LEVODOPA-BASED DEVICE-ASSISTED THERAPIES FOR THE TREATMENT OF ADVANCED PARKINSON'S DISEASE SROI

Report prepared by **HT**ANALYSTS
On behalf of AbbVie Pty Ltd

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abbvie

HTANALYSTS

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We thank all those who generously contributed their time and energy to help us develop this report, including people living with advanced Parkinson's disease, their partners and children, and the clinicians caring for them. We hope that this report provides useful insight that will help continued investment into levodopa-based device-assisted therapies for the treatment of advanced Parkinson's disease.

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Levodopa-Based Device-Assisted Therapies for the Treatment of Advanced Parkinson's Disease SROI

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FOREWORD BY HTANALYSTS

HTANALYSTS has been providing best-in-market strategic impact measurement services for over 20 years.

Our purpose is to have a powerful impact on the health of society by connecting people with the best treatments in the fastest amount of time.

This report details the rationale and methodology used to understand the social and economic impact of levodopa-based device-assisted therapies for the treatment of advanced Parkinson's disease on people living with Parkinson's disease, their partners, children, and the broader community. In preparing this report we listened to many people who have experience with Parkinson's disease, including those living with the disease, their partners, clinicians, and nurses caring for people living with Parkinson's disease, and patient advocacy organisations, all of whom had unique but equally important perspectives. In the following pages we have synthesised those experiences using the Social Return on Investment methodology to tell the story of how access to levodopa-based device-assisted therapies significantly impacts the lives of people living with Parkinson's disease, their partners and children, and the broader value of increasing access to these Parkinson's disease treatments.

We thank all those who generously contributed their time to help us develop this report, including people living with Parkinson's disease and their families.

GLOSSARY

ABS	Australian Bureau of Statistics
ADL	Activities of daily living
CADTH	Canadian Agency for Drugs and Technologies in Health
DAP	Daily Accommodation Payment
DAT	Device-assisted therapy
DBS	Deep brain stimulation
DSP	Disability Support Pension
HCP	Home Care Packages
HREC	Human Research Ethics Committee
MPIR	Multiple Permissible Interest Rate
NDIS	National Disability Insurance Scheme
NPV	Net present value
OOP	Out-of-pocket
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PD	Parkinson's disease
QoL	Quality of life
RAD	Refundable Accommodation Deposit
SROI	Social return on investment

EXECUTIVE SUMMARY

This project is a forecast Social Return on Investment (SROI) analysis, aimed at predicting the societal impacts that could be achieved if we invested in access to levodopa-based device-assisted therapies (DATs) for people living with advanced Parkinson's disease (aPD). The focus of this analysis are people living with aPD who reside in the community (i.e. not in nursing home, hospice, or palliative care) and their families, over a three-year period.

To capture this value, interviews were conducted with people living with aPD, their partners, and the nurses and doctors who care for them. Broader societal impacts for people living with aPD, their partners, children, and the Australian Government were evaluated. The analysis revealed wide-ranging impacts for both people living with aPD, their partners, and children. These impacts arose from improvements in both motor and non-motor symptoms of the disease, highlighting the importance of considering the breadth of Parkinson's disease (PD) symptoms.

This analysis is a valuable tool to shift the conversation from the cost of PD treatments to value and impact. This report captures insights into the real value of levodopa-based DATs for the treatment of aPD, and the difference they can make not only for people living with aPD but also for their partners and families.

SROI ratio

1 : 1.79

For every $1 invested in access to levodopa-based DATs, $1.79 of social value is created for people living with aPD, their partners, children, and the Australian Government.

TOTAL INVESTMENT

$227.16 MILLION

OVER 3 YEARS

$64,692

YEARLY INVESTMENT PER PERSON WITH PD

VALUE CREATED

$406.77 MILLION

OVER 3 YEARS

$179.61 MILLION

NET PRESENT VALUE

4,482

PEOPLE IMPACTED

INTRODUCTION

PD is a neurodegenerative disorder characterised by the progressive loss of dopamine-producing neurons in the brain, which impairs an individual's ability to control and coordinate movement (1). In its early stages, PD is characterised by three main symptoms: uncontrollable shaking (tremor), slowness of movement (bradykinesia), and muscle stiffness (rigidity). Other symptoms include postural instability, nerve pain, cognitive dysfunction, and mood and sleep disturbances (1). Whilst the average age of PD diagnosis is above 65, approximately 10% of people are diagnosed with PD before the age of 50 (2).

For the over 100,000 people living in Australia with PD, oral levodopa is the mainstay therapy for PD. Oral carbidopa may also be prescribed, ensuring that levodopa is metabolised in the central nervous system thereby reducing the required levodopa dose and preventing side effects (3). The goal of PD treatment is to achieve dopamine levels within a range that minimises PD symptoms. However, as PD advances, treatment effect shortens and patients experience periods of severe symptom onset between doses (referred to as "Off" periods) (4). To mitigate this, patients require higher and more frequent doses of oral levodopa/carbidopa, resulting in increased risk of medication side effects such as dyskinesia (involuntary, erratic movement of the limbs) and a greater medication-related burden (4). Research demonstrates the significant effect this has on quality of life (QoL), both for the person with PD and those around them. This includes increased physical, mental, social, and emotional burden due to the increased level of care required (5-7).

Clinical guidance recommends the use of device-assisted therapies (DATs) for people with advanced PD (aPD) (4, 8, 9). aPD is defined as PD which is poorly controlled by oral levodopa/carbidopa based on '5-2-1' criteria (≥ 5 times daily oral levodopa use ≥ 2 daily hours of "Off" time, or ≥ 1 daily hour with troublesome dyskinesia) (10). By providing continuous administration of medication, levodopa-based DATs aim to keep dopamine levels within an optimal range more consistently than oral medication. This then minimises both the symptoms of PD and the adverse side effects of increasing oral medications (11). However, despite suboptimal symptomatic control with oral treatments, it is estimated that less than 25% of aPD patients in Australia are receiving treatment with DATs.

Available DATs on the Australian market include apomorphine delivered by continuous subcutaneous infusion, deep brain stimulation (DBS), and levodopa/carbidopa intestinal gel (Duodopa®) (12). AbbVie Pty Ltd has recently conducted research into a novel levodopa-based DAT, Vyalev® (foslevodopa /foscarbidopa), a continuous subcutaneous infusion of levodopa/carbidopa prodrugs (medications that turn into an active form once they enter the body improving delivery, solubility, and stability (13)). Preliminary results from a double-blind, active-controlled, Phase III trial demonstrate that Vyalev® leads to significant improvements in aPD symptoms compared to oral levodopa/carbidopa (NCT04380142 or M15-736) (14). Knowing the effect PD, particularly aPD, has on families and carers, the benefit of this improved medication is expected to go beyond the outcomes traditionally measured in clinical trials.

As such, AbbVie Pty Ltd has commissioned **HT**ANALYSTS to determine the broader societal impact of investing in levodopa-based DATs, specifically Duodopa® and Vyalev®, for the treatment of aPD. The analysis will quantify the Social Return on Investment (SROI) through a process of understanding, measuring, and reporting the broader social, economic, and environmental outcomes for a variety of stakeholders, including people living with aPD and their families.

This analysis was informed by stakeholder consultation, supported by secondary research, and, where applicable, verified through aggregated, non-patient specific M15-736 clinical trial data. The aim was to model the impact of access to levodopa-based DATs for community-dwelling aPD patients (i.e. excluding people living in nursing home, palliative or hospice care) over a three-year time horizon.

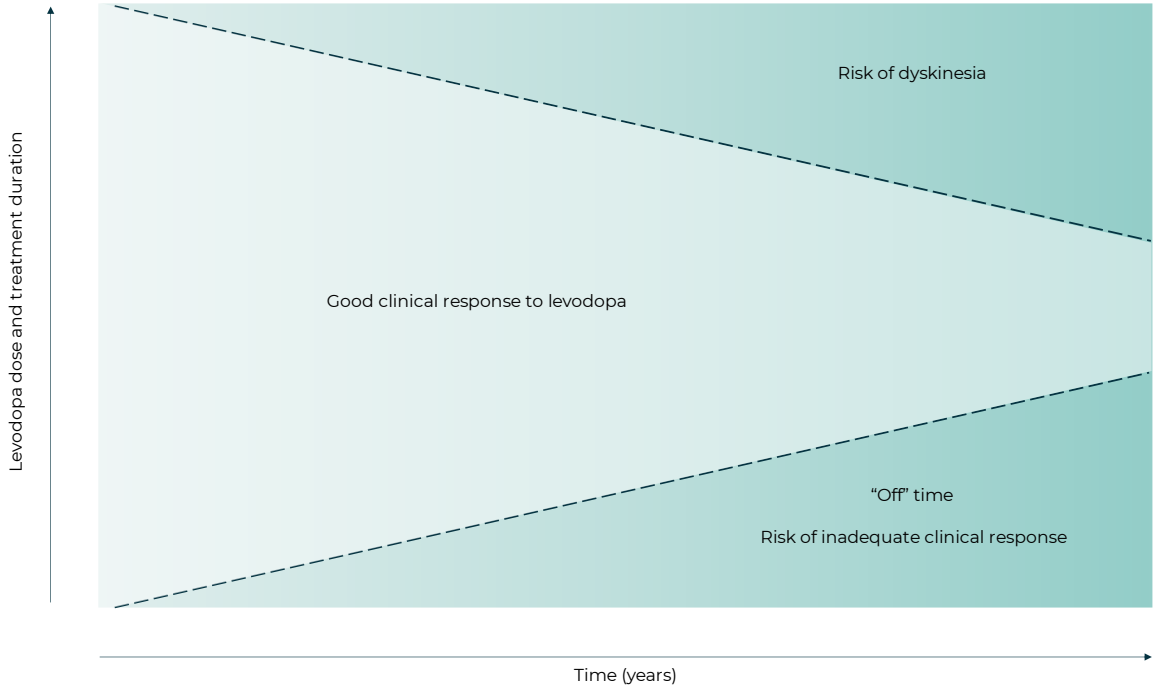
BACKGROUND

In Australia, there are currently more than 100,000 people living with PD. Of these, it is estimated that over 10% have aPD, based on the '5-2-1' criteria (15). Symptoms of aPD may include affected bilateral mobility, increased risk of falls, cognitive and mental health decline resulting in a significant impact on an individual's QoL and the lives of people caring for them (15).

The Deloitte Access Economics report *Living with Parkinson's Disease,* published on behalf of Parkinson's Australia, estimated that the total annual cost of PD in Australia in 2014 was over $1 billion, with direct health care system costs accounting for over 50% of this (16). Much of these PD-related health care costs were associated with the provision of aged care services, inpatient and outpatient services, and pharmaceuticals. The same report found that PD severity was a strong predictor of PD-related costs, highlighting the necessity for optimal treatment and management of aPD.

Current clinical guidance lists oral pharmacological intervention as the primary treatment option for people with PD, with the goal to best manage PD symptoms while reducing side effects (8, 9, 16). However, management of oral regimens can be complex, with continual and slight adjustments in dosages, timing, and combinations of drugs aimed at maintaining a good clinical response. In some cases, people living with PD need to take over 30 pills per day at regular intervals. This creates a substantial treatment burden, which places significant strain on people living with PD and their carers to remember when medication is due, and to time their planned activities around periods of optimal medication effectiveness. This high treatment burden, compounded by the fact PD also affects cognition, is associated with reduced medication compliance, and associated poorer control of PD symptoms (17-19). Nevertheless, as PD advances, the optimal levodopa range narrows (Figure 1). Increasing levodopa dose as the disease progresses causes a greater risk of dyskinesia as a result of increased plasma concentrations of levodopa. Lowering levodopa dose causes inadequate clinical response and symptom control, leading to increased "Off" time.

Figure 1 Progression of PD over time, showing the reduced probability of good clinical response to levodopa and increased risk of dyskinesia or inadequate clinical response



Source: Adapted from Calabresi Filippo, Ghiglieri et al. (2010)(11)

The Canadian Agency for Drugs and Technologies in Health (CADTH) review into Duodopa® investigated the burden associated with oral treatment regimens among over 900 survey responses from people living with PD and their carers (12). The study found that common difficulties with oral treatment regimens include

swallowing, remembering to take medication, and timing medication with meals (12). It also spoke of the frequent “peaks and troughs” experienced as PD advances, and the need for longer lasting medications that limit or eliminate “Off” periods. In Australia, AbbVie Pty Ltd market research estimates 76% of people living with aPD are being treated with an oral regimen that inadequately controls their disease.

DATs, including, DBS, continuous subcutaneous infusion of apomorphine, and Duodopa® are alternative treatments to oral levodopa-based medications, and are often indicated for advancing PD (4, 8, 9).

DBS is the second most common treatment in Australia for aPD (after oral medications), however, a relatively limited proportion of people living with aPD meet the DBS eligibility criteria. Eligibility for DBS is negatively affected by older age, cognitive impairment, and the presence of levodopa unresponsive symptoms, including gait and balance disturbance (4). Additionally, DBS is a highly invasive procedure requiring neurosurgical implantation of wires and electrodes into the brain (4).

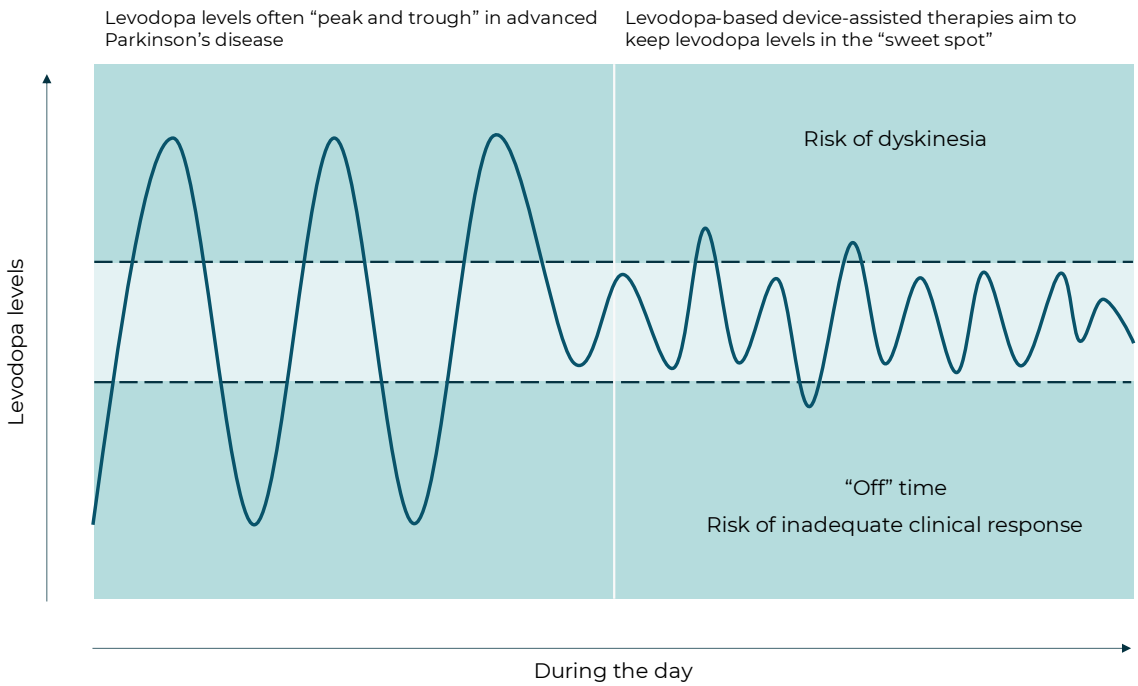
Apomorphine, a dopamine agonist delivered by continuous subcutaneous infusion is an alternative DAT option, however, is associated with impulse control disorders and other mental health issues such as anxiety and psychosis (4).

Duodopa® (levodopa/carbidopa intestinal gel) is an alternative DAT which may be prescribed for people living with aPD. The purpose of treatment with a levodopa-based DAT such as Duodopa® is to provide continuous administration of medication, ensuring the plasma concentration of levodopa is maintained within an optimal range. In turn, PD symptoms are adequately managed, limiting the side effects of medication, and “Off” time (see Figure 2) (4, 8, 9). Duodopa® has proven to be highly effective at managing PD symptoms, however, the insertion of a percutaneous endoscopic gastrostomy/jejunostomy tube (PEG/J) to deliver the gel directly to the jejunum has limited uptake, largely driven by capacity constraints to initiate Duodopa and patient hesitation to undergo surgery. Insertion of this tube requires a hospital stay of approximately one week, and clinicians have reported long wait times for the insertion procedure. In addition, the incision site for the tube needs to be maintained for as long as the patient remains on treatment, which can be challenging for patients and their carers (12).

These therapies are all available in Australia, however, clinicians have noted various limitations with their uptake, including patient hesitation, initiation delays, and limited accessibility to ongoing care. Consequently, it is estimated that only 24% of people living with aPD are treated with DATs despite inadequate symptom control with oral medications.

A new treatment developed by AbbVie Pty Ltd, Vyalev® (previous investigational name ABBV-951), provides a continuous subcutaneous infusion of levodopa/carbidopa prodrugs (foslevodopa/foscarbidopa) which are converted by the body into their active forms (13). The subcutaneous infusion device is less invasive than the PEG/J tube required for Duodopa® and does not require surgery for treatment initiation. Instead, patients can be initiated in an outpatient setting, reducing the burden on both patients and the health system. Whilst daily procedures and maintenance required of Vyalev® is similar to Duodopa®, the infusion pump for Vyalev® is notably smaller, making it easier for people living with aPD to carry and conceal.

Figure 2 The goal of treatment in advanced PD



Source: Adapted from How Parkinson's Disease Advances | DUOPA™ (carbidopa/levodopa)

RATIONALE FOR THE STUDY

The impacts of aPD and its management on broader stakeholders including partners, families, and carers of people living with aPD are poorly understood. Much of this misunderstanding is owed to the exclusion of stakeholders beyond the person living with aPD from traditional analyses such as a cost-effectiveness analysis. Although cost-effectiveness analyses provide a standardised way of evaluating the value provided by novel treatments, these are focused on the patient's clinical outcomes and costs, and often fail to capture the broader impacts on families and other people who may be impacted by PD.

The aim of this project is to evaluate the societal impact of investing in access to levodopa-based DATs (specifically Duodopa® and Vyalev®) for aPD, including the impact on people living with aPD, their partners and children, hospitals, and the Government.

