



**HAL**  
open science

## Incoming ethical issues for deep brain stimulation: when long-term treatment leads to a ‘new form of the disease’

Frederic Gilbert, Mathilde Lancelot

### ► To cite this version:

Frederic Gilbert, Mathilde Lancelot. Incoming ethical issues for deep brain stimulation: when long-term treatment leads to a ‘new form of the disease’. *Journal of Medical Ethics*, 2020, 47 (1), pp.20-25. 10.1136/medethics-2019-106052 . hal-03735041

**HAL Id: hal-03735041**

**<https://hal.science/hal-03735041>**

Submitted on 25 Jul 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Incoming Ethical Issues for Deep Brain Stimulation: When Long Term Treatment Leads to a ‘New Form of the Disease’”

*Journal of Medical Ethics* 2021; 47:20-25  
First published on 14 may 2020

Frédéric Gilbert<sup>1</sup> and Mathilde Lancelot<sup>2</sup>

## **Abstract:**

Deep Brain Stimulation (DBS) has been regarded as an efficient and safe treatment for Parkinson’s disease (PD) since being approved by the FDA in 1997. It is estimated that more than 150,000 patients have been implanted, with a forecasted rapid increase in uptake with population ageing. Recent longitudinal follow-up studies have reported a significant increase in postoperative survival rates of PD patients implanted with DBS as compared to those not implanted with DBS. Although DBS tends to increase life expectancy for most PD patients, this medical benefit does not come without attendant negative consequences. For example, emerging forms of iatrogenic harms are sometimes induced – harms which were not initially expected when clinicians proposed neurosurgery and patients or their guardians consented to the treatment.

We report and discuss the clinical case of a patient who was implanted with DBS more than 20 years ago (at the time of writing) and is now experiencing unexpected stages of PD. This case illustrates how extending the life span without improving quality of life may introduce a burden of harms for patients and families. As well, this case shows why we should prepare for the expanding numbers of PD implanted patients experiencing a gain of longevity but with severe stages of disease leading to diminution in quality of life. This newly-observed effect of DBS treatment requires us to explore ethical questions related to iatrogenic harms, informed consent, end-of-life and caregivers burden.

**Key words:** Deep Brain Stimulation, Life expectancy, Harms, End-of-Life, Informed Consent, Quality of life.

---

<sup>1</sup> School of Humanities, University of Tasmania, Hobart, Tasmania, Australia

<sup>2</sup> SPHERE UMR7219, Paris Diderot University / University of Paris, Paris, France

## 1. Introduction

Deep Brain Stimulation (DBS) has been regarded as an efficient and safe treatment for Parkinson's disease (PD) since being approved by the FDA in 1997 (for Subthalamic Nucleus and the internal segment of the globus pallidus). Historically prescribed as a last treatment option for patients, DBS has recently been established as a better treatment alternative than classical dopamine-antagonist drugs<sup>1</sup>. It is estimated that more than 150,000 patients have been implanted and the numbers are rapidly increasing with population ageing<sup>2</sup>.

In recent years, DBS has greatly gain attention in ethics due to intense lively debate about the putative effects of the technology on personality, identity, agency, autonomy, authenticity and self<sup>3-13</sup>. However, there is almost no ethical discussion in the evidenced-based neuroethics literature about emerging clinical studies demonstrating evidence that DBS may increase the life expectancy of PD patients<sup>14-19</sup>. In the longest and biggest longitudinal follow-up research study undertaken (to date), it has been demonstrated that PD patients implanted with DBS survive longer than non-implanted patients, with a median survival time of 12 years after surgery<sup>18</sup>. Evidence that DBS may be closely linked to an increase in longevity is further corroborated by two retrospective studies suggesting that DBS PD patients have significantly longer survival rates than those managed purely with medication<sup>14-16</sup>. Other studies that followed DBS-implanted PD patients for more than seven years post-surgery noted that death occurred in 30% of patients with a mean delay of 23 years after disease onset and 5.5 years after surgery<sup>16; 20-22</sup>. In contrast, a meta-analysis has shown that mortality occurs 7 to 15 years after disease onset in non-operated PD patients<sup>23</sup>.

However, along with this extension of life expectancy for DBS-implanted PD patients many symptoms of PD are reaching more severe stages that are lasting longer. Lau and colleagues' 2019 longitudinal follow-up study reported that symptoms such as akinesia, rigidity and axial symptoms worsened in DBS-implanted PD patients<sup>17</sup>. A Danish study of DBS-implanted PD patients showed that 10 years after implantation the surviving patients had an increased incidence of hallucination and dementia<sup>16</sup>. Elsewhere, it was reported that DBS-implanted PD women patients with comorbidities (such as lower cognition) were more likely to have repeated hospital visits<sup>24-25</sup>.

