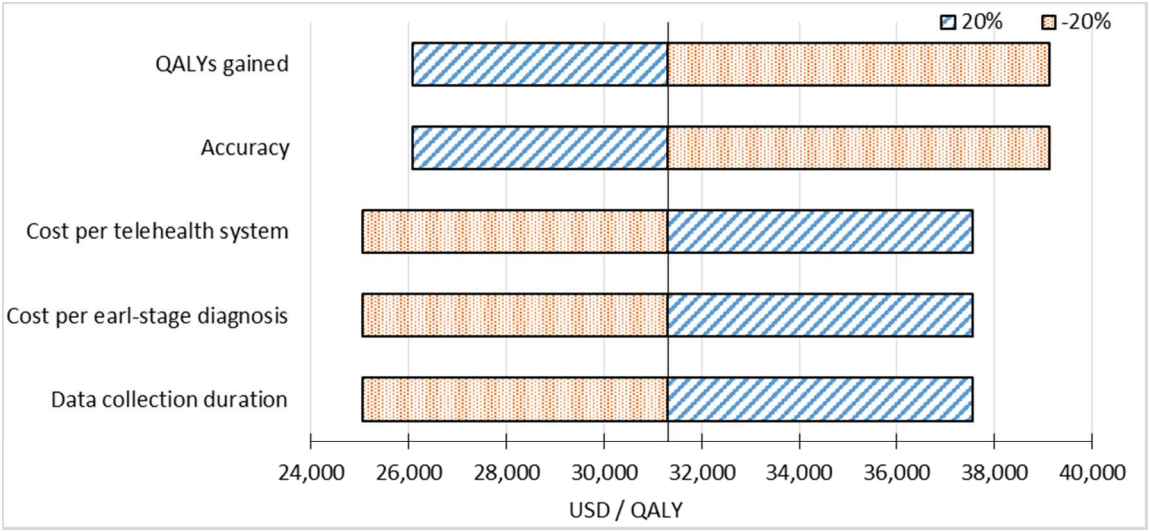

Figure 4: Cost-effectiveness tornado sensitivity for relevant parameters

4. Discussion

The burden of PD has impacted the populations' quality of life as well as its financial structure. One of the main remaining challenges for this disease is the ability to provide accurate mechanisms to allow its detection in earlier stages, something that will be even more important as disease-modifying regimens are discovered. Innovative healthcare technologies, such as the sensor-based telehealth system discussed in this study, can provide both health gains and economic benefits.

The lack of public funding to cover the health population needs has made cost-effectiveness analysis a relevant tool in the resource allocation processes. Technology advancements have impacted our ability to increase healthcare access, improve accuracy in medical treatments, and in some cases, reduce costs while achieving better health outcomes, among others. Both researchers and practitioners have started to look for opportunities in using existing technology to support medical decision to improve care and reduce healthcare costs. To increase the credibility and adoption of these innovative existing technologies, however, analyses that demonstrate their efficiency and effectiveness are needed. In this sense, CEA provides a "fair" mechanism to evaluate quantitatively whether these interventions provide substantial health gains given the costs involved, and compare different interventions to achieve the maximum health gains given the limited resources available. CEA may be seen, however, as a part of the roadmap for prioritizing healthcare interventions and not as a strict guideline. It is important to understand that some other considerations, typically difficult to quantify, might also be relevant when allocating resources that aim to improve the overall population's health.

A number of limitations exist in our study. First, our model did not account for discounting of cost items or health gains since a 1-year time horizon is used. Second, we assumed a simple linear deterioration of Q between HY stages due to lack of information in the literature. Third, we did not model PD-specific mortality rates and side effects. More comprehensive frameworks, such as Markov models mapping HY stages, are needed to account for such measures. Moreover, the CEA, as discussed in the literature, does not consider certain ethical and technical issues that may arise from screening of individuals in public spaces. Alternatives include implementing screening tools at community health fairs, in pharmacies, at annual physical exams, and even in the work place. The proposed telehealth system maintains patient privacy by only collecting the 3D unidentifiable skeleton data. Furthermore, the data collection does not require physical contact with the patient and the sensor can track skeletal joints, independent of the attire worn by the patient. This provides for patient convenience for screening.

5. Conclusions

Understanding the potential impact that an intervention has on the population is relevant for a proper allocation of resources. In this study, an intervention to support an earlier detection of Parkinson's Disease using a non-wearable sensor-based telehealth system was found to be cost-effective. The proposed intervention was estimated to have a cost-effectiveness of 31,305 $/QALY that is under the commonly accepted threshold used in the U.S. Moreover, according to the sensitivity analysis, the cost structure of the intervention is fairly robust, and hence, under various scenarios of different parameters, the intervention will still reach the typically used cost-effectiveness thresholds. An important consideration that might impact the practical attractiveness of these types of interventions is the setting in which they are expected to be implemented.

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Appendix

Using the cost data shown in Table 5, we estimate the annual cost per telehealth system as $28,160 for community-level implementation and $1,340 for household-level implementation. Assuming to reach 80% of the target population, the number of households in which a telehealth system is needed is 35,971,483 ($44{,}964{,}354 \times 0.8$). Thus, the total cost of the intervention is $48,201,787,488 for household-level implementation, which leads to an early-stage diagnosis cost of $2,298,535 ($\$48{,}201{,}787{,}488/20{,}971$). To calculate the total cost of the intervention for community-level implementation, we need to estimate the screening capacity of a telehealth system in a public setting. The average data collection duration is assumed to be 15 minutes (Tucker et al., 2015). Considering one hour for travel time to and from the screening location (e.g., a mall), we assume a nursing assistant can administer 28 screenings in a day ($(7 \times 60)/15$). This gives an annual screening capacity of 7000 for each telehealth system deployed in a public setting. To reach 80% of the target population ($53{,}615{,}124 = 67{,}018{,}905 \times 0.8$), 7,659 telehealth systems are needed ($53{,}615{,}124/7000$). Thus, the total cost of the intervention is $215,685,985 ($7{,}659 \times 28{,}160$) for community-level implementation, which leads to an early-stage diagnosis cost of $10,285 ($215{,}685{,}985/20{,}971$). In this scenario, the cost per screening is $4.02 ($215{,}685{,}985/53{,}615{,}124$).