OBJECTIVES OF THE STUDY

- To assess the broader value of investing in levodopa-based DATs for aPD in Australia
- To capture the stories of people living with aPD and their close family including partners and children
- To quantify the change stakeholders experience as a result of expanding access to levodopa-based DATs

TYPE OF ANALYSIS

This analysis is a prospective forecast SROI designed to measure the social impact created by investing in access to levodopa-based DATs (specifically Duodopa® and Vyalev®) for aPD. A three-year time horizon was selected to capture the short- and medium-term changes in health and social impacts expected to result from treatment with a levodopa-based DAT. This was supported by 36-month clinical trial data assessing the benefit of Duodopa® in aPD, which demonstrated stable clinical effect and dosing over this time period (20). A longer time horizon was not modelled to avoid any uncertainty associated with potential reduced clinical effectiveness over time.

Further, one of the levodopa-based DATs (Vyalev®) evaluated in this SROI was not registered in Australia at the time of the analysis and was an investigational product in clinical trial. As such, it was not possible to conduct a retrospective evaluation due to the limited number of people who had access to this therapy, and a forecast SROI was considered appropriate to measure the benefit that would be created when this treatment option becomes available in Australia.

SROI FRAMEWORK

PRINCIPLES AND METHODOLOGY

A forecast SROI analysis was conducted to assess the impact created by investing in improved access to levodopa-based DATs for people living with aPD.

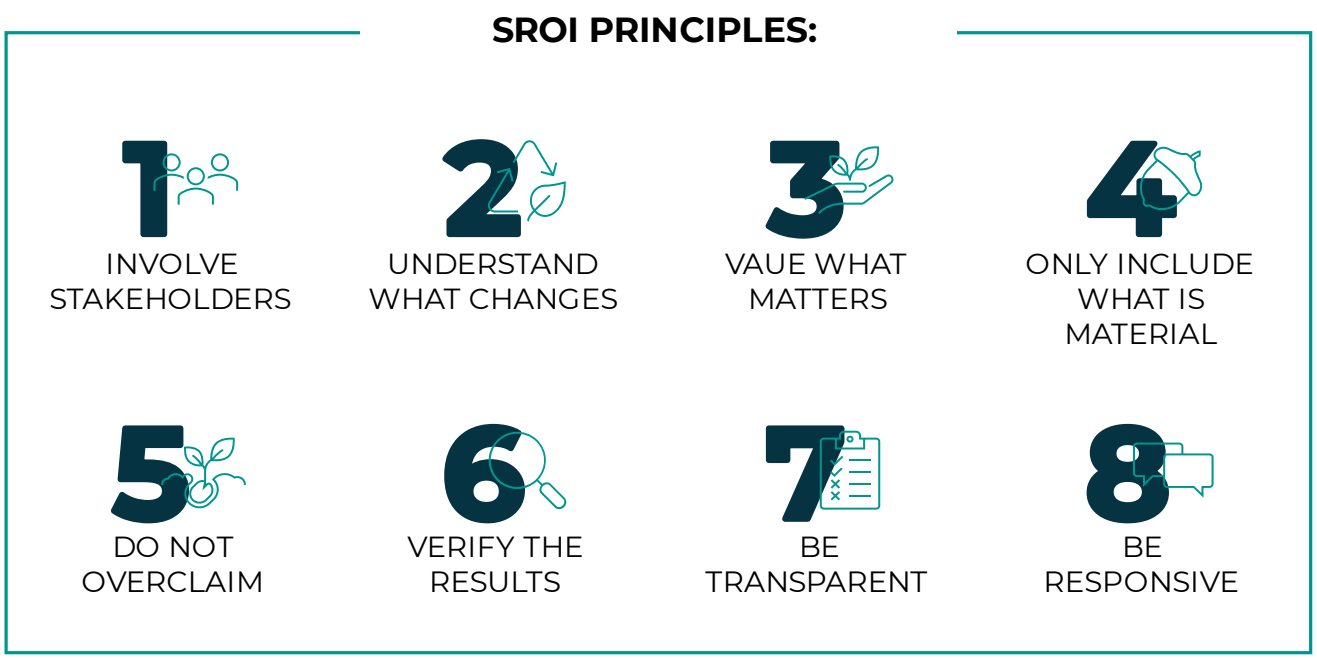
The SROI methodology is based on identifying key outcomes of an intervention, as informed by direct reporting of lived experience from stakeholders. As such, stakeholder engagement is essential in understanding what changes as a result of an activity and the value of these changes. Consultation with stakeholders also avoids self-referential thinking and incorrect assessment of impact.

The relationship between inputs, outputs, and outcomes is captured in the "Theory of Change". The Theory of Change visually maps how impact is created from the perspective of stakeholders, providing a chain-of-events towards each final outcome. In the case of this analysis, final outcomes are assigned a monetary value, representing the investment into levodopa-based DATs and increased access for people living with aPD (see Methodology).

The SROI framework produces both a quantitative and qualitative evaluation of outcomes. Whilst the investment required to provide levodopa-based DATs has a market price, the financial valuation of those outcomes that do not have a financial nature can represent a challenge. The SROI framework estimates the social value of providing access to levodopa-based DATs by assigning a financial proxy to each outcome for each stakeholder. The framework also considers adjustments to the social value that are made based on estimations of deadweight (what would have occurred anyway), attribution (what other organisations contributed to the outcomes), displacement (what activities were displaced by the intervention), and drop off (whether the outcomes experienced decline over time).

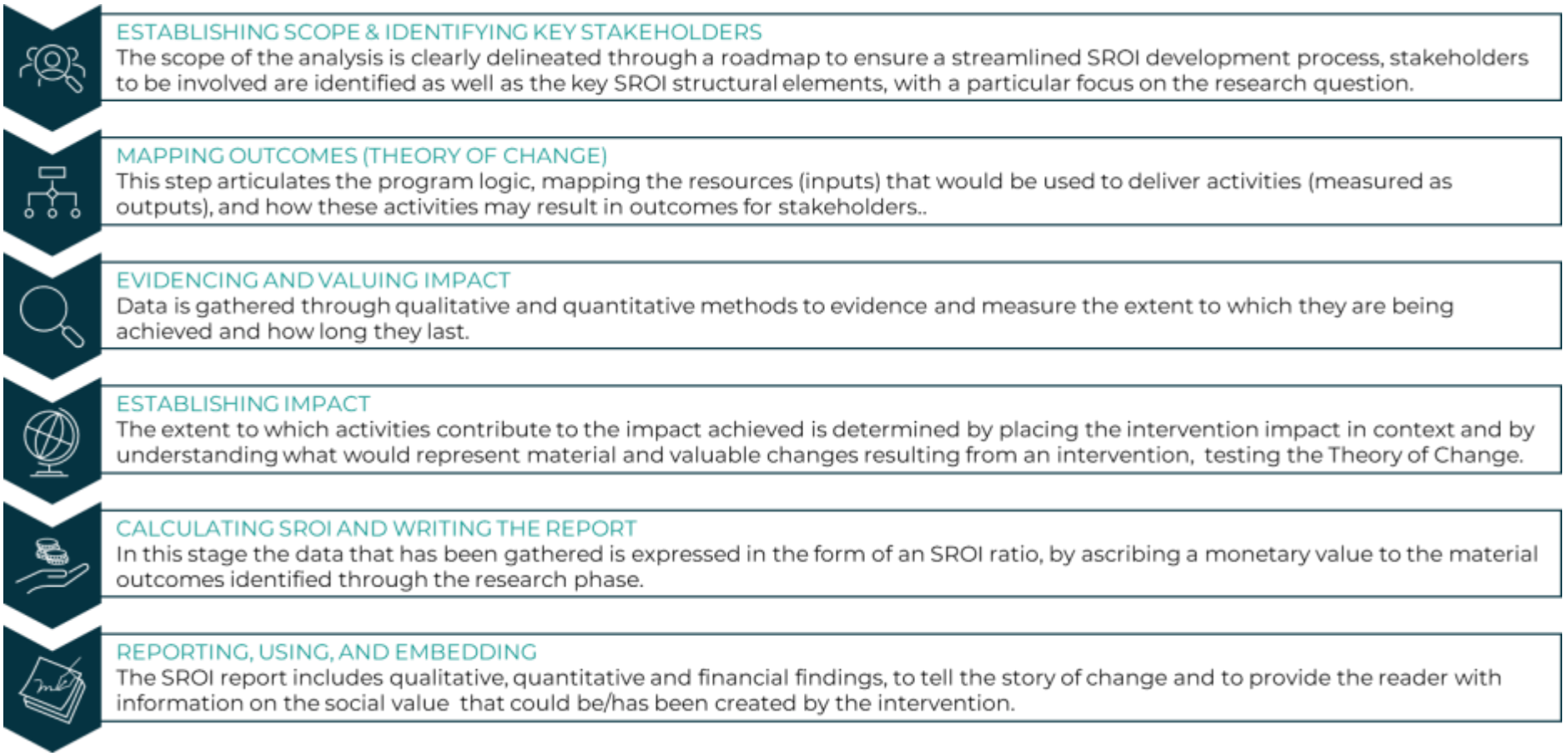
This process generates a story that fuses evidence, economics, and real-world experiences, to assess how access to treatment with a levodopa-based DAT affects people living with aPD, their partners and children, and broader society. Comparing the value of the investment with the value of the economic and social value created allows a SROI ratio to be calculated. This ratio shows the social value generated by each dollar invested.

Figure 3 Eight Principles of SROI



Guided by the above principles, there are six main steps involved in calculating the SROI (see Figure 4). These stages involve identifying and measuring outcomes and, where appropriate, applying financial proxies to valuate those outcomes. The overall value created is calculated and then compared to the investment required to generate it, to obtain the SROI ratio.

Figure 4 Six main steps in a SROI



LIMITATIONS AND CONSIDERATIONS

SROI is a form of stakeholder-driven evaluation blended with cost–benefit analysis tailored to social purposes. It tells the story of how change is being created, places a monetary value on that change, and compares it with the costs of inputs required to achieve it. This methodology accounts for a broader concept of value, measuring change in ways that are relevant to stakeholders impacted by a levodopa-based DAT (see Methodology section for further details). Thus, it is essential to understand that the values are derived from the lived experience of the stakeholders and not from traditional financial models of predictive analysis. The SROI values of one project should not be compared with that of a different project because the experiences and resulting benefits to the beneficiaries of different projects will vary. Within the SROI framework, changes and outcomes were identified and verified by the stakeholders. These abstract, narrative, or non-quantitative changes were then valued financially and adjusted according to stakeholders' perspectives and other factors such as deadweight, displacement, and attribution. To reduce the potential risk of error in any of the data or findings, all inputs and outputs were verified using robust clinical trial data, secondary literature, and extensive stakeholder consultation.

METHODOLOGY

ESTABLISHING THE SCOPE

The scope of this analysis was developed through a scoping phase, which began with a workshop held on 14 December 2021, facilitated by **HT**ANALYSTS and attended by team members of AbbVie Pty Ltd. The aim of the workshop was to gain a top-level understanding of the potential impacts of aPD and current treatments and support available to Australian patients. During the workshop, the potential stakeholders who might be impacted by investing in access to levodopa-based DATs were identified and the scope of the SROI analysis was defined (see Table 1).

Table 1 Scope of the SROI

Question	Scope
Organisation?	AbbVie Pty Ltd
What is the activity being analysed?	An investment to improve access to levodopa-based DATs (specifically Duodopa® and Vyalev®) to treat people with aPD living in the community.
How does the activity lead to the desired impact?	By improving access to levodopa-based DATs, people living with aPD will gain access to improved treatment options which reduces their PD symptoms. This will improve their overall QoL, reduce the burden of care for their partner and families, and increase their hope for the future.
What decisions will be influenced by this analysis?	By demonstrating the social impact of levodopa-based DATs, this analysis will be used to support advocacy for improved access to treatment, including to support a funding reimbursement application to the Australian Department of Health (via the Pharmaceutical Benefits Advisory Committee).
What is the duration of the activity?	A three-year time horizon was determined to be appropriate. Whilst people living with aPD may continue to receive access to a levodopa-based DAT beyond this time horizon, a three-year period limited uncertainty associated with extrapolating clinical effectiveness over time, while still captured the short- and medium-term changes in health and social impacts expected to arise from treatment.
Is this analysis a forecast or retrospective evaluation?	A forecast analysis was selected. One of the treatment options (Vyalev®) evaluated in this SROI was not registered in Australia at the time of the analysis and was an investigational product in clinical trial. As such, it was not possible to conduct a retrospective evaluation due to the limited number of people who had access to this therapy.

Abbreviations: aPD, advanced Parkinson's disease; DATs, device-assisted therapies; SROI, Social Return on Investment

STAKEHOLDER ENGAGEMENT

The direct involvement of stakeholders is one of the aspects distinguishing a SROI from a cost-effectiveness or cost–benefit analysis. Involving stakeholders allows the social value of a particular intervention to be measured and valued. Stakeholder engagement is vital to understand the importance of changes created and to identify how to quantify changes, based on how stakeholders value each outcome.

The stakeholder engagement process used for this analysis can be divided into five major stages:

- Stakeholder groups identification
- Participant recruitment
- Stakeholder interviews – to identify key outcomes and refine the Theory of Change
- Stakeholder survey – to validate and value outcomes
- Follow up interviews – to validate and verify final outcomes

For this research, two additional sources of stakeholder input were included. Specifically, secondary research on patient reported outcomes and clinical trial-based, validated, patient reported outcome measures were used to supplement the information collected through participant interviews and surveys.

STAKEHOLDER GROUPS IDENTIFICATION

All groups that may affect or be affected by improving access to levodopa-based DATs, whether the effect is intentional or unintentional, and whether that change is positive or negative, were comprehensively considered.

A preliminary list of stakeholders was developed by **HT**ANALYSTS and AbbVie Pty Ltd. Table 2 identifies the stakeholders considered and the rationale for including or excluding them from the SROI analysis. Some stakeholders were excluded from a value gained perspective, however, consulted as proxies to gain a complete understanding of the impact of improving access to levodopa-based DATs.

Table 2 List of stakeholders considered for the analysis

Stakeholders	Included/excluded	Rationale
People living with aPD	Included	As the people directly receiving the intervention being evaluated, people living with aPD were the primary stakeholder of this research. The decision was made to restrict this analysis to community-dwelling people (i.e. people with aPD who do not live in a nursing home, hospice, or are receiving palliative care) living with aPD. Clinicians consulted during the initial stages of the research noted that the majority of patients who receive active management and treatment for PD live at home. Those who live in nursing homes tend to be older and have other co-morbidities such as cognitive impairment which also impact their ability to remain independent at home (21). As such, it was expected that these people would experience different impacts. Given that people living in out-of-home care are the minority of PD patients, their exclusion from this analysis is unlikely to be material.
Partners of people living with aPD	Included	As PD advances, the symptoms can have significant impacts on partners of people living with aPD. Additionally, the person living with aPD will require greater assistance in everyday tasks, which is often provided by an informal carer such as a partner (5). Consultation with community-dwelling people living with aPD revealed partners were the primary carer in all instances. As such, it was expected that improving outcomes for people living with aPD will also benefit their partner.
Children of people living with aPD	Included	Children of people living with aPD were not identified as stakeholders during the initial scoping phase. This was because children were thought to be “one-step-removed” as they are typically adults, do not live in the same household as their parent living with aPD, and have families of their own. However, consultation with people living with aPD and their partners revealed PD has an impact on their children, including increased worry about their parent and affected ability to connect to their parent. These insights meant that children of people living with aPD were included as stakeholders via proxy in the evaluation, as it was expected that improving outcomes for people living with aPD will also benefit their children.
Friends and other family of people living with aPD	Excluded	Whilst people living with aPD identified they are less comfortable engaging in leisure and recreational activities which would plausibly be conducted with friends and other family, it was not considered that the impact of improved access to levodopa-based DATs on friends and other family would be material. Therefore, this stakeholder group was excluded from the analysis.
Employers	Excluded	Consultation with people living with aPD and their partners demonstrated how PD impacts an individual’s ability to remain in

		the workforce. As such, the ability for stakeholders to continue working was considered as part of this SROI. However, the majority of people living with aPD and their partners represent a small proportion of the workforce, are of or are nearing retirement age, and/or only working part-time. Additionally, when an employee leaves their job, their employer is likely to find someone to replace them. Whilst there are potential costs involved in this (e.g. recruitment and training), it is overall not considered likely to be material. As such, employers were excluded from the analysis.
Advocacy organisations (e.g. Parkinson's Australia and Shake It Up)	Excluded *(Consulted as proxy)*	PD advocacy organisations seek to improve the lives of people living with PD, their families, and the people caring for them. As their goals are intertwined with included stakeholder outcomes, they have not been included as an independent stakeholder to avoid double counting. Additionally, although advocacy organisations may provide financial support for the costs incurred by PD, these costs will be captured in our analysis of the patient stakeholder group. Professionals within some advocacy organisation (e.g. Parkinson's Australia and Shake It Up) were engaged to provide further insight via proxy into the lived experience of PD. As these organisations have contact with numerous people living with aPD, their partners, and children, they were able to share the lived experience of multiple patients, providing a broader perspective on the intervention being assessed.
Nurses caring for people living with aPD	Excluded *(Consulted as proxy)*	It was initially thought that nurses who provide care for people living with aPD would be impacted by levodopa-based DATs, as improvement in patient symptoms would reduce their care burden. However, once this analysis was restricted to community-dwelling aPD patients, it became evident that these patients generally did not have a nurse heavily involved in their care, as the majority of care was provided by a partner or other care provider (e.g. support worker). As such, nurses actively caring for people living with aPD were excluded from this analysis. Nurses acting as clinical trial coordinators or PD educators were engaged to provide further insight via proxy into the patient experience with levodopa-based DATs. As these nurses had contact with numerous patients who were receiving treatment with a levodopa-based DAT, they were able to share the lived experience of multiple patients, providing a broader perspective on the intervention being assessed.
Neurologists treating people living with aPD	Excluded *(Consulted as proxy)*	Although responding to the emotional needs and demanding treatment regimens of PD can be challenging, stakeholder consultations with neurologists revealed their physical and mental wellbeing was not significantly impacted by improved access to levodopa-based DATs for their patients. Additionally, neurologists reported they found their role rewarding irrespective of the available treatments. Although PD neurologists were excluded from this analysis, this stakeholder group were still engaged to provide further insight via proxy into the experience of other key stakeholder groups such as people living with aPD, hospitals, and the Government.
Hospitals	Excluded	Administration and commencement of treatment on Duodopa® requires hospital admission. To avoid double counting, this cost is being considered from the perspective of the Australian Government via the Department of Health, and thus hospitals are not included in this analysis.
The Australian Government	Included	The Australian Government provides investment for the purposes of funding the proposed intervention via the Pharmaceutical Benefits Scheme and the Medicare Benefits Schedule. Similarly, the Department of Social Services provides welfare services and Government funded income support payments (via the National Disability Insurance Scheme (NDIS) and Centrelink) to support people living with aPD and their partners who care for

		them, including welfare required from disability and early retirement. The Australian Government provide an input into the intervention and are monetarily impacted and are therefore included in this analysis.
Wider general population	Excluded	Although changes experienced by included stakeholders may have consequences for public expenditure that subsequently affects the general population, these changes were not considered material and thus were not included in the analysis.