The presence of the end stages of PD DBS has now changed such that we are seeing PD symptoms unlike what we normally would anticipate in the end stages of PD as observed to date. With these novel clinical observations, new questions are being introduced in the ethical debates over the long-term consequences of DBS treatments. What should we do about the fact that DBS currently promoted for treatment, which alleviate symptoms and increase life expectancy, at the same time can accentuate certain stages of disease and increase severity duration? Although the medical studies noted above report an increase in life expectancy, none of them have engaged PD patients to research their discourse of their experiences and the long-term outcomes of DBS treatment<sup>19</sup>. What are the health and well-being costs of this increase in life expectancy which could impact patients' – as well as their families' –diminution of quality of life?<sup>3</sup>

If life expectancy can be extended by DBS while inducing new and unexpected symptoms quite difficult to manage (for patients, their families and clinicians), then is there a point where de-activation or removal of the implanted device, if feasible, should be considered, if not ethically recommended? Indeed, from the moment that a DBS-implanted patient's quality of life becomes unbearable for the patients and their families, we need to ask, from an ethical standpoint<sup>26</sup>, whether a battery replacement makes sense, and whether removing or deactivating the device is what's really needed.

To illustrate these incoming ethical issues for DBS, this article first reports on a clinical case where DBS increased life expectancy while inducing severe stages of PD causing firstly, a burden of harm to the patient and her/his family and secondly, difficulties for clinicians trying to manage unexpected

---

<sup>3</sup> The notion of quality of life is used as a category framed by medical professionals.

symptoms. Next, we discuss concerns related to prolonged severe effects of PD. Finally, we address ethical questions related to DBS and end-of-life decision-making.

## 2. Clinical Case Report <sup>4</sup>

The case is that of a 66-year-old male patient who has experienced Parkinson's disease since age 36. The patient was among the first humans to be implanted in France when DBS for PD was still an experimental protocol<sup>5</sup>. Having been successfully stimulated by the implanted DBS device for more than 20 years, the patient is now presenting with unexpected stages of PD requiring intensive care. Severe stages of the symptoms include: 1) bucco-facial apraxia inducing a state where the patient's mouth is permanently open with his tongue inert and constantly slipping outside his mouth, thus forcing the patient to be fed with a gastric probe and to be continually lubricated; 2) fixed gaze; 3) incapacity to communicate aside from signals of thumbs "up" or "down" to express "yes" or "no"; 4) cognitive deficit/impairment manifesting as acute mental confusion.

His wife is increasingly worried about his state of confusion: She describes troubling episodes where her husband gets up in the middle of the night for no apparent reason and dresses himself over top of his pajamas. He also, for no apparent reason, sometimes requires having breakfast at 5 am. This patient now requires constant individualized and specialized medical support. However, French public hospitals or French institutions for dependent elderly people (named EHPAD "établissements d'hébergement pour personnes âgées dépendants" in France) are not designed to respond to his severe symptoms. His wife tried to place him in an adapted institution (EHPAD) but without success. Despite the daily care provided by way of home aids (housekeeper, nurses, caregivers), his wife ended up admitting in a medical consultation that she could not "go on like this anymore".

For the attending neurologist, this clinical case revealed an unexpected "iatrogenic effect of DBS". She further explains: "It is a new form of the disease. It is not a new pathology, but it is a new form [...] That is to say that... we are observing these forms that have thirty years of evolution! It didn't exist before, patients used to die before. We are extending patients survival rate with DBS. I'm almost convinced of that".

Checking the drug doses and stimulation parameters were the only therapeutic actions that remain possible for the neurologist. Eventually, hospitalization was recommended for a few days, including a complete check-up at the same time. Doing so would mean that there would need to be beds available in the hospital. In this case, the neurologist ended up referring the patient to so-called "comfort" and paramedical care (physiotherapy, possibly thermal cure, massages). She asserted that this was "the best" that she could do.

---

<sup>4</sup> This case belongs to a larger body of qualitative interviews and observations in clinical services which were initially developed and published in Ref. (19) as well in a PhD thesis in philosophy, epistemology, history of science and technology: M. Lancelot (2019) "Prise en charge de la maladie de Parkinson par stimulation cérébrale profonde : enjeux philosophiques d'un soin technologique" (directed by Marie Gaille), defended on September 20, 2019 - 424 pages (tel-02555639). Ethical approval to conduct interviews and field work were approved by the Comité d'Evaluation Ethique de l'Inserm (CEEI, France) IRB 403888 - Octobre 6, 2015 in the context of NormaStim research project (ANR-14-CE30- 0016) founded by the French National Research Agency. We are focusing in depth on this case study because it illustrates the surging trend among PD patients who have been implanted with DBS for many years. The increasing numbers of patients living longer with DBS will likely become prevalent, as such, this case is reflecting realities ahead for patients, caregivers and clinicians.

<sup>5</sup> French National Ethical Consultative Committee for Life Sciences and Health (CCNE) approved DBS for PD in 2002.