PARTICIPANT RECRUITMENT

Neurologists with patients either currently receiving or who had previously received treatment with Vyalev® or Duodopa® were identified and contacted by AbbVie Pty Ltd in the first instance. Clinicians were contacted via email which included information about the proposed study such as the purpose, proposed data collection method, and contact details of the investigators should the clinicians wish to seek any additional information or indicate their willingness to participate (see Appendix I). As one of the therapies being assessed (Vyalev®) was an investigational drug at the time of the study, the initial outreach also made clear that this research was being conducted separately from any ongoing clinical trials. Once clinicians indicated their willingness to participate, an introductory meeting was held where the project was outlined in more detail including the inclusion criteria and the process for patient recruitment.

People living with aPD who had received treatment with a levodopa-based DAT were identified by their treating clinician. Clinicians were asked to contact any patients who met the inclusion criteria by sharing a patient recruitment flyer via email (see Appendix I). If a patient was willing to participate in the research, the clinician could share their contact information with the AbbVie Pty Ltd's Communication and Patient Relations Manager, or the patient could reach out to **HT**ANALYSTS directly via phone or email. This process for patient contact was required by the AbbVie Pty Ltd's legal department. Partners and family members were identified by people living with aPD.

To further support recruitment efforts, **HT**ANALYSTS also reached out to PD advocacy and research organisations throughout Australia, specifically Parkinson's Australia and its state-based branches, and Shake It Up. Recruitment flyers for stakeholder interviews, follow up surveys, and follow up interviews were provided and disseminated across advocacy organisation networks. If a patient or their partner was willing to be interviewed, they could reach out to **HT**ANALYSTS directly via email. If a patient or their partner was willing to complete the follow up survey, they were directed to the online survey which was hosted via Qualtrics.

ETHICAL CONSIDERATIONS

Prior to commencing outreach to clinicians, ethics approval was sought from the Bellberry Human Research Ethics Committee (HREC). Ethics approval to conduct this research was received on the 27th of April 2022 (Application No. 2022-01-082) and permitted recruitment via private hospitals and organisations. As the Bellberry HREC is not currently part of the National Mutual Acceptance program, ethics approval was also sought via the Gold Coast Hospital and Health Service. Ethics approval was received on the 3rd of August 2022 (HREC/2022/QGC/87501), allowing recruitment via the public health sector.

Prior to conducting interviews with clinicians, nurses, and patients, certain hospitals required Site Specific Approval via their Research Governance Office to commence. This approval was sought where necessary.

Patient privacy was maintained by having clinicians or advocacy organisations reach out to patients to explain the study, and having patients contact **HT**ANALYSTS directly if they were interested in participating. Contact information was not to be shared with **HT**ANALYSTS, except by the patient themselves. Similarly, the contact information of partners of patients was not shared with **HT**ANALYSTS, unless provided by the partners themselves.

Interviews with neurologists, nurses, patients, and family members were recorded and kept on a secure server by **HT**ANALYSTS. It was emphasised to participants that their decision whether or not to participate in an interview would not impact their relationship with the study sponsor or jeopardise their current or future treatment for PD or any other condition.

STAKEHOLDER INTERVIEWS

Stakeholder interviews were conducted virtually via telephone, Microsoft Teams, and Zoom from April 2022 to February 2023. Interview guides were developed by **HT**ANALYSTS and reviewed by the Bellberry and GCHHS HRECs (Appendix I).

Eight neurologists were contacted to explain the research and request an interview. As Vyalev® was in only available in Australia through clinical trial at the time of the research, these constituted all clinicians in Australia who had experience with Vyalev®. Four neurologists responded and interviews were conducted with all four clinicians between May 2022 and June 2022. No response was received from the remaining four clinicians, despite follow up contact being attempted. Clinician interviews focused on explaining the purpose of the research, outlining the inclusion criteria, and seeking support to recruit eligible patients. Clinician interviews were also used during the initial stages of developing the Theory of Change to understand any changes they had observed in their patients, what clinical outcomes were important to them, and what they understood to be important to their patients. Whilst all four clinicians interviewed initially expressed willingness to contact their patients regarding the study, only two clinicians referred patients to be included in the study. The remaining clinicians were followed up on at least one occasion after the initial interview, however, no response was received.

Due to the fact that clinicians and nurses were to contact patients without including **HT**ANALYSTS in the initial outreach, it is not known by the researchers how many patients were contacted to participate in this study.

Interviews were conducted with four aPD patients (two receiving Vyalev® and two receiving Duodopa®) and their partners. After explaining the purpose of the research and confirming consent to record, participants were asked introductory questions about their PD diagnosis and how it affected them and their family. Interviews then focused on the impacts of their current treatment compared to their previous experience on oral therapy. The interviews aimed to understand what symptoms of PD are most important to patients and how these relate to downstream effects on their QoL. Information from these interviews was used to develop and refine the Theory of Change. Additionally, 2 clinical trial nurses with experience with PD and 2 patient advocacy organisations were interviewed as proxy, to gain insight into the patient experience with aPD.

Table 3 Initial stakeholder interviews conducted

Stakeholder	Number of unique interviewees
People living with aPD	4
Partners of people living with aPD	4
Neurologists *(as proxy)*	4
Nurses *(as proxy)*	2
Patient advocacy groups *(as proxy)*	2
Total	**16**

Abbreviations: aPD, advanced Parkinson's disease

STAKEHOLDER SURVEYS

Follow up surveys were sent via email to stakeholders who had completed an interview and disseminated through Parkinson's Australia state-based branches and Shake It Up (see Appendix III). The surveys aimed to understand the relative importance of PD symptoms to patients and their families, as well as the importance of the final outcomes to be included in this analysis.

Survey responses were collected between December 2022 and January 2023 via Qualtrics. Thirty-eight survey responses from people living with PD and 17 survey responses from partners of people living with PD were included in this analysis (see Table 4).

Table 4 Stakeholder surveys

Stakeholder	Number of unique survey responses
People living with aPD	38
Partners of people living with aPD	17
Total	**55**

Abbreviations: aPD, advanced Parkinson's disease

FOLLOW UP INTERVIEWS

Follow up interviews were conducted with people living with PD to verify the Theory of Change, range of outcomes, and relative importance of outcomes to be included in the analysis. Participants were recruited through flyers disseminated through Parkinson's Australia state branches and Shake It Up. Participants made direct contact with **HT**ANALYSTS via email. In total, five people living with PD and one partner of a person living with PD were interviewed as follow up (see Table 5). Additionally, two clinical nurse consultants who provide support to people living with PD were interviewed to further verify the results (see Table 5).

Table 5 Follow up interviews

Stakeholder	Number of unique follow up interviewees
People living with aPD	5
Partners of people living with aPD	1
Nurses *(as proxy)*	2
Total	**8**

Abbreviations: aPD, advanced Parkinson's disease

As there are a limited number of people in Australia who have received or are receiving treatment with levodopa-based DATs (especially Vyalev®), stakeholder recruitment proved challenging. As such, not all survey or interview participants had direct experience with aPD or levodopa-based DATs, however, they all had experience with PD as a condition. Their experience was considered relevant to this research, as it was used to establish a baseline of the average person living with PD and the impact of the disease symptoms on QoL. The impact of treatment with a levodopa-based DAT in reducing aPD symptoms and alleviating the associated burden on QoL was measured through M15-736 clinical trial data. This approach was validated with PD patient advocacy organisations and nurses caring for people living with aPD.

SECONDARY RESEARCH OF STAKEHOLDER-REPORTED OUTCOMES

Due to the limited number of aPD patients who have experience with the interventions being evaluated, secondary research was conducted to supplement the interview responses and understand how the impacts of aPD are valued by patients and their families. The research identified a range of patient reported outcomes that highlighted the substantial impact of aPD on patients and their carers.

In 2018, CADTH conducted a review into Duodopa® which included patient stores from PD patients and their caring partners across Canada who had experience with Duodopa® (12). The report included input from three patient groups: *Parkinson Canada*, *Parkinson Association of Alberta*, and *Parkinson Society BC*. Surveys were conducted by all three associations, resulting in responses from 960 people living with PD and their caring partners. In addition, interviews were conducted with 26 patients who had experience with Duodopa® and their caring partners.

This study was considered a valuable addition to this SROI, as it includes a wide range of patient and carer perspectives on the impacts of aPD on QoL. Surveys and interviews captured both positive and negative impacts of Duodopa® treatment, as well as the importance placed by the stakeholders on these impacts, consistent with the SROI principles. Patients included in the interviews had been receiving Duodopa® for a range of time, which was considered important as PD is a degenerative condition, and the effectiveness of therapies may change over time. The results of this comprehensive research were consistent with the themes which emerged during the interviews conducted with the Australian aPD patients and partners.

In addition, the surveys conducted by the *Parkinson Association of Alberta* included a relative ranking of the areas of their life most impacted by PD and the symptoms they considered most important to manage. The areas most impacted include QoL, participation in social/recreational activities, family obligations, relationships, confidence, and independence. The most important symptoms to manage were mood, sleep, speech and swallowing issues, tremors and rigidity, cognition and memory, and balance (12).

One additional study assessing the impact of starting Duodopa® treatment was identified (22). This study included 12 patients and their care partners and followed up patients for six months from commencing treatment with Duodopa®. QoL was assessed using the Schedule for the Evaluation of Individual Quality of Life – Questionnaire (SEIQoL-Q). Four SEIQoL-Q domains were consistently named as most important by patients: family, relationships, health, and independence. Caregivers had similar concerns, but rated friends and money over health and independence.

Although no representative from the Australian Government was consulted during the SROI due to recruitment feasibility, secondary research and insights from consultation with neurologists, nurses, and patient advocacy organisations informed the outcomes considered for this stakeholder group. The inclusion of outcomes was supported by the authors' extensive experience in the health sector, health economics, and outcomes research, including long-term collaborations with the Department of Health. Specifically, outcomes relating to health care resource utilisation and financial outcomes are considered highly relevant to the Australian Government when conducting economic evaluations.

TRIAL-BASED OUTCOME ASSESSMENT

Patient reported outcome data from the Phase III trial comparing Vyalev® and oral levodopa/carbidopa was used as an indicator to inform the Impact Map. This trial captured pre-and post-treatment PD QoL data using the PD Questionnaire-39 (PDQ-39), a disease-specific instrument designed to measure aspects of health that are relevant to subjects with PD (see PDQ-39 Questionnaire). The PDQ-39 assesses whether a person has experienced difficulties (occurrence) with their PD symptoms across 8 domains and, if so, to what extent (magnitude). The domains assessed include activities of daily living, attention and working memory, cognition, communication, depression, functional mobility, QoL, social relationships, and social support.

Data from individual domains of the PDQ-39 or total scores (i.e. the Summary Index) were used to further verify outcomes included in the Impact Map. For example, people living with aPD receiving treatment with levodopa-based DATs indicated they experienced an increased ability to perform ADL which led to increased independence. Data from the PDQ-39 ADL domain was then used to understand whether a change had objectively occurred following treatment with a levodopa-based DAT and, if so, to what extent (see Table 6).

Table 6 Excerpt from PDQ-39 - ADL domain

Due to having Parkinson's disease, how often during the last month have you...					
	Never	**Occasionally**	**Sometimes**	**Often**	**Always** or cannot do at all
Had difficulty washing yourself?	☐	☐	☐	☐	☐
Had difficulty dressing yourself?	☐	☐	☐	☐	☐
Had problems doing up your shoelaces?	☐	☐	☐	☐	☐
Had problem writing clearly?	☐	☐	☐	☐	☐
Had difficulty cutting up food?	☐	☐	☐	☐	☐
Had difficulty holding a drink without spilling it?	☐	☐	☐	☐	☐

Source: (34)

Where an outcome was considered to be largely the result of an improvement in a single PD domain (e.g. reduced need for aids is related primarily to improved mobility), that domain was used to measure the magnitude of change. Where an outcome is related to a range of PD domains (e.g. ability to remain in the workforce is related to an improvement in all PD symptoms), an average improvement in all relevant domains was used.

SUMMARY OF STAKEHOLDER ENGAGEMENT

A summary of stakeholder engagement throughout the SROI process is provided in Table 7.

Table 7 Summary of stakeholder engagement throughout the SROI process

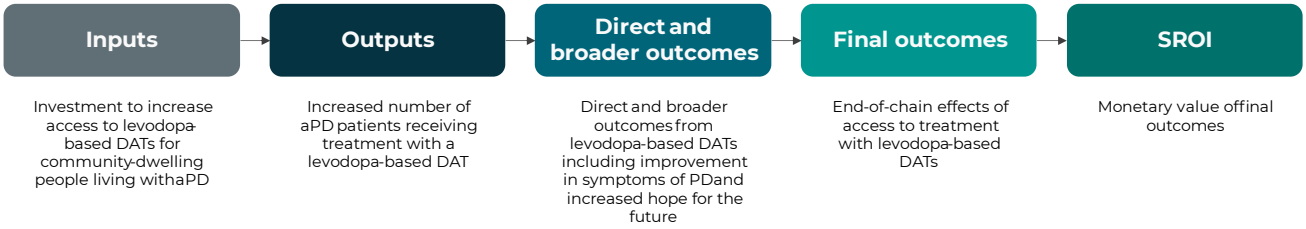
Stakeholder	Number of stakeholders uniquely engaged	Mode of engagement
People living with aPD	47	• Interviews with people living with aPD (n=4) • Surveys with people living with aPD (n=38) • Follow up interviews with people living with aPD (n=5) • Secondary research • M15-736 clinical trial-based outcome assessment
Partners of people living with aPD	22	• Interviews with partners of people living with aPD (n=4) • Surveys with partners of people living with aPD (n=17) • Follow up interviews with partners of people living with aPD (n=1) • Secondary research
Children of people living with aPD	--	• Indirectly via interviews with people living with aPD and their partners • Indirectly via surveys with people living with aPD and their partners • Indirectly via follow up interviews with aPD and their partners • Secondary research
Australian Government	--	• Indirectly via interviews with neurologists (n=4), nurses (n=2), and patient advocacy organisations (n=2) • Indirectly via follow up interviews with nurses (n=2) • Secondary research • Authors' experience consulting with Department of Health

Abbreviations: aPD, advanced Parkinson's disease

THEORY OF CHANGE

In a SROI, the Theory of Change maps the sequence of events resulting in impact for a stakeholder group. The Theory of Change is informed and guided by stakeholders, and aims to identify the relationship between the inputs, outputs, and outcomes of an intervention to capture the real-world experience of those affected (see Figure 5). To avoid overclaiming and overvaluation, only final outcomes were valued to assess the social return of levodopa-based DATs.

Figure 5 Relationship between inputs, outputs, and outcomes for levodopa-based DATs for aPD SROI



Theory of Change maps outline how inputs and outputs are linked, providing a chain-of-events towards each final outcome (23). The following Theory of Change maps outline the sequence of events forecast to occur with increased access to levodopa-based DATs for community-dwelling people living with aPD, their partners and children, and the Australian Government.

Outcome indicators for people living with aPD and their partners were derived from consultations with these stakeholder groups. For children of people living with aPD and the Australian Government, outcome indicators were informed indirectly via interviews (including follow up interviews) with people living with aPD and their partners, neurologists, nurses, and patient advocacy organisations. Given that final outcomes were indicated and verified by multiple sources, it is unlikely that there are other key material outcomes which have not been included in this report.

A summary of indicators for stakeholder outcomes with increased access to levodopa-based DATs is provided in Table 8.

Table 8 Indicators of stakeholder outcomes

Stakeholder	Outcome	Indicator(s) of change
People living with aPD	Reduced out-of-pocket costs for aids and modifications	• Reduced need for aids and other modifications • Change in M15-736 clinical trial data (PDQ-39 Mobility domain)
	Increased connection to family and friends	• Increased ability and willingness to connect and spend time with family and friends • Change in M15-736 clinical trial data (PDQ-39 Stigma domain)
	Increased independence	• Increased ability to perform activities of daily living independently • Change in M15-736 clinical trial data (PDQ-39 ADL domain)
	Increased ability to remain in the workforce	• Continued presence in the workforce and therefore a maintained income stream • Change in M15-736 clinical trial data (PDQ-39 Summary Index)
	Increased hope for the future	• Increased feeling of being in control of disease and increased excitement for future prospects • Change in M15-736 clinical trial data (PDQ-39 Summary Index)
	Increased burden of discomfort	• Discomfort experienced with levodopa-based DAT infusion site, tube, and pump
Partners of people living with aPD	Reduced worry about partner's health	• Reduced worry about the day-to-day wellbeing of partner living with aPD • Reduced carer burden • Indirectly via change in M15-736 clinical trial data (PDQ-39 ADL domain)
	Increased connection to family and friends	• Increased ability to attend social events with family and friends (including socialising alongside partner living with aPD) • Indirectly via change in M15-736 clinical trial data (PDQ-39 ADL domain
	Increased carer wellbeing	• Reduced carer burden • Increased leisure time

Stakeholder	Outcome	Indicator(s) of change
		• Indirectly via change in M15-736 clinical trial data (PDQ-39 Summary Index)
	Increased hope for the future	• Increased excitement for future life with partner • Indirectly via M15-736 clinical trial data (PDQ-39 Stigma domain)
	Increased ability to remain in the workforce	• Continued presence in the workforce and therefore a maintained income stream • Indirectly via M15-736 clinical trial data (PDQ-39 Summary Index)
Children of people living with aPD	Increased connection to parent	• Ability to speak to parent living with aPD over the phone • Indirectly via M15-736 clinical trial data (PDQ-39 Stigma domain)
	Reduced worry about parent	• Reduced worry about the day-to-day wellbeing of parent living with aPD • Indirectly via M15-736 clinical trial data (PDQ-39 Summary Index)
The Australian Government	Avoided cost of healthcare services	• Reduced hospitalisations and health care resource use • Indirectly via M15-736 clinical trial data (PDQ-39 Summary Index)
	Avoided cost of welfare services and support payments	• Reduced need for welfare services and support payments • Indirectly via M15-736 clinical trial data (PDQ-39 Summary Index)

Abbreviations: aPD, advanced Parkinson's disease

The indicators included in this SROI were heavily influenced by the feasibility of data collection, given the forecast nature of this analysis. Future analyses should include a broader range of indicators specific to each stakeholder group. Proposed indicators of change to compare against this forecast are summarised in Table 9. The proposed indicators aim to include both subjective and objective indicators. It is acknowledged that some of the proposed objective indicators may not be feasible to capture in future analyses due to the number and range of people who may access treatment, however, they are included here for completeness. Ideally, indicators of change should be measured pre- and post-initiation of treatment with a levodopa-based DAT.