### 3. Discussion

#### 3.1 DBS as a “new form” of iatrogenic harms?

The clinical case above reflects recent findings concerning the extension of PD patients’ survival rates, where extension of the life span is accompanied by manifest unexpected stages of the disease<sup>14-18</sup>. This situation suggests DBS may accentuate the natural progressive neurodegenerative trajectory of PD. The natural neurodegenerative progression of PD is characterised by worsening of motor and non-motor symptoms such as akinesia, speech, postural stability, freezing of gait, and cognitive function.<sup>27</sup> In addition to physical disability and psychological deterioration, loss of identity and reduction in social interactions may also occur over time.<sup>28</sup> With PD, the burden of non-motor symptoms increases over time with the development of orthostatic hypotension (35 %), dementia (49 %), and psychosis (60 %).<sup>29</sup> See Table 1. While there is evidence for a longer life expectancy and related consequences, there is also clear evidence for a time period of reduced symptoms and care needs.<sup>1</sup> Statistically speaking, up to a certain point in the neurodegenerative trajectory, most patients will highly benefit from DBS. Since 2003 at least, it has been clearly established that DBS treatment for PD is alleviating some symptoms, with worsening of neurotypical symptoms consistent with the natural neurodegenerative trajectory of PD.<sup>30</sup> With recent longitudinal DBS follow-up research findings—as also exemplified in our clinical case above—we observe forms of PD have thirty years of evolution which “didn't exist before” because patients used to pass away before. As a result, symptoms in Table 1 are likely going to be manifested longer, and at a potentially higher levels of severity. The hypothesis that the DBS care management induces new forms of PD suggests DBS pushes the natural progression of the neurodegenerative symptoms further down their neurotypical expression and beyond their natural trajectory limits. As disease progress and symptoms advance, the ratio between *iatrogenic harms* and *extending life benefits* seems to favour the former. If DBS comes as a kind of “iatrogenic effect” (like many other kind of treatment), then this effect is associated with the problem of monitoring and treating new forms of PD and new symptoms.

Nevertheless, it is crucial to note that it is not “DBS” *solely* that seems to shape and prolong the life trajectory of these patients or the prolongation of their symptoms. Instead, the full disease management and medical treatment regiment, including DBS with pre- to post-operative follow up care, are implicated. From a history of medicine perspective, these issues of an expanding disease trajectory are not novel, but new for DBS-related discussions and treatment. Some hypothesis about potential long-term severe effects of PD were evoked in neurology back in 1996.<sup>31</sup> This intuition takes place in a broader debate in the history of medicine. We can refer to an extant literature dating from the second half of the 20th century onwards where the relevant questions of expanding symptoms trajectory of various diseases have already been developed.<sup>31-34</sup> In sum, by extending life, modern medicine seems to have contributed to prolonging various disease states or creating new diseases, including new forms, symptoms, and treatments. This is the case for many others chronic conditions. The novelty for DBS is that we are observing recently and for the first-time confirmation of the phenomenon. As such, the ethical question we must ask is how will the new forms and symptoms of Parkinson’s be managed as life expectancy increases for DBS implanted PD patients?

#### 3.2 Informed consent and advance directives.

Although the technology remains safe and effective, patients clearly need to be warned that embracing DBS might lead to them spending more time with reduced quality of life in later years. This information must be incorporated in the informed consent process, and be explicit in the signed form by patients. This new inclusion in the consent process should provided patients with the option of refusing treatment later on (presuming that this does ameliorate the life extending effects of DBS). How can a medical prescription to stop stimulation (by turning off the mechanism or simply not replacing the battery) ensure that this is acceptable to and for the patient? Expanding the life span is ethically desirable as long as the extended life meets an acceptable threshold for quality of living. As Gaille has worded it, “the quest for longevity with DBS is never only about the length of existence, but also about a meaningful existence”.<sup>35</sup> A prolonged existence makes sense insofar it aligns with a patient’s own definition and understanding of what an acceptable life is. For instance, when quality of life does not

match a patient's expectations for self-respect, dignity and autonomy, it may be ethically appropriate to examine the desirability of stopping the stimulation, or simply not replacing the battery of the implanted DBS device when it requires maintenance. This issue is raised by the study of Sankary et al. (2019).<sup>26</sup> They propose a model for remediating problem cases (like the one discussed above). Accordingly, they recommend consultation with the patient and the family in which an "off-trial" period is proposed. During this time the attending medical team evaluate whether the patient experiences the transition from being *on* to *off* battery as desirable. This remediation model also proposes that it may be medically prescribed to not replace the battery.<sup>26</sup>

The magnitude of the problem of respecting patient's autonomy increases when patients no longer possess the capacity to consent. The harms at stake highlight the importance for patients to be fully informed of the increasing long-term risks associated with DBS for PD ahead. This suggests that implanted patients at the point of consent should be made aware of their rights to stop treatment and should be offered to stop stimulation whenever it is advisable to do so or—presuming they have capacity to understand their best interests—whenever they wish to do so. In cases where patients lack capacity to understand their best interests in choosing to maintain or stop a course of treatment, this decision may need to be made for them by their guardian in conjunction with their attending medical team. The reality of anticipated fluctuating or loss of mental capacity associated with PD means that PD patients should strongly consider articulating advance directives prior to signing a DBS PD informed consent agreement. In some countries, such as France, patients have the right to have treatment stopped at any point. In countries where there is no such right, the argument could be made that the option to stop stimulation should be provided for patients in the case of prolonged survival when they experienced a situation similar to the case we report above.

### **3.3 End-of-life.**

We believe that medical systems that support or fund DBS need to do more to invest in hospices or palliative care facilities for patients at the end of life given that this is a foreseeable consequence of the treatment. Physicians, families and caregivers to persons living with PD must proactively focus on respecting patient autonomy and diminishing disease burden. Some have suggested that disease burden and unmet needs in advanced PD call for integration of palliative care into DBS practices.<sup>26; 36</sup> The World Health Organization places palliative care within the overall mission of medical practices, in particular in a palliative context, to improve the quality of life of patients and their families facing the problems associated with life-threatening symptoms.<sup>37</sup> Palliative care practices for DBS should be operated through the prevention and relief of symptoms by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. Physicians should continue to explain to patients and their families the reality of the disease progression and its long-term symptoms. They also need to discuss all potential outcomes, in appropriate contexts. PD implanted patients and families should be apprised of the possible risks associated with prolonged survival and medical doctors should be prepared to care on a long-term perspective these ageing DBS-implanted PD patients, while being aware of the limits to providing effective therapy within the disease progression.<sup>32</sup>

### **3.4 Addressing caregiver burden**

Health services are not well designed to support the care of patients manifesting certain symptoms which are not currently a typical and expected part of PD's trajectory. Providing cares in these circumstances is difficult, especially when care is under resource scarcity (too many patients for too little available places). It directly impacts families and caregivers who have to provide the care, as we have seen in our care above.

As DBS care extends the life-span trajectory of the disease, caregiver burden is also expected to increase as PD progresses. Table 2 indicates findings from the literature on psychosocial burden experienced by caregivers to PD patients. Qualitative studies reflect essential information regarding the difficult challenges faced by PD caregivers.<sup>28; 38-41</sup> As described in the literature, as the disease progresses many

partners report changing their primary relationship role to caregiver; as seen in our clinical case as well. Understanding caregiver experience is invaluable; caregivers have expert knowledge that is crucial for capturing faithfully the psycho-social adversities lived by patients.<sup>27</sup> The needs and experiences of caregivers should be included in the treatment-related protocols. Neurologists and clinical teams prescribing DBS need to understand and be well informed about the potential for diminished quality of life and extending caregiver burden associated with prolonged treatment of PD with DBS. They also need to provide guidance to patients and families to avoid unnecessary harms and, ultimately, help patients to die in accordance to a meaningful concept of self-respect, dignity they identify and endorse.<sup>26</sup>

#### 4. Recommendations

Extending life expectancy with DBS care has an ethical cost. Patients and families need to be prepared and guided with respect to novel knowledge gain about the long-term impact of DBS. The unexpected forms of PD's symptoms may be correlated with an increase in patients' life expectancy, but also interrelated with severe consequences regarding experiencing PD symptoms beyond natural standard limits. Patients and families need to be properly informed about potential long-term consequences of stimulation prior consenting for treatment. Description of advance manifestation of PD symptoms (See Table 1) may suggests symptoms are incompatible with sustained quality of life. The prospect of increased longevity for PD patients treated with DBS will result in an increased need to assist these patients in coping with their illness trajectory.<sup>29</sup> If DBS extends life expectancy for PD patients without improved quality of life for the long term, then it raises ethical questions about better supporting palliative care for PD patients. This includes the need for advance directives should PD patients lose capacity for consenting or refusing treatment decisions in the late stages of the disease.

Below we are formulating recommendation addressing the ethical issues introduced in section 3.

<b>Ethical issues</b>	<b>Recommendations</b>
New form of disease and iatrogenic harms	Created better channels contributing to public understanding, in particular prospective patients, families or caregiver for informing them of risk of harms in late stages.
Informed consent	At the point of consenting, patient and family/caregiver should be made aware of their rights to stop treatment (for instance, not replacing battery).  Given risks of impaired mental capacity in late PD stages, it should be required articulating advance directives prior to signing a DBS informed consent agreement.
End-of-life	With PD neurodegenerative trajectory still progresses to unexpected stages, palliative care should be supported and integrated into DBS practices
Caregiver burdens	Caregivers' needs and experiences should be included in the treatment-related protocols

## Conclusion:

Reports of success with DBS surgery to treat PD patients, providing them with longer lives and increased motor functioning, can be traced back to 2006.<sup>42</sup> The drive to improve quality of life when a technology has reached its limit for providing therapeutic benefit raise ethical concerns. This article has highlighted incoming ethical issues related to long-term DBS for PD as patients face a prolonged disease course with unexpected symptoms; in particular iatrogenic harms, informed consent, end-of-life and caregivers' burden.