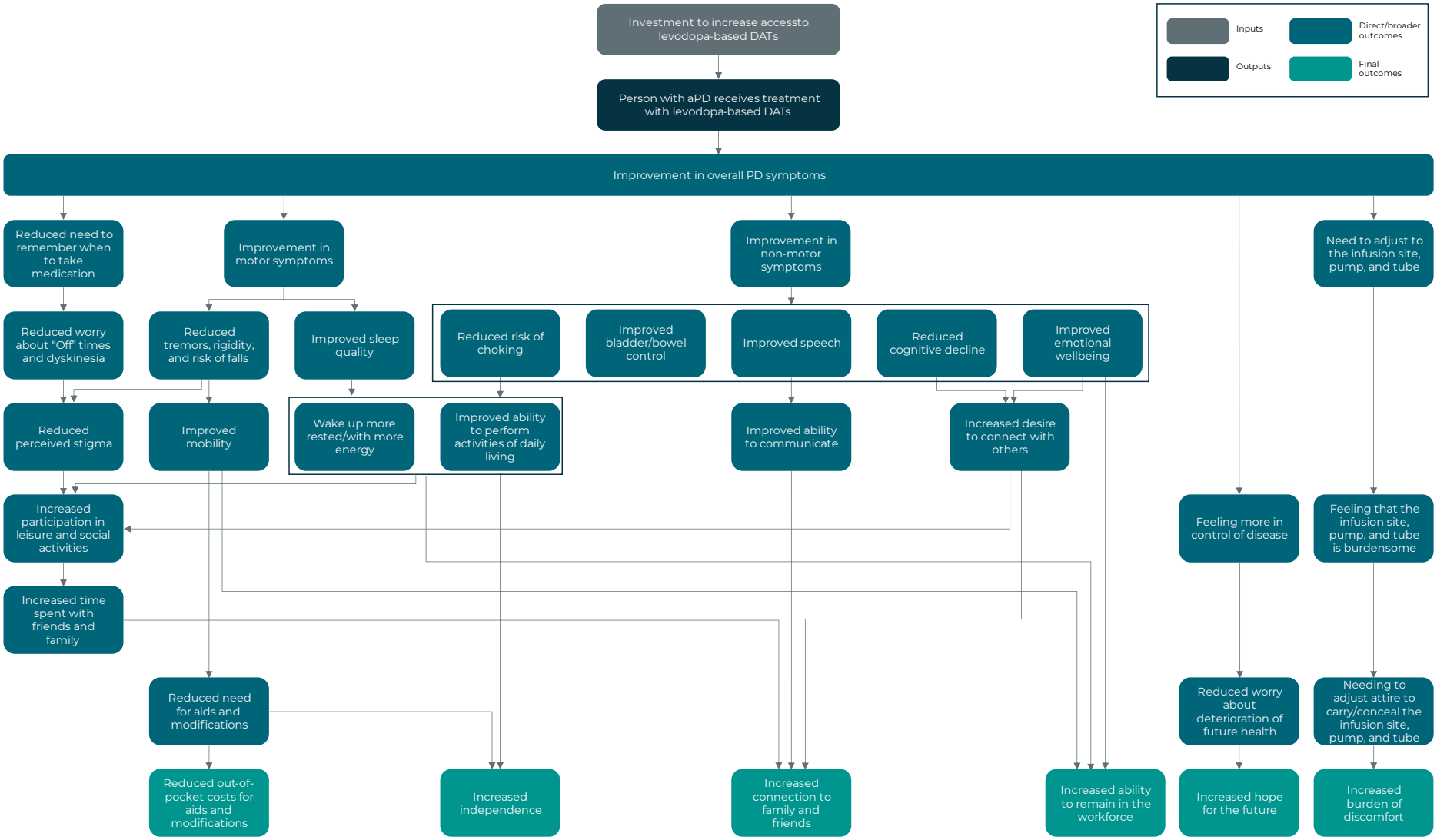
Table 9 Proposed indicators of stakeholder outcomes for future evaluation

Stakeholder	Outcome	Subjective indicator of change	Objective indicator of change
People living with aPD	Reduced out-of-pocket costs for aids and modifications	• Reduced need for aids and modifications	• Change in spend on aids and modifications
	Increased connection to family and friends	• Increased ability and willingness to connect and spend time with family and friends	• Change in average number of social interactions per week (including phone calls and face-to-face)
	Increased independence	• Increased ability to perform activities of daily living independently • Reduced reliance on formal and informal care	• Change in number of hours of formal/informal care required to support independence per week
	Ability to remain in the workforce	• Continued presence in the workforce and maintained an income stream	• Change in number of people living with aPD who remain in full-time and part-time work
	Increased hope for the future	• Increased feeling of being in control of disease and increased excitement for future prospects	• Change in proportion of people living with aPD who report making medium to long-term plans (e.g. plans to travel)
	Increased burden of discomfort	• Experience of discomfort experienced with levodopa-based DAT infusion site, tube, and pump	• Change in proportion of people who report discomfort from pump
Partners of people living with aPD	Reduced worry about partner's health	• Reduced worry about the day-to-day wellbeing of partner living with aPD	• Change in validated measures of perceived stress (e.g. Perceived Stress Scale)
	Increased connection to family and friends	• Increased ability to attend social events with family and friends (including socialising alongside partner living with aPD)	• Change in average number of social interactions per week (including phone calls and face-to-face)
	Increased carer wellbeing	• Reduced burden of care for partner • Increased leisure time	• Change in validated measures of quality of life (e.g. SF-36) or subjective wellbeing (e.g.
	Increased hope for the future	• Increased excitement for future life with partner	• Change in proportion of partners who report making medium to long-term plans (e.g. plans to travel)
	Increased ability to remain in the workforce	• Continued presence in the workforce and maintained an income stream	• Change in number of partners of people living with aPD who remain in full-time and part-time work
Children of people living with aPD	Increased connection to parent	• Increased social time spent with parent	• Change in average number of social interactions with parent per week
	Reduced worry about parent	• Reduced worry about the day-to-day wellbeing of parent living with aPD	• Change in validated measures of perceived stress (e.g. Perceived Stress Scale)

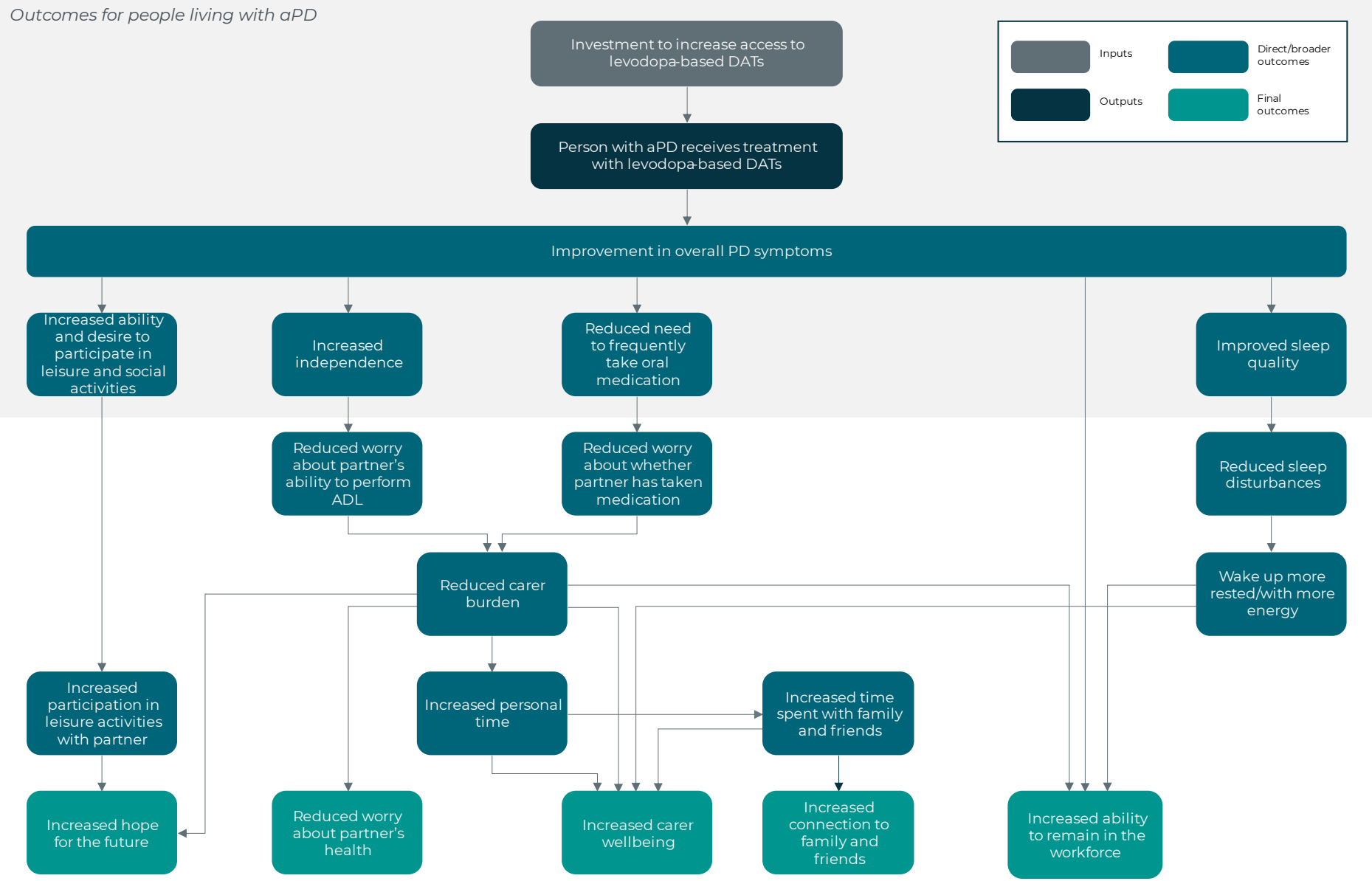
Stakeholder	Outcome	Subjective indicator of change	Objective indicator of change
The Australian Government	Avoided cost of healthcare services	• N/A	• Change in number of hospital admissions and emergency department presentations relating to aPD
	Avoided cost of welfare services and support payments	• N/A	• Change in number of people living with aPD and their partners requiring welfare services and support payments from the Australian Government

Abbreviations: aPD, advanced Parkinson's disease

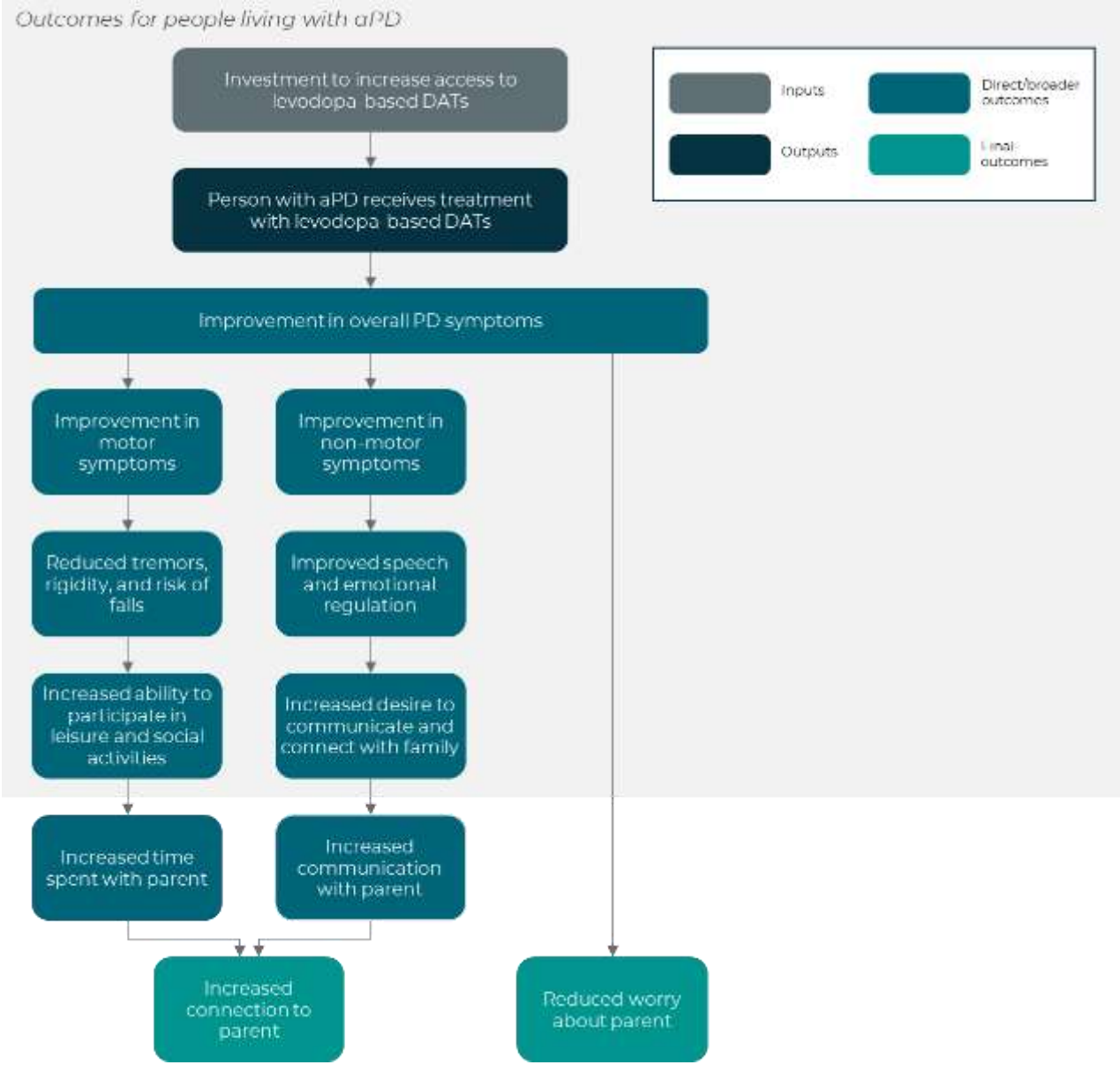
THEORY OF CHANGE FOR PEOPLE LIVING WITH APD



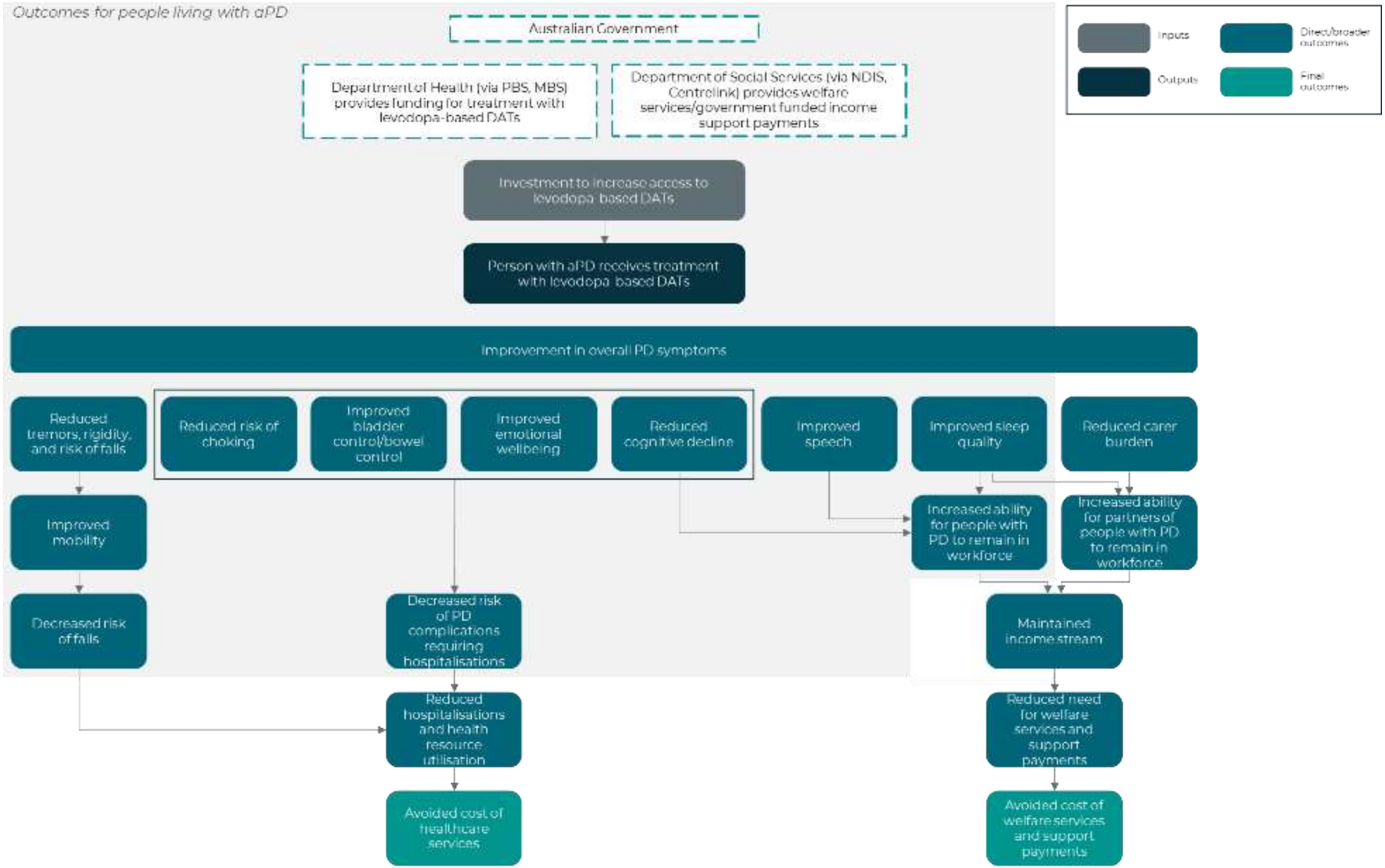
THEORY OF CHANGE FOR PARTNER'S OF PEOPLE LIVING WITH APD



THEORY OF CHANGE FOR CHILDREN OF PARENTS LIVING WITH APD



THEORY OF CHANGE FOR THE AUSTRALIAN GOVERNMENT



MEASURING MATERIAL CHANGE

One of the principles of a SROI is to "only include what is material" (23). This principle ensures that included information and evidence gives a true and fair picture, such that reasonable conclusions about impact can be drawn.

The materiality of an outcome was determined by its relevance and significance to the stakeholder. Relevance means the outcome has a clear impact on stakeholders and stakeholders perceive the outcome as important to them. Significance means the outcome has scale enough to influence decisions and actions, based upon its causality, quantity, and duration (23).

The materiality of each final outcome was assessed using the following criteria:

1. **Was the change indicated?**

   Indicators are ways of knowing that change has happened (23). They are applied to outcomes as a way to measure change. Importantly, indicators are best informed by stakeholders, and supported by secondary research or complementary data.

   For this SROI, change was indicated if the final outcome was:

   - Indicated by stakeholders during consultation; and/or
   - Supported by secondary research; and/or
   - Verified by M15-736 clinical trial data.

2. **Was the change important?**

   Importance determines the relevance, value, and impact of an outcome as perceived by stakeholders (23).

   For this SROI, the change was considered important if:

   - The weighted average importance of the outcome was at least 50%; or
   - The outcome was already financial in nature, and thus the importance was 100%; or
   - The outcome was considered negative or detrimental to stakeholders.

3. **What caused the change?**

   For this SROI, any change in outcomes is expected to be almost entirely due to treatment with a levodopa-based DAT. Change in final outcomes was considered material if:

   - The change was almost entirely the result of the intervention. That is, attribution is less than or equal to 20% (see Appendix VI); and
   - The change would have very probably not occurred without the intervention. That is, deadweight is less than or equal to 20% (unless otherwise justified) (see Appendix VII).

4. **What was the quantity of change?**

   For this SROI, quantity of change was assessed using M15-736 clinical trial data and was considered material if:

   - The proportion who experienced the outcome was at least 50% (unless otherwise justified).

5. **What was the magnitude of change?**

   This SROI assessed magnitude of change using the following methods (unless otherwise justified):

- For outcomes with corresponding PDQ-39 data, pre- and post-initiation scores were used to assess the magnitude of change resulting from treatment with levodopa-based DATs. This includes the indirect use of PDQ-39 data for partners and children of people living with aPD. If the magnitude of change of an outcome was ≥ 15% (i.e. ≥ 15% reduction in PDQ-39 scores), then it was considered material.
- Based on the authors' experience consulting with the Department of Health for over a decade, cost savings are always included in economic modelling of health interventions. Nevertheless, for this SROI financial outcomes for the Australian Government were also considered in the context of their overall spending in PD to further verify their materiality. As such, if the financial saving associated with an outcome was ≥10% of the total spend, then it was considered material.

6. **What was the duration of change?**

   The duration of change determines how long an outcome lasts after the intervention (23).

   For this SROI, the duration of change was considered material if:

   - The outcome lasts at least six months. This is expected to exclude acute outcomes that may arise from surgical initiation of Duodopa®, but still capture meaningful short- and medium-term outcomes associated with levodopa-based DAT treatment.

If the above criteria were met, then a final outcome was considered relevant, significant, and thus material. The assessment of materiality for each stakeholder and outcome included in this SROI is summarised in Table 10.

Table 10 Measuring materiality – outcomes for people living with aPD

		Relevance			Significance		
Stakeholder	**Outcome**	**Indicator of change**	**Importance**	**Causality of change**	**Quantity of change**	**Magnitude of change**	**Duration of change**
People living with aPD	Reduced out-of-pocket costs for aids and modifications	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – the outcome is financial in nature	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased connection to family and friends	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased independence	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased ability to remain in the workforce	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – the outcome is financial in nature	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of working aged stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months

		Relevance			Significance		
Stakeholder	**Outcome**	**Indicator of change**	**Importance**	**Causality of change**	**Quantity of change**	**Magnitude of change**	**Duration of change**
	Increased hope for the future	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased burden discomfort	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is negative or detrimental to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – 100% change pre- and post-initiation with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
Partners of people living with aPD	Reduced worry about partner's health	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased connection to family and friends	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months

		Relevance			Significance		
Stakeholder	**Outcome**	**Indicator of change**	**Importance**	**Causality of change**	**Quantity of change**	**Magnitude of change**	**Duration of change**
	Increased carer wellbeing	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased hope for the future	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
	Increased ability to remain in the workforce	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – the outcome is financial in nature	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of working aged stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
Children of people living with aPD	Increased connection to parent	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months

		Relevance			Significance		
Stakeholder	**Outcome**	**Indicator of change**	**Importance**	**Causality of change**	**Quantity of change**	**Magnitude of change**	**Duration of change**
	Reduced worry about parent	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – stakeholders expressed that this outcome is important to them	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – a material proportion of stakeholders are expected to experience this outcome	**Yes** – ≥ 15% change in corresponding PDQ-39 domain pre- and post-initiation treatment with a levodopa-based DAT	**Yes** – this outcome is expected to last at least 6 months
Australian Government	Avoided cost of healthcare services	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – the outcome is financial in nature	**Yes** - change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – the Australian Government represents one stakeholder and is always impacted by financial outcomes	**Yes** – cost saving accounts for >10% of the annual health system spend in PD (excluding aged care)	**Yes** – this outcome is expected to last at least 6 months
	Avoided cost of welfare services and support payments	**Yes** – indicated during consultation, supported by secondary research, or verified through M15-736 clinical trial data	**Yes** – the outcome is financial in nature	**Yes** – change in outcome is expected to be almost entirely due to treatment with a levodopa-based DAT	**Yes** – the Australian Government represents one stakeholder and is always impacted by financial outcomes	**Yes** – cost saving accounts for >10% of the annual welfare and support payment spend in PD (including DSP and carer payments)	**Yes** – this outcome is expected to last at least 6 months

HOW MANY PEOPLE ARE IMPACTED BY INCREASED ACCESS TO LEVODOPA-BASED DATS?

NUMBER OF PEOPLE LIVING WITH APD

The number of people living with aPD who are currently receiving or are expected to receive treatment with a levodopa-based DAT was calculated from AbbVie Pty Ltd market research based on analysis of Pharmaceutical Benefits Scheme (PBS) data, clinician feedback, and experience in PD treatment uptake both in Australia and globally. Specifically, the number of people initiating either Duodopa® or Vyalev® per year was calculated based on the number of people living with aPD based on '5-2-1' criteria and analysis of PBS data. The proportion of people who would be eligible for treatment with a levodopa-based DAT and who would uptake treatment was based on clinician feedback and expertise. This was then added to the number of people already receiving treatment with either levodopa-based DAT. Whilst people initiate treatment with Duodopa® and Vyalev® each year, the total number of people receiving treatment was expected to remain stable due to an equal number of prevalent patients discontinuing treatment each year. The calculation for the number of people living with aPD with access to treatment with levodopa-based DATs each year is summarised in Table 11.

Table 11 Calculation for the number of people living with aPD with access to treatment with levodopa-based DATs

Description	Value	Source
Number of people initiating Duodopa® per year	93	AbbVie Pty Ltd commercial-in-confidence assumptions
Number of people initiating Vyalev® per year	468	AbbVie Pty Ltd commercial-in-confidence assumptions
Number of people receiving treatment with Duodopa®	527	AbbVie Pty Ltd analysis of PBS data and commercial insight into PD treatment uptake both in Australia and globally
Number of people receiving treatment with Vyalev®	701	AbbVie Pty Ltd commercial insight into PD treatment uptake both in Australia and globally
Total number of people living with aPD with access to treatment with levodopa-based DATs	**1,228**	Calculated

Sources: AbbVie Pty Ltd commercial-in-confidence assumptions, analysis of PBS data, clinician feedback, and commercial insight into PD treatment uptake both in Australia and globally

NUMBER OF PARTNERS OF PEOPLE LIVING WITH APD

The number of partners of people living with aPD was calculated using the proportion of people aged 45+ years registered as married or de facto as per the most recently published Australian Census (24). This proportion was applied to the total number of people living with aPD with access to treatment with levodopa-based DATs (see Table 11). The calculation for the number of partners of people living with aPD is summarised in Table 12.

Table 12 Calculation for the number of partners of people living with aPD

Description	Value	Source
Proportion of people aged 45+ years registered as married or de facto	65%	Household and families | Census 2021 (24)
Total number of partners of people living with aPD	**798**	Calculated based on total number of people with aPD and proportion married or de facto

Sources: Household and families | Census 2021 (24)

NUMBER OF CHILDREN OF PEOPLE LIVING WITH APD

The number of children with parents living with aPD was calculated using data detailing dynamics of a typical Australian family (25). The most common family size in Australia includes 2 children. It is expected that the average person living with aPD will have 2 children. The calculation for the number of children of people living with aPD is summarised in Table 13.

Table 13 Calculation for number of children of people living with aPD

Description	Value	Source
Number of children per family	2	Families Then & Now: Having children | Australian Institute of Family Studies (25)
Total number of children of people living with aPD	**2,456**	Calculated based on total number of people with aPD and number of children per family

Sources: Families Then & Now: Having children | Australian Institute of Family Studies (25)

THE AUSTRALIAN GOVERNMENT

The Australian Government is considered a single stakeholder for the purposes of this analysis, as the Government is a single organisation responsible for decision-making and funding of healthcare services.

VALUING OUTCOMES

Valuing outcomes involves the monetisation of non-financial outcomes by assigning them appropriate financial proxies. Financial proxies reflect the value of change from the perspective of the lived experience of the stakeholder. Given many outcomes are non-financial in nature, stakeholder consultation was used to inform appropriate financial proxies. To ensure the perspective of all stakeholders was accurately captured, the chosen financial proxy was validated by secondary research and further consultation with stakeholders.

Three main techniques were used to value outcomes:

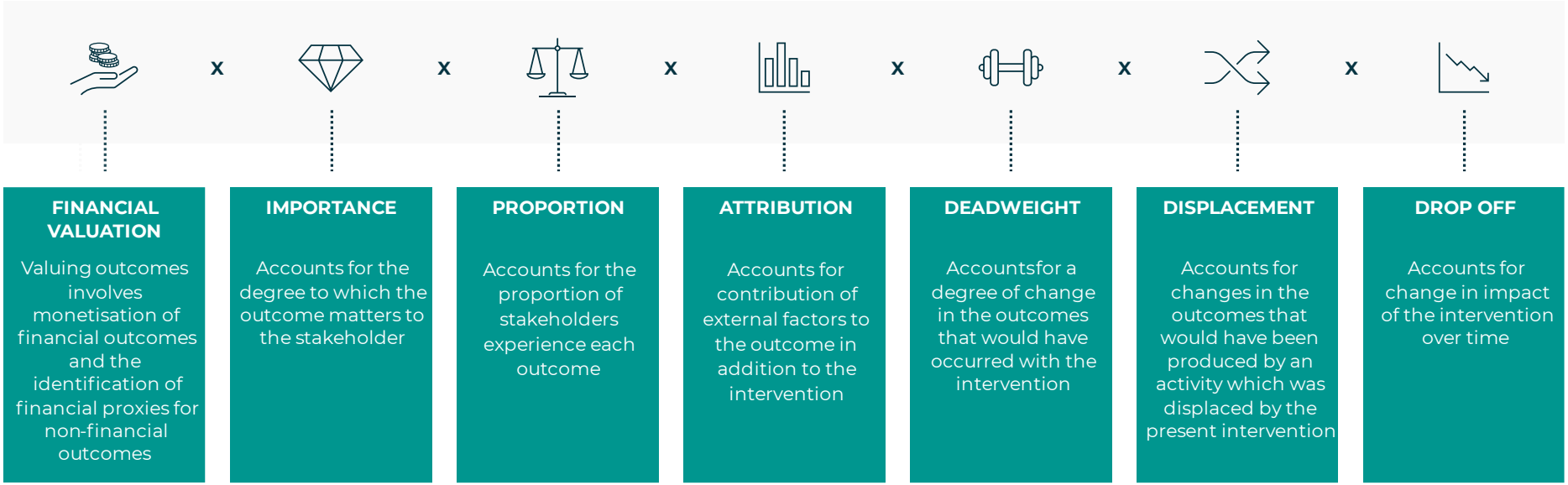
1. **Economic valuation** – the financial value representing the actual savings/cost to the stakeholder
2. **Willingness to pay/accept** – the value of an outcome based on how much stakeholders are willing to pay/accept
3. **Replacement valuation** – the cost of other service(s) and/or good(s) that would achieve the same amount of change

The financial proxy and valuation approach for each outcome for people living with aPD, their partners and children, and the Australian Government is detailed in Appendix V.

CALCULATING THE VALUE

This report aims to quantify the social value created from access to levodopa-based DATs for people living with aPD, their partners and children, and the Australian Government. Outcomes were derived from stakeholder consultation and secondary research. To calculate the total value, the value of each outcome was calculated by multiplying the financial valuation (Appendix V) with the importance weighting (Appendix VII), proportion of stakeholders impacted (Appendix VI), duration (Appendix VIII), and SROI filters, including attribution (Appendix VIII), deadweight (Appendix X), displacement (Appendix XI), and drop off (Appendix XII) (see Figure 6). As described above, stakeholders were engaged where possible to inform the variables used in the calculation process. However, due to issues with stakeholder recruitment (as described above in Methodology), the majority of people who were consulted did not have direct experience with a levodopa-based DAT. As such, they were not able to inform estimates of SROI filters. Interviews and surveys were instead used to inform how symptoms relate to downstream impacts (i.e. final outcomes) to form the Theory of Change. SROI filters were informed using the authors' judgement in consultation with patient advocacy organisations, neurologists and nurses treating people living with aPD. Further detail is provided in Appendix VIII to Appendix XII.

Figure 6 Calculating the value



LEVODOPA-BASED DATS FOR PARKINSON'S DISEASE

Only through lived experience is one truly able to understand the impact of a disease, and ultimately tell the story of how change is created. This is one of the core tenants of SROI. Part of conducting this analysis involved consulting people living with aPD, their partners, and the healthcare providers caring for them, to understand how access to a levodopa-based DAT impacts their lives (see Methodology for additional detail). Their stories demonstrate that access to a levodopa-based DAT has profound social, health, and economic impacts on people's lives.

People living with aPD

"[Levodopa-based DATs] *have* ***IMPROVED MY LIFE ENORMOUSLY*** *compared to what it was like on the tablets... I just don't have the down times anymore.*"
– Person living with aPD receiving treatment with a levodopa-based DAT

"*For the people that* [levodopa-based DATs] *has worked for,* [there has been] *a* ***MASSIVE CHANGE IN THEIR LIFE.***"
– Nurse caring for people living with advanced PD receiving treatment with DATs

Partners of people living with aPD

"[Treatment with levodopa-based DATs] *straightens out your life a little bit more. It* ***GIVES YOU A BIT MORE HOPE FOR THE FUTURE***"
– Partner of patient with aPD receiving treatment with a levodopa-based DAT

"[Treatment with levodopa-based DATs] ***REALLY GIVES US A BIT MORE INDEPENDENCE TO STILL MOVE AROUND... TO TRAVEL****... with the more consistent supply of medicine.*"
– Partner of a person living with aPD receiving treatment with a levodopa-based DAT

Children of people living with aPD

"[The voice of the person living with aPD had] *become very weak and he really couldn't have phone conversations with his sons who both live interstate. That had become a real issue because he felt he was losing touch...* [After starting treatment with a levodopa-based DAT] ***HIS SONS WERE REALLY BLOWN AWAY BY HAVING THESE GREAT LONG CONVERSATIONS WITH THEIR DAD.***"
– Nurse caring for people living with aPD receiving treatment with a levodopa-based DAT

IMPACT OF LEVODOPA-BASED DATS

For every **$1** invested in levodopa-based DATS...