If DBS applications for PD continue to prolong life for PD patients, the prevalence of clinical cases involving DBS-PD with late stages of severe symptoms will increase. These ethical concerns are novel complexities for PD DBS which add knowledge to pre-existing debates in ethics about DBS, in particular issues linked to putative effect of DBS on personality,<sup>3; 43-44</sup> value of DBS solutionism within a regime of care,<sup>45</sup> and doubt about reversible nature of the innovation.<sup>46</sup>

**Table 1.** Clinical and disability features of advanced, long-term, and/or end-stage Parkinson's disease. <sup>47-51</sup>

Classification	Symptom	Prevalence	Reference: study type, sample
<b>Motor</b>	Dyskinesia	94% at 15 years*; 100% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	End of dose failure	96% at 15 years*; 100% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Dystonia	56% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
	Gait disturbances	49 to 83% at ≥20 years <sup>#</sup>	<sup>#</sup> Cilia et al. (2015): cross- sectional, 401 patients
	Postural instability	47 to 83% at ≥20 years <sup>#</sup>	<sup>#</sup> Cilia et al. (2015): cross- sectional, 401 patients
	Classification	Symptom	Prevalence
<b>Psychiatric and Cognitive</b>	Mild cognitive impairment	36% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
	Dementia	48% at 15 years*; 83% at 20 years**; 17 to 42% at ≥20 years <sup>#</sup>	Coelho and Ferreira (2012): review; *Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients
	Psychosis	6% at 15 years*; 22 to 42% at ≥20 years <sup>#</sup>	*Hely et al. (2005): prospective, 52 survivors; <sup>#</sup> Cilia et al. (2015): cross- sectional, 401 patients
	Visual hallucinations	50% (formed) at 15 years*; 21% (treatment-adjusted) at 15 years*; 74% at 20 years**	Coelho and Ferreira (2012): review; *Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors



	Depression	46% (mild) at 15 years*; 7% (definite) at 15 years*; 70% at 20 years**; 10 to 25% at ≥20 years (depression and apathy) <sup>#</sup>	*Hely et al. (2005): prospective, 41 survivors who took the GDS; **Hely et al. (2008): prospective, 10 survivors who took the GDS; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients
	Agitation	29% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
	Anxiety, often associated with irritability	66% of PD patients with motor fluctuations <sup>@</sup>	*Lokk and Delbari (2012): review
	Nightmares	44% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
	Marked paranoia and violence	2% at 15 years*; 3% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Pathologic gambling	2% at 15 years*; 7% at 10 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Suicide	3% at 20 years**	**Hely et al. (2008): prospective, 30 survivors
	Hypersexuality	3% at 20 years**	**Hely et al. (2008): prospective, 30 survivors
<b>Classification</b>	<b>Symptom</b>	<b>Prevalence</b>	<b>Reference: study type, sample</b>
<b>Autonomic failure</b>	Symptomatic postural hypotension	35% at 15 years*; 48% at 20 years**; 13 to 19% at ≥20 years <sup>#</sup>	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients
	Urinary incontinence	41% at 15 years*; 71% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Faecal incontinence	17% at 20 years**	**Hely et al. (2008): prospective, 30 survivors
	Constipation	40% at 20 years**	**Hely et al. (2008): prospective, 30 survivors
	Pain	50% of PD patients <sup>@</sup>	<sup>@</sup> Lokk and Delbari (2012): review
<b>Classification</b>	<b>Symptom</b>	<b>Prevalence</b>	<b>Reference: study type, sample</b>
<b>Activities of daily living</b>	Dysphagia	50% at 15 years*; 48% at 20 years**; 9 to 25% at ≥20 years <sup>#</sup>	*Hely et al. (2005): prospective, 52 survivors; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients
	Speech impediment	27% at 15 years*; 81% at 20 years**; 51 to 68% at ≥20 years <sup>#</sup>	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients

	Daytime sleepiness	79% at 15 years*; 70% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Sleep disturbance	60% of PD patients <sup>@</sup>	<sup>@</sup> Lokk and Delbari (2012): review
	Falls	81% at 15 years*; 87% at 20 years**; 20 to 37% at $\geq 20$ years <sup>#</sup>	Coelho and Ferreira (2012): review; *Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors; <sup>#</sup> Cilia et al. (2015): cross-sectional, 401 patients
	Freezing	81% at 15 years*; 81% at 20 years**; 43 to 55% at $\geq 20$ years <sup>#</sup>	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors; <sup>#</sup> Cilia et al. (2015): cross- sectional, 401 patients
	Start hesitation	90% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
	Fractures	23% at 15 years*; 35% at 20 years**	*Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
<b>Classification</b>	<b>Symptom</b>	<b>Prevalence</b>	<b>Reference: study type, sample</b>
<b>Living arrangement</b>	Residential home admission	40% at 15 years*; 48% at 20 years**	Coelho and Ferreira (2012): review; *Hely et al. (2005): prospective, 52 survivors; **Hely et al. (2008): prospective, 30 survivors
	Inability to live alone	58% at 15 years*	*Hely et al. (2005): prospective, 52 survivors
<b>Classification</b>	<b>Symptom</b>	<b>Prevalence</b>	<b>Reference: study type, sample</b>
<b>Mortality</b>	Death	60% by 15 years*; 74% by 20 years**	Coelho and Ferreira (2012): review; *Hely et al. (2005): prospective, 136 people originally recruited; **Hely et al. (2008): prospective, 136 people originally recruited

Notes: GDS – Geriatric Depression Scale. The studies of Hely et al. (2005) and Hely et al. (2008) followed people with Parkinson’s disease who are part of a 5-year trial comparing low-dose bromocriptine with low-dose levodopa-carbidopa. The “at 15 years” statistics reported by Hely et al. (2005) indicate prevalence of certain clinical and disability features 15 years from onset of treatment and approximately 17 years from onset of symptoms indicative of Parkinson’s disease.