...**$1.79** of social value is created

TOTAL INVESTMENT

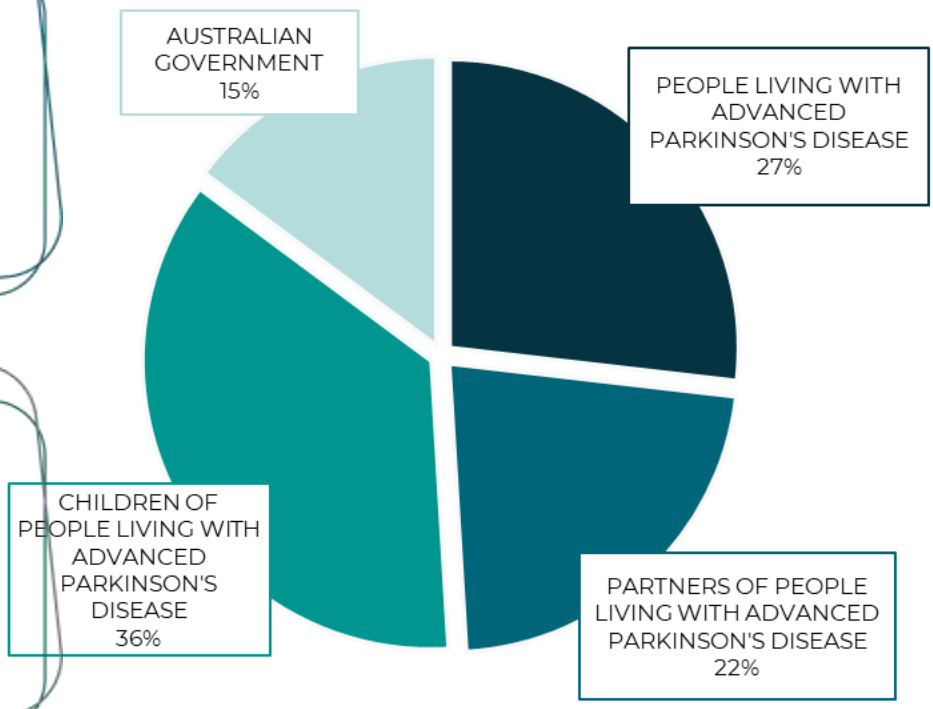
$227.16 MILLION
OVER 3 YEARS

$64,692
YEARLY INVESTMENT PER PERSON WITH PD

VALUE CREATED

$406.77 MILLION
OVER 3 YEARS

$179.61 MILLION
NET PRESENT VALUE



1 : 1.79
SROI ratio

$$= \frac{\text{\$406.77 MILLION (Present value of benefits)}}{\text{\$227.16 MILLION (Present value of investment)}}$$

INVESTMENT

In a SROI, an input refers to what the stakeholders are contributing in order to make the outputs and outcomes possible (23). This includes both monetary and 'in-kind' (e.g. time) contributions. Australia has a public healthcare system funded by a federal Government, which provides free or subsidised access to listed medicines (via the PBS), and healthcare services and medical procedures (via the Medicare Benefits Schedule (MBS)) (see Appendix XIII).

The drug costs of Duodopa® and Vyalev® were used as inputs for the cost of medicines. This cost was separated into PBS costs (paid by the Australian Government) and the co-payment (paid by the patient), based on the current price of Duodopa® on the PBS. The current list price of Duodopa® was taken from PBS Item 11919H ($5,902.22) and the average daily dose (1.1 cassettes based on Duodopa® Product Information) was used to calculate an annual average cost per patient. The average patient co-payment amount ($8.33 per dispensed script) was calculated based on PBS utilisation data for PBS Item 11919H (Duodopa®) and the 2023 patient co-payments. It was assumed that the price of Vyalev® would be equal to the cost of Duodopa®. In Australia, medicines funded on the PBS can also include a 'Special Pricing Arrangement' where the true cost of the medicine to the Government (also called the 'effective price' or 'net price') is not known to the public, as a confidential rebate is paid by the drug sponsor. The current average rebate was calculated based on publicly available PBS expenditure reports for the financial year 2020-2021 (26). The average rebate across all medicines listed on the PBS was calculated to be 22%. This was applied to the price of levodopa-based DATs in the evaluation.

The cost of medical services associated with commencing levodopa-based DATs was also included as an input, based on hospital costs and appointment costs with specialists including neurologists.

In order to avoid double counting, it was assumed that other stakeholders (e.g. partners and children of people living with PD) did not have any monetary or in-kind investment into treatment, and all financial inputs was incurred by the patient themselves.

The total investment into levodopa-based DATs over the three-year time horizon was calculated to be $227.16 million, or $79.44 million per year (see Table 14). This cost was primarily incurred by the Australian Government, with patients contributing an average of $133 each per year.

Table 14 Total input costs

Stakeholders	Financial value of investment for entire stakeholder group	Financial value of investment per person living with aPD
People living with aPD	$163,538 per year	$133 per year
Australian Government	$79,278,096 per year	$64,559 per year
Total annual investment	**$79,441,634 per year**	**$64,692 per year**
Total present value investment	**$227.16 MILLION over 3 years**	

1,228

Total number of people living with aPD impacted by the intervention

$64,692

Yearly investment per person living with aPD

$79.44 MIL

Total amount invested per year in access to treatment with levodopa-based DATs

VALUE CREATED

FINAL OUTCOMES FOR PEOPLE LIVING WITH APD

REDUCED OUT-OF-POCKET COSTS FOR AIDS AND MODIFICATIONS

As PD advances, people may experience worsening symptoms which affects their mobility and increases dependence on aids and modifications (including walkers, wheelchairs, grab bars, and railings). However, with access to levodopa-based DATs, people living with aPD experience improved motor symptoms including a reduction in tremors, rigidity, and risk of falls (3). This leads to improved mobility, reducing the need for and costs associated with aids and other modifications.

"[Oral medication] *just didn't work for me at all. So, I had three months in which I had a number of falls, and I damaged my shoulder quite badly... and then when I went on the* [levodopa-based DAT] *infusions, things changed rapidly... and for the first year of the infusion I* [was] *doing quite well."* – Person living with aPD receiving treatment with a levodopa-based DAT

INCREASED CONNECTION TO FAMILY AND FRIENDS

With access to levodopa-based DATs, people living with aPD experience an improvement in their overall PD symptoms, including sleep quality and ability to communicate (3). Additionally, reduced worry about "Off" times and dyskinesia, leads to a reduction in perceived stigma and increases an individual's ability and desire to participate in leisure and social activities with family and friends. During consultation, stakeholders described how people living with aPD were able to connect, or in some cases reconnect, with family and friends after commencing treatment with levodopa-based DATs.

"To know that I didn't have to worry about not being "On" or having dyskinesia during work meetings or in social situations would increase my confidence, decrease my anxiety, and stress levels and would let me feel more like myself" – Person living with aPD receiving treatment with a levodopa-based DAT (12)

"The best part is we have a social life again! Reconnecting with my friends and spending time with my family has brought me so much joy and happiness." – Person living with aPD receiving treatment with a levodopa-based DAT (12)

INCREASED INDEPENDENCE

Consultation with stakeholders demonstrated when people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in their overall PD symptoms and ability to perform activities of daily living (ADL). This was supported by clinical trial data (3). This leads to increased independence.

"[Treatment with levodopa-based DATs] *really gives us a bit more independence to still move around... to travel... with the more consistent supply of medicine."* – Partner of a person living with aPD receiving treatment with a levodopa-based DAT

"I spend approximately 65% of my waking day in the "Off" state when my medication is not working. This causes me to have difficulty moving independently, feeding myself,

and performing basic tasks. The 35% I manage in the "On" state is with troublesome dyskinesia, very violent movements that again prevent me from doing most basic activities… I have many severe symptoms that cause me to need help with my activities of daily living" – Person living with aPD discussing the burden of disease progression (12)

INCREASED ABILITY TO REMAIN IN THE WORKFORCE

When people living with aPD have access to treatment with a levodopa-based DAT, they experience an improvement in their overall PD symptoms including reduced motor difficulties and cognitive decline, and improved ability to perform ADL (3). As such, they have an increased ability to remain in the workforce. During consultation, nurses caring for people living with aPD explained people living with aPD who are of working age may continue to work.

"We know from research the majority of [people living with aPD] *will retire earlier than they had planned… many of them move to working part-time as opposed to maintaining a full-time position…"* – Nurse caring for people living with aPD

"My primary goal was to stay at work and retire when I want to retire, not when Parkinson's makes me retire…" – Person living with aPD discussing DAT treatment goals

INCREASED HOPE FOR THE FUTURE

During consultation, people living with aPD explained how their ability to plan for the future and hopes for retirement were impacted by their PD diagnosis (12). This was supported by secondary research. However, after commencing treatment with a levodopa-based DAT, people living with aPD explained they were able to continue making travel plans, as they felt more in control of their PD and were less worried about their future health status.

"[Access to treatment with a levodopa-based DAT] *has improved my life enormously compared to what it was like on the tablets… I just don't have the down times anymore."* – Person living with aPD receiving treatment with a levodopa-based DAT

INCREASED BURDEN OF DISCOMFORT

When people living with aPD commence treatment with a levodopa-based DAT, they need to adjust to the infusion site, pump, and tube, which can initially feel burdensome. During consultation, people living with aPD explained they needed to adjust their attire to carry and/or conceal the infusion site, pump, and tube, leading to an increased burden of discomfort. Despite this, during consultation, people living with aPD explained the benefit gained through access to a levodopa-based DAT was "worth it"

"…[the levodopa-based DAT] *tube and pump took some time getting used to, but the independence is worth it…"* – Person living with aPD receiving treatment with a levodopa-based DAT (12)

TOTAL VALUE CREATED FOR PEOPLE LIVING WITH APD

The value of each final outcome for people living with aPD was calculated (see Figure 6 for details). The value created from increased access to levodopa-based DATs for people living with aPD is outlined in Table 15.

Table 15 Total present value created for people living with aPD

Stakeholder	Outcomes	Total present value for entire stakeholder group	Total present value created per individual stakeholder
People living with aPD	Reduced out-of-pocket costs for aids and modifications	$1,043,763	$850
	Increased connection to family and friends	$13,901,423	$11,320
	Increased independence	$75,018,926	$61,090
	Increased ability to remain in the workforce	$12,161,556	$9,904
	Increased hope for the future	$6,239,937	$5,081
	Increased burden of discomfort	-$805,330	-$656
	Total present value created	$109,111,543	$88,853

Abbreviations: aPD, advanced PD; PD, Parkinson's disease
NB rounding applies

FINAL OUTCOMES FOR PARTNERS OF PEOPLE LIVING WITH APD

REDUCED WORRY ABOUT PARTNER

When people living with aPD receive treatment with a levodopa-based DAT, they experience a greater independence and a reduced need to remember when to take their medication. As a result, their partners experience reduced worry about their ability to perform ADLs, including whether they have taken their oral medication. This leads to reduced carer burden, resulting in a reduction in the overall worry partners of people living with aPD experience.

"We are so much happier. We were given life back. My wife doesn't have to worry anymore." – Person living with aPD receiving treatment with a levodopa-based DAT (12)

"He just needed supervision so I could go out… I sat with my phone on my lap the whole time I was at the hairdresser, just in case." – Partner of person living with PD

INCREASED CONNECTION TO FAMILY AND FRIENDS

When people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in independence and reduced need to frequently take oral medication, thus requiring less supportive care. As a result, their partner experiences a reduced carer burden. This leads to an increase in personal time and ability to spend time with family and friends, thus increasing connection to family and friends.

"His wife can now go quilting for a few hours each week without being concerned that her husband has forgotten to take a dose of medication" – Partner of person living with aPD receiving treatment with a levodopa-based DAT (12)

INCREASED CARER WELLBEING

When people living with aPD receive treatment with a levodopa-based DAT, they experience improved sleep quality and increased independence. As a result, their partner experiences fewer sleep disturbances and reduced carer burden, which leads to more personal time and time spent with family and friends. This leads to increased carer wellbeing.

"When he was just on the tablets he would constantly thrash around and kick and punch [me in bed] *but that hasn't happened since beginning* [treatment with levodopa-based DATs]" – Partner of person living with aPD receiving treatment with a levodopa-based DAT

"I used to ask him if he could just give me some respite because there was only me" – Partner of person living with PD

"My caregiving role has changed dramatically since my spouse started receiving the Duodopa treatment. For several years it was a very demanding role, 24 hours a day… I had no independent life… But now with Duodopa most of that no longer applies" – Partner of person living with aPD receiving treatment with a levodopa-based DAT (12)

"The disease has a direct impact on every aspect of life for the caregiver. As the symptoms develop and increase in severity, everything becomes unpredictable. Managing household chores, planning for the day's and week's activities, etc. all become difficult. The stress takes its toll on the caregiver…" – Partner of person living with aPD receiving treatment with a levodopa-based DAT (12)

INCREASED HOPE FOR THE FUTURE

When people living with aPD receive treatment with a levodopa-based DAT, they experience an increased ability and desire to participate in leisure and social activities with their partner. For partners of people living with PD, this, coupled with a reduced carer burden, leads to an increased hope for the future.

"[Treatment with levodopa-based DATs] *straightens out your life a little bit more. It gives you a bit more hope for the future."* – Partner of patient with aPD receiving treatment with a levodopa-based DAT

INCREASED ABILITY TO REMAIN IN THE WORKFORCE

When people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in their overall PD symptoms. As a result, their partners experience a reduced carer burden and fewer sleep disturbances, increasing their ability to remain in the workforce.

"I could go for walks with my husband, go to the movies, go back to work" – Partner of person living with aPD receiving treatment wi th a levodopa-based DAT (12)

TOTAL VALUE CREATED FOR PARTNERS OF PEOPLE LIVING WITH APD

The value of each final outcome for partners of people living with aPD was calculated (see Figure 6 for details). The value created from increased access to levodopa-based DATs for partners of people living with aPD is outlined in Table 16.

Table 16 Total present value created for partners of people living with aPD

Stakeholder	Outcomes	Present value calculation	Total present value created per individual stakeholder
Partners of people living with aPD	Reduced worry about partner's health	$42,335,021	$53,051
	Increased connection to family and friends	$5,579,602	$9,498
	Increased carer wellbeing	$20,058,610	$25,136
	Increased hope for the future	$5,172,817	$6,482
	Increased ability to remain in the workforce	$15,275,384	$19,142
	Total present value created	$90,421,435	$113,310

Abbreviations: aPD, advanced PD; PD, Parkinson's disease
NB rounding applies

FINAL OUTCOMES FOR CHILDREN OF PEOPLE LIVING WITH APD

INCREASED CONNECTION TO PARENT

When people living with aPD receive treatment with a levodopa-based DAT, they experience an overall improvement in their PD symptoms. This leads to an increased ability to participate in leisure and social activities and a greater desire to connect and communicate with family. As a result, children of people living with aPD experience an increased connection to their parent.

> "[The voice of the person living with aPD had] *become very weak and he really couldn't have phone conversations with his sons who both live interstate. That had become a real issue because he felt he was losing touch…* [After starting treatment with a levodopa-based DAT] *his sons were really blown away by having these great long conversations with their dad."* – Nurse caring for people living with aPD receiving treatment with levodopa-based DATs

REDUCED WORRY ABOUT PARENT

When people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in overall PD symptoms. As a result, children of people living with aPD experience reduced worry about their parent.

> *"They told us to go to a retirement village"* – Person living with aPD talking about their children

TOTAL VALUE CREATED FOR CHILDREN OF PEOPLE LIVING WITH APD

The value of each final outcome for children of people living with aPD was calculated (see Figure 6 for details). The value created from increased access to levodopa-based DATs for children of people living with aPD is outlined in Table 17.

Table 17 Total value created for children of people living with aPD

Stakeholder	Outcomes	Value calculation	Total present value created per individual stakeholder
Children of people living with aPD	Increased connection to parent	$1,913,508	$779
	Reduced worry about parent	$145,000,725	$59,039
	Total value created	**$146,914,233**	**$59,819**

Abbreviations: aPD, advanced PD; PD, Parkinson's disease
NB rounding applies

FINAL OUTCOMES FOR THE AUSTRALIAN GOVERNMENT

AVOIDED COST OF HEALTHCARE SERVICES

When people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in overall PD symptoms. This leads to reduced hospitalisations and health resource utilisation. Thus, there is an avoided cost of healthcare services.

AVOIDED COST OF WELFARE SERVICES AND SUPPORT PAYMENTS

When people living with aPD receive treatment with a levodopa-based DAT, they experience an improvement in overall PD symptoms. This leads to an ability for people living with aPD and their partners to remain in the workforce, reducing the need for welfare services and support payments. Thus, there is an avoided cost of required welfare services and support payments.

TOTAL VALUE CREATED FOR THE AUSTRALIAN GOVERNMENT

The value of each final outcome for the Australian Government was calculated (see Figure 6 for details). The value created from increased access to levodopa-based DATs for the Australian Government is outlined in Table 18.

Table 18 Total value gained for the Australian Government

Stakeholder	Outcomes	Value calculation
Australian Government	Avoided cost of healthcare services	$51,917,934
	Avoided cost of welfare services and support payments	$8,405,032
	Total value created	**$60,322,966**

NB rounding applies

SENSITIVITY ANALYSIS

A SROI analysis, like all types of economic evaluations, should include sensitivity analyses to assess the impact of certain assumptions on the results. Since the results of this assessment are often based on hypotheses and variables that are based on interviews and surveys it is important to test plausible ranges of key assumptions to understand how the results would change.

The following variables were tested in the sensitivity analysis:

- Discount rates
- Cost inputs
- Valuation approaches
- Time horizon and duration
- SROI filters

The number of stakeholders in each stakeholder group was not examined in a sensitivity analysis. This is because the stakeholder numbers were sourced from real-world evidence based on published Australian epidemiology, PBS claims data, clinician feedback, and experience in PD treatment uptake both in Australia and globally (24, 25). Similarly, the proportion of stakeholders experiencing each outcome was calculated using M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (see Appendix VI). As these inputs were based directly on published data, they were not tested in a sensitivity analysis.

DISCOUNT RATE

Alternative discount rates are commonly tested in economic evaluations. The discount rate is intended to reflect how society values future outcomes compared to present outcomes. As per the PBAC (27), alternative rates of 3.5% and 0% were tested (Table 19). Overall, the change in discount rate did not significantly impact the final SROI ratio.

Table 19 Discount rate sensitivity analysis

Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
Base case	5.00%	1:1.79 $179.61 million	-	Recommended base case discount rate for PBAC submissions (27)
Sensitivity analysis	3.50%	1:1.79 $181.50 million	+0.16%	Alternative discount rate suggested in PBAC guidelines (27)
Sensitivity analysis	0.00%	1:1.78 $186.19 million	+0.53%	Alternative discount rate suggested in PBAC guidelines (27)

Sources: DATs_SROI_Impact Map
Abbreviations: NPV, net present value; PBAC, Pharmaceutical Benefits Advisory Committee; SROI, Social Return on Investment
NB rounding applies

COST INPUTS

To examine the impact of using different cost inputs on the value created the price of medication for Duodopa® and Vyalev® was changed. The sensitivity analysis presented in Table 20 demonstrates how alternative cost inputs impact the calculated SROI ratio. Although the model is sensitive to cost changes, this analysis shows that a positive SROI ratio is likely to be realised over a range of plausible cost inputs.