**Table 2.** Psychosocial Effects of Parkinson’s disease on caregivers.<sup>52-55</sup>

Effects on Caregivers	Reference (study type; sample size)
Frustration and sadness as predominant emotions regarding caregiving	Boersma et al. (2017): qualitative (interview and focus group)
Taking on new roles and responsibilities, such as becoming the primary decision maker	
Assuming a greater responsibility for household tasks, acting as a chaperone, and spending less time doing and planning recreational activities	
Difficulties in communicating with the person with PD	
Impact of PD’s clinical features on caregiver’s sleep, physical caregiving, and social embarrassment	
Concerns for physical safety when a person with PD experiences psychosis	
Concerns related to finances, housing/living situation, and taking care of their spouses in advanced stages	
Guilt in acknowledging significant financial, physical, and emotional caregiving burden	Fox et al. (2017): qualitative (semi-structured interview)
Social isolation as the person with PD becomes more dependant and requires full-time care	
Bereavement due to the loss of the person with PD or loss of their loved one’s personality	
Difficulty in making tough decisions about the care of their loved one	
Feelings of guilt and despair when it is no longer possible or preferential to care for the person with PD at home	
Change in capability to perform family duties and leisure activities	Tessitore et al. (2018): cross-sectional
Change in work	
65% of caregivers experienced physical aggression and 27% experienced sexual aggression in their first visit to the Movement Disorders Palliative Care Clinic	Bruno et al. (2016): caregivers’ report

Notes: ZBI – Zarit Burden Inventory

**Acknowledgements:** The authors are grateful to the anonymous reviewers for their valuable comments. The authors are also thankful to Marie Gaille, Tim Krahn, John Noel Viana, and the EPPE research group at the ARC Centre of Excellence for Electromaterials Science for their feedback.

**Contributors:** FG: primary author; design and conceptualised research project; analysed the data; drafted majority of the manuscript for intellectual content. ML: conducted the interview and analysed it through a previous publication; contribute to design and conception of study; analysed the data; drafted the manuscript for intellectual content.

**Funding:** FG was funded by Australian Research Council (DECRA award Project Number DE150101390). ML was funded by a French National Research Agency Project NormaStim 14-CE30- 0016.

**Competing interests:** None declared.

**Patient consent for publication:** Not required.

**Ethics approval:** Ethical approval to conduct interviews and field work were approved by the Comité d’Evaluation Ethique de l’Inserm (CEEI, France) IRB 403888 - Octobre 6, 2015 in the context of NormaStim research project (ANR-14-CE30- 0016) founded by the French National Research Agency.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

## References:

1. **Schuepbach W. M. M.**, Rau J, Knudsen K, *et al.* Neurostimulation for Parkinson's Disease with Early Motor Complications. *The New England Journal of Medicine* 2013, DOI: 10.1056/NEJMoa1205158
2. **Medtronic 2016.** FDA Approves Medtronic Deep Brain Stimulation for People with Parkinson's Disease with Recent Onset of Motor Complications, 2016, <http://newsroom.medtronic.com/phoenix.zhtml?c=251324&p=RssLanding&cat=news&id=2279215> . (Accessed 8 Apr 2018).
3. **Gilbert, F, Viaña, J.N.M, Ineichen, C.** Deflating the “DBS causes personality changes” bubble. *Neuroethics* (2018). doi:10.1007/s12152-018-9373-8
4. **Gaillard, M.** Neuroessentialism, our Technological Future, and DBS Bubbles. *Neuroethics* (2019). doi:10.1007/s12152-019-09407-6
5. **Kubu, C.S.**, Ford, P.J., Wilt, J.A., *et al.* Pragmatism and the Importance of Interdisciplinary Teams in Investigating Personality Changes Following DBS. *Neuroethics* (2019). doi:10.1007/s12152-019-09418-3
6. **Pugh, J.**, Pycroft, L., Maslen, H., *et al.* Evidence-Based Neuroethics, Deep Brain Stimulation and Personality - Deflating, but not Bursting, the Bubble. *Neuroethics* (2018). doi:10.1007/s12152-018-9392-5
7. **Erler, A.** Discussions of DBS in Neuroethics: Can We Deflate the Bubble Without Deflating Ethics? *Neuroethics* (2019). doi:10.1007/s12152-019-09412-9
8. **Zuk, P., Lázaro-Muñoz, G.** DBS and Autonomy: Clarifying the Role of Theoretical Neuroethics. *Neuroethics* (2019). doi:10.1007/s12152-019-09417-4
9. **Thomson, C.J., Segrave, R.A., Carter, A.:**Changes in Personality Associated with Deep Brain Stimulation: a Qualitative Evaluation of Clinician Perspectives. *Neuroethics* (2019). doi:10.1007/s12152-019-09419-2
10. **Bluhm, R., Cabrera, L.Y.** It's Not Just Counting that Counts: a Reply to Gilbert, Viaña, and Ineichen. *Neuroethics* (2018). doi:10.1007/s12152-018-9391-6
11. **Snoek, A.**, de Haan, S., Schermer, M., Horstkötter, D. On the Significance of the Identity Debate in DBS and the Need of an Inclusive Research Agenda. A Reply to Gilbert, Viana and Ineichen. *Neuroethics* (2019). doi:10.1007/s12152-019-09411-w
12. **Pugh, J.** Clarifying the Normative Significance of ‘Personality Changes’ Following Deep Brain Stimulation. *Sci Eng Ethics* (2020). <https://doi.org/10.1007/s11948-020-00207-3>
13. **Gilbert, F.**, Goddard, E., Viaña, J. N. M., Carter, A., & Horne, M.. I miss being me: Phenomenological effects of deep brain stimulation. *AJOB Neuroscience* (2017) 8(2), 96–109. <https://doi.org/10.1080/21507740.2017.1320319>
14. **Ngoga D**, Mitchell R, Kausar J, *et al.* Deep brain stimulation improves survival in severe Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry* 2014; 85:17-22.
15. **Merola A**, Rizzi L, Zibetti M, *et al.* Medical therapy and subthalamic deep brain stimulation in advanced Parkinson's disease: a different long-term outcome? *Journal of Neurology, Neurosurgery & Psychiatry* 2014; 83:251-257.
16. **Bang Henriksen M**, Johnsen EL, Sunde N, *et al.* Surviving 10 years with deep brain stimulation for Parkinson's disease - a follow-up of 79 patients. *European Journal of Neurology* 2014; 23(1):53-61.
17. **Weaver FM**, Stroupe KT, Smith B, *et al.* Survival in patients with Parkinson's disease after deep brain stimulation or medical management. *Movement Disorders* 2017; 32(13):1756–1763.
18. **Lau B**, Meier N, Serra G, *et al.* Axial symptoms predict mortality in Parkinson's disease patients with subthalamic stimulation. *Neurology* 2019, DOI: 10.1212/WNL.0000000000007562

19. **Lancelot M**, Des « attentes décalées »? Examen et analyse d'attentes propres au soin par stimulation cérébrale profonde. In: Desmoulin-Canselier S, Gaille M, Moutaud B, eds. *La stimulation cérébrale profonde, de l'innovation au soin - Les neurosciences cliniques la lumière des sciences humaines et sociales*. Paris: Hermann, 2019: 129–48. (halshs-02555663)
20. **Rizzone MG**, Fasano A, Daniele A, *et al.* Long-term outcome of subthalamic nucleus DBS in Parkinson's disease: From the advanced phase towards the late stage of the disease? *Parkinsonism & Related Disorders* 2014, 20(4):376-381.
21. **Castrioto A**, Lozano AM, Poon YY, *et al.* Ten-Year Outcome of Subthalamic Stimulation in Parkinson Disease: A Blinded Evaluation. *Archives of Neurology* 2011; 68:1550-1556.
22. **Fasano A**, Romito LM, Daniele A, *et al.* Motor and cognitive outcome in patients with Parkinson's disease 8 years after subthalamic implants. *Brain* 2010; 133(9):2664-2676.
23. **Macleod AD**, Taylor KS, Counsell CE. Mortality in Parkinson's disease: a systematic review and meta-analysis. *Movement Disorders* 2014; 29(13):1615-1622.
24. **Hassan A**, Wu SS, Schmidt P, *et al.* High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease. *Parkinsonism & Related Disorders* 2013; 19(11):949–954.
25. **Hassan A**, Wu SS, Schmidt P, *et al.* What are the issues facing Parkinson's disease patients at ten years of disease and beyond? Data from the NPF-QII study. *Parkinsonism & Related Disorders* 2012; 18 Suppl 3:S10–4.
26. **Sankary LR**, Ford PJ, Machado AG, *et al.* Deep Brain Stimulation at End of Life: Clinical and Ethical Considerations. *Palliative Medicine*, July 2019, DOI: 10.1089/jpm.2019.0129
27. **Miyasaki JM**, **Kluger B**. Palliative Care for Parkinson's Disease: Has the Time Come? *Current Neurology and Neuroscience Reports* 2015; 15(5): 26 DOI: 10.1007/s11910-015-0542-4.
28. **Hudson PL**, Toyne C, Kirstjanson LJ. Would people with Parkinson's disease benefit from palliative care. *Palliative Medicine*, 2006; 20(2):87–94.
29. **Auyeung M**, Tsoi TH, Mok V, *et al.* Ten year survival and outcomes in a prospective cohort of new onset Chinese Parkinson's disease patients. *Journal of Neurology, Neurosurgery & Psychiatry* 2012; 83:607–611.
30. **Krack P**, Batir A, Van Blercom N, *et al.* Five-Year Follow-up of Bilateral Stimulation of the Subthalamic Nucleus in Advanced Parkinson's Disease. *The New England Journal of Medicine* 2003; 349(20):1925-1934.
31. **Mercer B-S**. A randomized study of the efficacy of the PROPATH Program for patients with Parkinson disease. *Archives of Neurology* 1996, 53:881–884.
32. **Canguilhem G**. Une pédagogie de la guérison est-elle possible ? *Nouvelle Revue de Psychanalyse*, 1978 ; 17:13-26.
33. **Plough A-L**. Medical technology and the crisis of experience: the cost of clinical legitimation. *Social Science & Medicine* 1981; 15(2-3):89-101.
34. **Strauss A-L**, **Glaser B**. « Maladie et Trajectoires » (1985) in *La Trame de la Négociation, Sociologie qualitative et interactionnisme, Sociologie qualitative et interactionnisme*. Textes réunis et présentés par Baszanger I, Paris, L'Harmattan, 1992, p. 143-189.
35. **Gaille M**. La longévité: un désir à l'épreuve de la vieillesse ? *Gérontologie et société* 2016 – n° 151 – vol. 38, p. 151-164.
36. **Farris S**, Ford P, DeMarco J, Giroux ML. Deep brain stimulation and the ethics of protection and caring for the patient with Parkinson's dementia. *Movement Disorders* 2008; 23(14):1973–1976.