Table 20 Cost inputs sensitivity analysis

Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
Base case	$64,692 per person living with aPD ($79.44 million total annual investment)	1:1.79 $179.61 million	-	Average annual cost of treatment with a levodopa-based DAT based on current medicine costs for Duodopa®, estimated Special Pricing Arrangement rebate, and initiation costs for DATs
Sensitivity analysis – No confidential rebate on drug price	$83,324 per person living with aPD ($102.32 million total annual investment)	1:1.39 $114.20 million	-22%	Published price of Duodopa® and Vyalev®
Threshold analysis – Cost of levodopa-based DATs for NPV to equal $0	$115,844 per person living with aPD ($142.26 million total annual investment)	1:1 $0	-44.16%	Cost needed to reach SROI ratio of 1:1

Sources: DATs_SROI_Impact Map
Abbreviations: aPD, advanced PD, NPV, net present value; PBAC, Pharmaceutical Benefits Advisory Committee; PD, Parkinson's disease; SROI, Social Return on Investment
NB rounding applies

VALUATION APPROACHES

The valuation approach and financial proxy used for each outcome were informed via stakeholder consultation, providing insights into the lived experience of aPD. To reflect variations in the lived experience of aPD, alternative scenarios were used to conduct a sensitivity analysis (see Table 21). Notably, alternative scenarios were also informed by stakeholder consultation. All the alternative scenarios yielded a positive SROI.

Table 21 Valuation approaches sensitivity analysis

Scenario	Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
Increased independence for people living with aPD	Base case	$53,268.10	1:1.79 $179.61 million	-	People living with aPD may require additional support within their home to maintain independence. Home Care Packages help people access these supports. In the base case, 'High Care Needs' (Level 4) package was assumed. This would provide approximately 17-19 hours of support per week

Scenario	Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
	Sensitivity analysis – lower Care Needs for Home Care Package	$35,138.55	1:1.68 $154.08 million	-6.28%	Alternative scenario assuming 'Intermediate Care Needs' (Level 3). This would provide approximately 11-13 hours of support per week
Increased carer wellbeing for partners of people living with aPD	Base case	$22,330.35	1:1.79 $179.61 million	-	It was assumed, partners of people living with aPD rely on respite care to temporarily relieve their carers burden. As such, the cost of 63 days of respite care per year based on the average cost of a support worker to provide this care was used as the financial proxy in the base case
	Sensitivity analysis – cost of aged care reflects the value of increased wellbeing	$48,535.77	1:1.89 $203.15 million	+5.79%	Alternative scenario using the average cost of aged care homes that provide support and accommodation for people living with aPD who can no longer be safely and reasonably cared for by their partners as the financial proxy (28)
Increased connection to parent for children of people living with aPD	Base case	$972.00	1:1.79 $179.61 million	-	Economic valuation approach using the average cost of a monthly phone-on-a-plan mobile phone contract in Australia as a financial proxy
	Sensitivity analysis – family therapy reflects the cost of connection to parent	$2,411.47	1:1.80 $182.45 million	+0.70%	Alternative scenario using a replacement valuation approach and average cost of family therapy was used as a financial proxy (inflated to 2021) (29), as children may feel a lack of emotional connection to their parent with PD due to difficulties with emotional regulation and expression
	Sensitivity analysis – international flight reflects the cost of connection to parent	$1,400.00	1:1.79 $180.46 million	+0.21%	Alternative scenario using the average cost of an international flight, assuming that children would need to travel to visit their parents to maintain connection (30)
Avoided cost of healthcare services for the Australian Government	Base case	$28,180.00 ($26.10 million total cost avoided for people living with aPD)	1:1.79 $179.61 million	-	Economic valuation, the actual health system cost of PD health care resource utilisation per person living with mild (Hoehn & Yahr Stage I – II) vs moderate-to-severe (Hoehn & Yahr Stage III – IV) PD, inflated to 2021 values (31)

Scenario	Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
	Sensitivity analysis – Deloitte Access Economics report used to inform healthcare resource cost	$5,720.50 ($5.36 million total cost avoided for people living with aPD)	1:1.61 $138.36 million	-10.42%	Alternative source of actual health system cost of PD care resource utilisation per person living with mild (Hoehn & Yahr Stage I – II) vs moderate-to-severe (Hoehn & Yahr Stage III – IV) PD, inflated to 2021 values (32)

Sources: DATs_SROI_Impact Map
Abbreviations: aPD, advanced PD, NPV, net present value; PD, Parkinson's disease; SROI, Social Return on Investment
NB rounding applies

TIME HORIZON AND DURATION

The sensitivity analysis presented in Table 22 demonstrates how the chosen time horizon and duration of each outcome impacts the calculated SROI ratio. For each case, the time horizon and duration period were matched. Whilst all scenarios lead to a SROI ratio greater than 1, the time horizon and duration chosen in the base case limits uncertainty associated with reduced clinical effectiveness over time and captures the short- and medium-term changes in health and social impacts expected to result from treatment with a levodopa-based DAT, which would not be expected to be captured with a shorter time horizon.

Table 22 Time horizon and duration sensitivity analysis

Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
Base case	3 years	1:1.79 $179.61 million	-	A three-year period limits uncertainty associated with reduced clinical effectiveness over time and captures the short- and medium-term changes in health and social impacts expected to result from treatment with a levodopa-based DAT
Sensitivity analysis – shorter time horizon	1 year	1:2.08 $85.67 million	+16.06%	An alternative scenario, forecasting a one-year time period. This limits uncertainty associated with reduced clinical effectiveness of levodopa-based DATs over time, however, captures short-term changes in health and social impacts only
Sensitivity analysis – longer time horizon	5 years	1:1.56 $202.93 million	-12.78%	An alternative scenario, forecasting a five-year time period. This may introduce some uncertainty associated with clinical effectiveness over time, and overestimate the long-term changes in health and social impact from access to levodopa-based DATs

Sources: DATs_SROI_Impact Map
Abbreviations: aPD, advanced PD; DAT, device-assisted therapy; NPV, net present value; SROI, Social Return on Investment
* Excluding "increased burden of discomfort" as this final outcome is expected to last for one-year
NB rounding applies

SROI FILTERS

Estimates of SROI filters, including attribution, deadweight, displacement, and drop off, were informed by stakeholder consultation, secondary research, and clinical trial data. Estimates were further verified by AbbVie Pty Ltd commercial-in-confidence assumptions, analysis of PBS data, clinician feedback, and commercial insight into PD treatment uptake both in Australia and globally. Alternative scenarios for the SROI filters and for each outcome were used to conduct a sensitivity analysis (see Table 23). Drop off was not included in the sensitivity analysis. Long-term follow up data from a real-world observational study was used to inform the base case analysis (20). This included data up to 36-months, the time horizon of this assessment. As such, it was considered that any uncertainty in the drop off rate was negligible. Although the base case calculated SROI ratio (1:1.83) was influenced by the chosen attribution, displacement, and drop off values, alternative estimates all yielded a positive SROI.

Table 23 SROI filters sensitivity analysis

SROI filter	Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
Attribution	Base case	0%	1:1.79 $179.61 million	-	As per the randomisation process of the M15-736 clinical trial, it were assumed the outcomes included in this SROI were completely the result of access to treatment with levodopa-based DATs (see Appendix IX) (33)
	Sensitivity analysis – increased attribution from base case	+20% for each outcome*	1:1.43 $98.26 million	-20.00%	Alternative scenario if it were assumed the outcomes included in this SROI were almost entirely the result of access to treatment with levodopa-based DATs (33)
	Sensitivity analysis – increased attribution from base case	+40% for each outcome*	1:1.07 $16.91 million	-40.00%	Alternative scenario if it were assumed the outcomes included in this SROI were largely the result of access to treatment with levodopa-based DATs (33)
Deadweight	Base case	20%	1:1.79 $179.61 million	-	As PD is a progressive neurodegenerative disease, the outcomes included in this SROI would very probably not occur without access to treatment with levodopa-based DATs (see Appendix X) (33)
	Sensitivity analysis – decreased deadweight from base case	-20% for each outcome*	1:2.24 $281.51 million	+25.05%	Alternative scenario if it were assumed the outcomes included in this SROI would never have occurred without access to treatment with levodopa-based DATs (33)
	Sensitivity analysis – increased deadweight from base case	+20% for each outcome*	1:1.34 $77.72 million	-25.05%	Alternative scenario if it were assumed the outcomes included in this SROI might have occurred without access to treatment with levodopa-based DATs (33)
Displacement	Base case	0%	1:1.79 $179.61 million	-	Treatment with a levodopa-based DAT is displacing

SROI filter	Type	Value	SROI ratio, NPV	% change in SROI ratio	Description
					treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0% (see Appendix XI)
	Sensitivity analysis – increased displacement from base case	+20% for each outcome*	1:1.43 $98.01 million	-20.04%	Alternative scenario if displacement was assumed to be 20%
	Sensitivity analysis – increased displacement from base case	+40% for each outcome*	1:1.07 $16.58 million	-40.08%	Alternative scenario if displacement was assumed to be 40%

Sources: DATs_SROI_Impact Map
Abbreviations: aPD, advanced PD; DATs, device-assisted therapies; NPV, net present value; PBAC, Pharmaceutical Benefits Advisory Committee; PD, Parkinson's disease; SROI, Social Return on Investment
* Excluding "increased burden of discomfort" as this final outcome is a direct result of initiating levodopa-based DATs.
NB rounding applies

OVERALL IMPACT OF UNCERTAINTY

Attempts have been made to verify the results of this SROI analysis, including validating outcomes with people living with aPD, their partners, nurses, and patient advocacy organisations. Additionally, sensitivity analyses of various inputs show the impact of various assumptions made throughout the analysis (see Sensitivity Analysis). There is nevertheless the possibility that the cumulative impact of these assumptions could influence the overall result. In particular, lack of robust data on the proportion and magnitude of change, as well as long-term data on the duration and drop off of outcomes experienced is a limitation of the current research.

The nature of the Phase III data used in this analysis reduces the risk of selection or reporting bias, as participants in the trial were 'blinded' to their treatment allocation. This means that they are not likely to alter their reporting of outcomes based on their perception of treatment efficacy. However, this SROI did not directly measure the occurrence of the included outcomes. Instead, this SROI used proxy indicators based on clinical trial data which measured the change in PD symptom domains. This was necessary due to limitations with stakeholder recruitment and the small number of stakeholders who have experience with levodopa-based DATs in Australia. However, it is acknowledged that by measuring the upstream symptoms of aPD instead of specific outcomes, this analysis has indirectly captured outcome data. This is particularly true for the partners and children of people who live with aPD, as there were no stakeholder-specific indicators available for use in this analysis. Recommendations have been provided as to the direction of future research, including potential indicators which could be used to verify the occurrence of the identified outcomes.

There is also the possibility that the current analysis underestimates the benefit of treatment with levodopa-based DATs. The clinical trial data used in this SROI compare treatment with a levodopa-based DAT to continuation on oral levodopa over a 12-week period. Whilst real-world evidence demonstrates the effectiveness of levodopa-based DATs is expected to persist for at least 36-months (20), the progressive nature of PD means patients who continue treatment with oral levodopa are likely to experience worsening symptoms, and therefore a deterioration in many of the outcomes reported here. As such, the difference between levodopa-based DATs and oral levodopa may in fact increase over time, an element not considered in the current analysis.

VERIFICATION AND DISSEMINATION OF RESULTS

Stakeholders were engaged throughout the SROI process, to ensure the information in the survey, results, and analysis expresses their lived experience. The results and assumptions of this forecast analysis were discussed and shared with people living with aPD, their partners, patient advocacy groups, and nurses caring for them. Following the initial stakeholder interviews, follow up surveys were conducted in a separate sample of people living with PD and their partners, to verify the outcomes considered most important to them. Additional interviews with people living with PD and their partners were also conducted to ensure that the Theory of Change reflects their experiences with the disease.

The results and report of this analysis will be disseminated to relevant audiences. The dissemination plan is not yet finalised, but is expected to include:

- A manuscript to be written and published in a chosen journal. This manuscript is primarily expected to reach a clinical audience, including neurologists and nurses caring for people living with PD. The manuscript peer-review process will serve as an additional verification of the methodology applied to this research.
- A communication report will be developed to be public facing and disseminated among patient advocacy groups and non-technical groups more broadly. This report will also be shared with decision makers, including funders of PD treatments in Australia.
- Short communication briefs including 1-2 page documents to communicate the key results of the analysis to specific audiences selected by AbbVie Pty Ltd.

IMPLICATIONS AND RECOMMENDATIONS

This report is the first SROI analysis which investigates the impact of improving access to levodopa-based DATs for people living with aPD. Whilst a SROI provides a ratio of return to investment, this research also tells the story of how value is created and reveals wide-ranging impacts for a diverse array of stakeholders. Through engagement with stakeholders, this research reveals the impact of investing in levodopa-based DATs is expected to be substantially further reaching than the outcomes captured in a traditional clinical trial or cost-effectiveness analysis.

For Government agencies, this analysis demonstrates that the investment required to improve access to levodopa-based DATs for people living with aPD who are currently poorly controlled on oral medication will result in positive social value being created. This is due to the immense social and economic value created not just for people living with aPD themselves, but for their partners, children, and broader community, which are often neglected in traditional economic and financial evaluations.

It is recommended that the results of this analysis are verified in the future through a retrospective evaluation, once a greater number of people have access to Vyalev® and can speak to its impact. Considerations for future research include:

- **Addressing challenges with stakeholder recruitment**
  This research faced significant difficulties reaching people living with aPD and their families. Whilst this was partially attributed to the limited number of people who had exposure to the treatment being evaluated (Duodopa ® and Vyalev®) compared to those on oral medication, clinicians also noted that people living with PD are often approached to participate in research and as such may be 'burnt out'. Early engagement with patient advocacy groups is essential to connecting with people living with aPD and their families. Additionally, the feasibility of directly recruiting Government stakeholders should be considered in future works, including identifying appropriate Government representatives, requesting participation in the study, and allowing lead time for interviews.
- **Considering aPD populations in alternative settings**
  This research evaluated the impact of levodopa-based DATs specifically in people living with aPD in a community-based setting. This was a pragmatic decision, as engaging people who live in out-of-home care (e.g. a aged care homes) was not likely to be feasible given the time and scoping restraints of this research. As such, any extrapolation of these outcomes to people living in aged care homes should be done with caution. Future work should assess differences in the impact of levodopa-based DATs in this population. Additionally, in these settings, nurses caring for people living with aPD would likely be impacted, thus included/excluded stakeholders should also be re-evaluated.
- **Considering the impact of young onset PD**
  Further research should assess the potential differential impact of young onset PD. Whilst the average age of PD diagnosis is above 65, approximately 10% of people are diagnosed with PD before the age of 50 (2). These people are more likely to have younger, dependent children, and will likely still be part of the workforce. As such, they may experience additional or different outcomes compared to the broader aPD population assessed in this SROI. Whilst a number of people living with young onset PD were consulted as part of this research, additional research focusing exclusively on this population may reveal additional impacts.

- **Considering the influence of alternative treatments for aPD**
  This research focused on the impact of investing in improving access to levodopa-based DATs. Based on current Australian data, it was assumed that patients commencing treatment with levodopa-based DATs would have otherwise received treatment with oral levodopa/carbidopa. As such, outcomes of levodopa-based DATs were compared to the outcomes of people who continued receiving treatment with oral therapy. However, other aPD treatments are available in Australia, for example DBS and continuous subcutaneous infusion of apomorphine. Whilst these treatments are associated with significant limitations (see Introduction for more information), understanding the impact of levodopa-based DATs compared to alternative treatments for aPD would be informative.
- **Understanding the current gaps in health care for aPD**
  Further research is needed to understand the current gaps in aPD care. Throughout the consultation process, nurses emphasised the need for increased patient access to specialised nurses, with expertise in aPD and DATs. The role of these nurses is to provide patients with support relating to the infusion site, pump, tube (including leaks, discolouration, and blockages), cassettes (broken, malfunctioning, discolouration), PEG/J site concerns, and more. These specialist nurses play an important role in patient education and support, which is an essential element of successful treatment and was noted to reduce the perceived burden associated with the DATs. However, access to these nurses can be limited. Lack of access to nurse specialists was noted by nurses as a barrier to uptake of levodopa-based DATs.

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APPENDIX I RECRUITMENT FLYERS

HEALTHCARE PROFESSIONALS INTERVIEW RECRUITMENT FLYER

Sharing your experiences of Parkinson's disease and the value of advanced treatment options

A new research study is aiming to understand how Parkinson's disease is affecting people living with the condition, their families, communities, and society. The study is looking to identify people living with or involved in the care of Parkinson's disease to provide their perspective and experiences.

Who can participate?

- Healthcare professionals such as clinicians and nurses who have experience with Parkinson's disease and device-aided therapy for advanced Parkinson's disease.

What do I need to do?

- Take part in a 30 minute to 1 hour interview. The interview will be conducted over a video conference platform such as Microsoft Teams.

What types of questions will I be asked?

- Your patients' Parkinson's disease diagnosis, treatment options and treatment experience.
- The potential impact Parkinson's disease has on your patients.
- Your patients' mental health and outlook and how these might be influenced by Parkinson's disease.
- Changes in your patients' daily life.
- How your patients' experience Parkinson's disease today.

How will my information be used?

- Your interview will be used to inform a report about the broader impacts of Parkinson's disease.
- No personal details will be shared and anything you share will remain anonymous.
- The intention is that this report will be made public by AbbVie to inform additional research and potential new treatments.

The research is being commissioned by AbbVie and will be undertaken by the research agency HTANALYSTS.

If you are interested in participating, contact HTANALYSTS to register your interest and to receive further information on the study. Please email: **irene.deltetto@htanalysts.com.au**

- Before taking part in the study, a consent form containing details about privacy and ethics standards will be provided.

AbbVie Australia Pty Ltd, Level 7, 241 O'Riordan St, Mascot, NSW, 2020. [illegible] May [illegible]

abbvie

PEOPLE LIVING WITH APD AND FAMILY INTERVIEW RECRUITMENT FLYER

Sharing your experiences of Parkinson's disease and the value of advanced treatment options

A new research study is aiming to understand how Parkinson's disease is affecting people living with the condition, their families, communities, and society. The study is looking to identify people living with or involved in the care of Parkinson's disease to provide their perspective and experiences.

Who can participate?

- People living with Parkinson's disease who are eligible for device-aided therapy.
- Family members or carers (over age 18) of persons with Parkinson's disease who are eligible for device-aided therapy.

What do I need to do?

- Take part in a 30 minute to 1 hour interview. The interview will be conducted over a video conference platform such as Microsoft Teams or via telephone.
- Support will be available should you experience distress during the interview.

What questions will I be asked?