37. World Health Organisation <https://www.who.int/cancer/palliative/definition/en/> Last retrieved December 09 2022
38. **Hasson F**, Kernohan WG, McLaughlin M, *et al.* An exploration into the palliative and end-of life experiences of carers of people with Parkinson's disease. *Palliative Medicine* 2010; 24(7):731–736.
39. **McLaughlin D**, Hasson F, Kernohan WG, *et al.* Living and coping with Parkinson's disease: perceptions of informal carers. *Palliative Medicine* 2011; 25(2):177–182.
40. **Giles S, Miyasaki J.** Palliative stage Parkinson's disease: patient and family experiences of health-care services. *Palliative Medicine* 2009; 23(2): 120–125.
41. **Goy ER**, Carter JH, Ganzini L. Parkinson disease at the end of life: caregiver perspectives. *Neurology* 2007; 69(6):611–612.
42. **Bunting-Perry LK.** Palliative care in Parkinson's disease: implications for neuroscience nursing. *Journal of Neuroscience Nursing* 2006; (38)2:106-113
43. **Gilbert F.**, “Deep Brain Stimulation: Inducing Self-Estrangement,” *Neuroethics* **11**, no. 2 (2018): 157– 65
44. **Gilbert F** The burden of normality: from 'chronically ill' to 'symptom free'. New ethical challenges for deep brain stimulation postoperative treatment. *J Med Ethics* 2012;**38**:408–12.[doi:10.1136/medethics-2011-100044](https://doi.org/10.1136/medethics-2011-100044)
45. **Gardner JG**, Warren NL, 2018 Learning from Deep Brain Stimulation: The fallacy of techno-solutionism and the need for 'regimes of care'. *Medicine, Health Care and Philosophy.* 10.1007/s11019-018-9858-6
46. **Pugh J** No going back? Reversibility and why it matters for deep brain stimulation. *Med Ethics* 2019;**45**:225–230. [doi:10.1136/medethics-2018-105139](https://doi.org/10.1136/medethics-2018-105139)
47. **Hely MA**, Morris JG, Reid WG, Trafficante R. Sydney Multicenter Study of Parkinson's disease: non-L-dopa-responsive problems dominate at 15 years. *Movement Disorders* 2005; 20(2):190-199.
48. **Hely MA**, Reid WG, Adena MA, *et al.* The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. *Movement Disorders* 2008; 23(6):837-844.
49. **Cilia R**, Cereda E, Klersy C, *et al.* Parkinson's disease beyond 20 years. *Journal of Neurology, Neurosurgery & Psychiatry* 2015; 86(8):849-855.
50. **Coelho M, Ferreira JJ.** Late-stage Parkinson disease. *Nature Reviews Neurology* 2012; 8(8):435-442.
51. **Lokk J, Delbari A.** Clinical aspects of palliative care in advanced Parkinson's disease. *BMC Palliative Care* 2012; 11:20, DOI: 0.1186/1472-684X-11-20.
52. **Boersma I**, Jones J, Coughlan C, *et al.* Palliative Care and Parkinson's Disease: Caregiver Perspectives. *Palliative Medicine* 2017; 20(9):930-938.
53. **Fox S**, Cashell A, Kernohan WG, *et al.* Palliative care for Parkinson's disease: Patient and carer's perspectives explored through qualitative interview. *Palliative Medicine* 2017; 31(7):634-641.
54. **Tessitore A**, Marano P, Modugno N, *et al.* Caregiver burden and its related factors in advanced Parkinson's disease: data from the PREDICT study. *Journal of Neurology* 2018; 265(5):1124-1137.
55. **Bruno V**, Mancini D, Ghoche R, *et al.* High prevalence of physical and sexual aggression to caregivers in advanced Parkinson's disease. Experience in the Palliative Care Program. *Parkinsonism & Related Disorders* 2016; 24:141-142.