- You or your family member's diagnosis, treatment options and treatment experience.
- How Parkinson's disease has impacted your or your family member's health, personal life and relationships.
- Your mental health and outlook and how this is influenced by Parkinson's disease.
- Changes in your daily life.
- How you think about Parkinson's disease today.

How will my information be used?

- Your interview will be used to inform a report about the broader impacts of Parkinson's disease.
- No personal details will be shared and anything you share will remain anonymous.
- The intention is that this report will be made public by AbbVie to inform additional research and potential new treatments.

The research is being commissioned by AbbVie, a pharmaceutical company, and will be undertaken by the research agency HTANALYSTS.

If you are interested in participating, contact HTANALYSTS to register your interest and to receive further information on the study. Please email **irene.deltetto@htanalysts.com.au**

- Before taking part in the study, a consent form containing details about privacy and ethics standards will be provided.

AbbVie Australia Pty Ltd, Level 7, 24 Chandler St Mascot, NSW, 2020. ABBV-AU-00158 NV May 2022

abbvie

PEOPLE LIVING WITH APD AND FAMILY SURVEY RECRUITMENT FLYER

Sharing your experiences of Parkinson's disease and the value of advanced treatment options

A new research study is aiming to understand how Parkinson's disease is affecting people living with the condition, their families, communities, and society. The study is looking to identify people living with or involved in the care of Parkinson's disease to provide their perspective and experiences.

Who can participate?

- People living with Parkinson's disease who are eligible for device-aided therapy.
- Family members or carers (over age 18) of persons with Parkinson's disease who are eligible for device-aided therapy.

What do I need to do?

- Take part in a short online survey. Instructions for the online survey will be provided to you during a short phone call and you can complete the survey over the phone if you prefer.
- Support will be available should you experience distress during the interview.

What questions will I be asked?

- You or your family member's diagnosis, treatment options and treatment experience.
- How Parkinson's disease has impacted your or your family member's health, personal life and relationships.
- Your mental health and outlook and how this is influenced by Parkinson's disease.
- Changes in your daily life.
- How you think about Parkinson's disease today.

How will my information be used?

- Your interview will be used to inform a report about the broader impacts of Parkinson's disease.
- No personal details will be shared and anything you share will remain anonymous.
- The intention is that this report will be made public by AbbVie to inform additional research and potential new treatments.

The research is being commissioned by AbbVie, a pharmaceutical company, and will be undertaken by the research agency HTANALYSTS.

If you are interested in participating, contact HTANALYSTS to register your interest and to receive further information on the study. Please email: **irene.deltetto@htanalysts.com.au**

- Before taking part in the study, a consent form containing details about privacy and ethics standards will be provided.

AbbVie Australia Pty Ltd, Level 7, 241 O'Riordan St, Mascot, NSW 2020 ABN 67 601 683 FM, May 2022.

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APPENDIX II INTERVIEW GUIDES

PATIENT INTERVIEW GUIDE

We would first like to begin with a brief introduction about you and your experience with Parkinson's disease.

1. When you were first diagnosed with Parkinson's disease, what were your thoughts and feelings?
2. What were the initial treatments you received for Parkinson's disease?
    a. What was your experience with these treatments?
3. Once these treatments were no longer as effective, what treatment options were presented to you?
    a. Did you undergo treatment with any other therapies for advanced Parkinson's disease before commencing ABBV-951/Duodopa® (e.g., apomorphine)?
    b. How did these treatments impact your life?
4. What are your main treatment goals?
    a. What outcomes are most important to you?
    b. Probe: what is it about these outcomes that is important? What relationship do they have to downstream effects?
5. What made you decide to commence treatment with ABBV-951/Duodopa®/other?
6. How has your health been since commencing treatment?
    a. What have been the main benefits/disadvantages of this treatment?
        i. Probe: ADL, non-motor, sexual dysfunction, cognitive, mental health
        ii. Probe: How important are these activities to you?
7. Are there any activities that you been able to do now as a result of your treatment with ABBV-951/Duodopa®/other that you were previously unable to do?
8. Have your carer requirements changed since commencing treatment with ABBV-951/Duodopa®?
    a. Probe: changing need for formal care
    b. Probe: changing need for informal care

The following questions are to explore other aspects of life that may have been impacted by advanced Parkinson's disease. We are interested to know if you think these are relevant to you, and how you would describe your experience of each of these areas of your life.

9. When you commenced treatment with ABBV-951/Duodopa®/other, did you experience any impacts on your social and family life?
10. When you commenced treatment with ABBV-951/Duodopa®/other, did you experience any impacts on your ability to work (depending on patient age), spend time with family, and do tasks around the house?
11. When you commenced treatment with ABBV-951/Duodopa®/other, did you experience any economic impacts?
12. When you commenced treatment with ABBV-951/Duodopa®/other, did you experience any mental health impacts?

For the next section of the interview, I am hoping to ask about the impacts of your diagnosis and treatment on other members of your family, such as your children or partner.

13. Did you notice your treatment having an impact on your partner/children/friends/carer?
14. What kind of support did you previously receive from friends or family?

15. Has this support changed over time and how so?

PARTNER INTERVIEW GUIDE

We would first like to begin with a brief introduction about you and your experience with your partner's Parkinson's disease.

1. When your partner was first diagnosed with Parkinson's disease, what were your thoughts and feelings?
2. What were the initial treatments your partner received for Parkinson's disease?
    a. How did these treatments impact your life?
3. Once these treatments were no longer as effective, how did you feel?
    a. What adjustments did your family make during this time?
4. What are your main treatment goals for your partner's treatment?
    a. What outcomes are most important to you?
    b. Probe: what is it about these outcomes that is important? What relationship do they have to downstream effects?
5. What made you and your partner decide to commence treatment with ABBV-951/Duodopa®/other?
6. How has your partner's health been since commencing treatment?
    a. What have been the main benefits and disadvantages of treatment?
    b. What are the most important outcomes of treatment for you and your partner?
        i. Probe: ADL, non-motor, sexual dysfunction, cognitive, mental health
        ii. Probe: Why are these outcomes important? What is their link to downstream effects?
7. What have you been able to do now as a result of your partner's treatment with ABBV-951/Duodopa® that you were previously unable to do?
    a. How important are these activities to you?
8. Have your partner's carer requirements changed since commencing treatment with ABBV-951/Duodopa®?
    a. Probe: changing need for formal care
    b. Probe: changing need for informal care

The following questions are to explore other aspects of life that may have been impacted by Parkinson's disease. We are interested to know if you think these are relevant to you, and how you would describe your experience of each of these areas of your life.

9. When your partner commenced treatment with ABBV-951/Duodopa®/other, did you experience any impacts on your social and family life?
10. When your partner commenced treatment with ABBV-951/Duodopa®/other, did you experience any impacts on your ability to work (depending on patient age), spend time with family, and do tasks around the house?
11. When your partner commenced treatment with ABBV-951/Duodopa®/other, did you experience any economic impacts?
12. When your partner commenced treatment with ABBV-951/Duodopa®/other, did you experience any mental health impacts?

For the next section of the interview, I am hoping to ask about the impacts of your partner's diagnosis and treatment on other members of your family, such as your children or close friends.

13. Did you notice your partner's treatment having an impact on your children/friends?
14. What kind of support did you previously receive from friends or family?
15. Has this support changed over time and how so?

Finally, we would like to briefly touch on how your employer responded to your partner's aPD diagnosis and what support what provided to you.

16. Were there any changes to the amount you worked after your partner's diagnosis?
17. Did these changes differ when your partner changed treatment?
18. What adjustments were made at your workplace to support your needs as you managed the changing needs of your family?

NEUROLOGIST INTERVIEW GUIDE

General

1. How many Parkinson's disease patients are you currently treating?
    a. How many of these patients would be classified as having 'advanced' Parkinson's disease?
2. From your perspective, what are the main impacts of aPD on patients' and their families' lives?

Recruitment and administration

3. How many of your patients do you think would be willing to participate in this research?
4. What would be the most convenient way to engage them? (survey vs interview)
5. What should be our main considerations regarding survey engagement? (access to technology, ability to complete online survey, go through family members)
6. Who do you think would benefit most from increasing access to DATs (family, nurses, patients)

Treatments

7. Of your aPD patients, what would be the rough breakdown of the treatments they are currently receiving? (orals, Duodopa®, apomorphine, DBS)
    a. What are the main drivers of treatment choice for those patients?
    b. Do patients ever come off these advanced therapies and back onto oral levodopa/carbidopa?
        i. If yes, what are the main reasons for this?
    c. What are the main disadvantages of current treatments?
8. Specifically relating to Duodopa® and DBS: what are the wait times like for implantation of the tube or electrodes?
    a. What impact does this wait time have on patients?
    b. What impact does this wait time have on the health system more broadly?
9. If ABBV-951 becomes available in Australia, how many of those patients would you like to transition to this new treatment?
10. What are the main goals of treatment from your perspective?
    a. What outcomes are most important to your work?
        i. Probe: mental health, motor symptoms, non-motor symptoms
11. What are the perceived benefits of ABBV-951 from your perspective?
    a. How do improved treatment outcomes for patients impact your work?

i. Probe: capacity, burnout, professional satisfaction

b. How do you think this will impact patients and their families?

Care requirements

12. Other than medication, aPD patients may require a range of formal and informal care. From your understanding, what level of care do aPD patient generally require?
    a. What is the burden of this care on family (partners and offspring) and friends of aPD patients?
    b. Would all patients require some level of formal care for aPD?
13. Roughly what proportion of patients with aPD would still be living at home vs in an assisted living facility?
    a. Is there a general 'threshold' after which patients would move to assisted living?

Health system

14. Other than patients and their families, who else do you think might be impacted by improving access to aPD DATs?
15. Based on your experience, what are the broader impacts on the health care system of treating someone with aPD?
    a. Probe: staff requirements, emergency capacity, end-of-life care
16. Based on your experience, how might this change with improved access to DATs?

NURSE INTERVIEW GUIDE

General

1. In what setting are you currently providing PD care? (at home, assisted living, other)
2. How many PD patients do you currently treat?
    a. Approximately what proportion of these patients would classify as having aPD?
3. From your perspective, what are the main impacts of aPD on patients' and their families' lives?

Treatments

4. Of the aPD patients you currently work with, what would be the approximate breakdown of treatments they are currently receiving?
5. What are the main goals of treatment from your perspective?
    a. What outcomes are most important to your work?
        i. Probe: mental health, motor symptoms, non-motor symptoms
6. What are the main advantages/disadvantages of current treatment options from your perspective?
    a. Probe: any issues specific to Duodopa® that could plausibly be alleviated with ABBV-951
    b. Probe: any issues specific to ABBV-951 that should be considered
7. How do you think ABBV-951 will impact patients and their families?
    a. How do improved treatment outcomes for patients impact your work?
        i. Probe: capacity, physical and mental health, emergency care, burnout, satisfaction

Health system

8. Based on your experience, what are the broader impacts on the health care system of treating someone with aPD?

   a. Probe: staff requirements, emergency capacity, end-of-life care

9. Based on your experience, how might this change with improved access to DATs?

APPENDIX III STAKEHOLDER SURVEY

SURVEY FOR PEOPLE LIVING WITH PD

1. How old are you?
    - <50 years
    - 50-60 years
    - 60-70 years
    - 70-80 years
    - 80+ years

2. How long ago were you diagnosed with Parkinson's disease?
    - 1-5 years ago
    - 5-10 years ago
    - 10-15 years ago
    - 15+ years ago

3. Please select the answer that best describes you:
    - I am receiving treatment with oral (carbidopa/levodopa) medication
    - I am receiving treatment with Duodopa® (levodopa/carbidopa intestinal gel)
    - I am receiving another treatment

4. Which of these symptoms is important to you in the management of your Parkinson's disease? Please click and drag each symptom to rank them in order from most important to least important.
    - "Off" times and dyskinesia
    - Tremors and rigidity
    - Choking and trouble swallowing
    - Bladder/bowel control
    - Altered speech
    - Changes in cognition and memory
    - Changes in mood
    - Sleep issues and fatigue
    - Impaired balance and worry about falling

5. Which treatment outcomes are most important to you? Please click and drag each outcome to rank them in order from most important.
    - Reduced worry about "Off" times and dyskinesia
    - Reduced tremors, rigidity, and risk of falls

- Ability to perform activities of daily living e.g. cooking or housework
- Ability to communicate with family and friends e.g. over the phone or via video call
- Increased independence
- Ability to participate in leisure and social activities
- Improved mental health and emotional wellbeing
- Increased sense of hope for the future
- Ability to connect with others in social settings

If "I am receiving another treatment" is selected:
Please describe the Parkinson's disease treatment you are currently receiving.

If "I am receiving treatment with Duodopa® (levodopa/carbidopa intestinal gel)" is selected:

Which of the following outcomes did you experience after you commenced treatment with Duodopa® (levodopa/carbidopa intestinal gel)?

- Reduced worry about "Off" times and dyskinesia
- Reduced tremors, rigidity, and risk of falls
- Ability to perform activities of daily living e.g. cooking or housework
- Ability to communicate with family and friends e.g. over the phone or via video call
- Increased independence
- Ability to participate in leisure and social activities
- Improved mental health and emotional wellbeing
- Increased sense of hope for the future
- Ability to connect with others in social settings

How much did your commencing treatment with Duodopa® (levodopa/carbidopa intestinal gel) influence this outcome?

	Not at all	A little	A moderate amount	A lot	Completely
Reduced worry about "Off" times and dyskinesia	O	O	O	O	O
Reduced tremors, rigidity, and risk of falls	O	O	O	O	O
Ability to perform activities of daily living e.g. cooking or housework	O	O	O	O	O
Ability to communicate with family and friends e.g. over the phone or via video call	O	O	O	O	O
Increased independence	O	O	O	O	O
Ability to participate in leisure and social activities	O	O	O	O	O

	Not at all	A little	A moderate amount	A lot	Completely
Improved mental health and emotional wellbeing	O	O	O	O	O
Increased sense of hope for the future	O	O	O	O	O
Ability to connect with others in social settings	O	O	O	O	O

Is there anything else about your experience with Duodopa® (levodopa/carbidopa intestinal gel) that has impacted your life?

6. Is there anything else about your experience with Parkinson's disease you would like to share?

SURVEY FOR PARTNERS OF PEOPLE LIVING WITH PD

1. How old are you?
    - <50 years
    - 50-60 years
    - 60-70 years
    - 70-80 years
    - 80+ years

2. How long ago was your partner diagnosed with Parkinson's disease?
    - 1-5 years ago
    - 5-10 years ago
    - 10-15 years ago
    - 15+ years ago

3. Please select the answer that best describes your partner living with Parkinson's disease.
    - My partner is receiving treatment with oral (carbidopa/levodopa) medication
    - My partner is receiving treatment with Duodopa® (levodopa/carbidopa intestinal gel)
    - My partner is receiving another treatment

4. Which of these symptoms is most important to you in the management of your partner's Parkinson's disease? Please click and drag each symptom to rank them in order from most important to least important.
    - "Off" times and dyskinesia
    - Tremors and rigidity
    - Bladder/bowel control
    - Altered speech
    - Changes in cognition and memory

- Changes in mood
- Sleep issues and fatigue
- Impaired balance and worry about falling

5. Which of the following outcomes is most important to you? Please click and drag each outcome to rank them in order from most important to least important.
    - Reduced worry about whether my partner has taken their medication
    - Increased personal time
    - Ability to spend time with family and friends
    - Ability to participate in leisure activities and friends
    - Reduced sleep disturbances
    - Ability to connect with others in social settings
    - Increased sense of hope for the future

If "I am receiving another treatment" is selected:
Please describe the Parkinson's disease treatment your partner is currently receiving.

If "I am receiving treatment with Duodopa® (levodopa/carbidopa intestinal gel)" is selected:

Which of the following outcomes did you experience after your partner commenced treatment with Duodopa® (levodopa/carbidopa intestinal gel)?

- Reduced worry about whether my partner has taken their medication
- Reduced need to support and provide care for partner
- Increased personal time
- Ability to spend time with family and friends
- Ability to participate in leisure activities with partner
- Reduced sleep disturbances
- Ability to connect with others in social settings
- Increased sense of hope for the future

	Not at all	A little	A moderate amount	A lot	Completely
Reduced worry about whether my partner has taken their medication	O	O	O	O	O
Reduced need to support and provide care for partner	O	O	O	O	O
Increased personal time	O	O	O	O	O
Ability to spend time with family and friends	O	O	O	O	O

	Not at all	A little	A moderate amount	A lot	Completely
Ability to participate in leisure activities with partner	O	O	O	O	O
Reduced sleep disturbances	O	O	O	O	O
Ability to connect with others in social settings	O	O	O	O	O
Increased sense of hope for the future	O	O	O	O	O

Is there anything else about your partner's experience with Parkinson's disease that you would like to share?

6. Is there anything else about your partner's experience with Parkinson's disease that you would like to share?

APPENDIX IV PDQ-39 QUESTIONNAIRE

Due to having Parkinson's disease, how often during the last month have you...

MOBILITY	
1.	Had difficulty doing the leisure activities which you would like to do?
2.	Had difficulty looking after your home, e.g. DIY, housework, cooking?
3.	Had difficulty carrying bags of shopping?
4.	Had problems walking half a mile?
5.	Had problems walking 100 yards?
6.	Had problems getting around the house as easily as you would like?
7.	Had difficulty getting around in public?
8.	Needed someone else to accompany you when you went out?
9.	Felt frightened or worried about falling over in public?
10.	Been confined to the house more than you would like?
ACTIVITIES OF DAILY LIVING (ADL)	
11.	Had difficulty washing yourself?
12.	Had difficulty dressing yourself?
13.	Had problems doing up your shoe laces?
14.	Had problem writing clearly?
15.	Had difficulty cutting up your food?
16.	Had difficulty holding a drink without spilling it?
EMOTIONAL WELLBEING	
17.	Felt depressed?
18.	Felt isolated or lonely?
19.	Felt weepy or tearful?
20.	Felt angry or bitter?
21.	Felt anxious?
22.	Felt worried about your future?
STIGMA	
23.	Felt you had to conceal your Parkinson's from people?
24.	Avoided situations which involve earing or drinking in public?
25.	Felt embarrassed in public due to having Parkinson's disease?
26.	Felt worried by other people's reaction to you?
SOCIAL SUPPORT	
27.	Had problems with your close personal relationships?
28.	Lacked support in the ways you need from your spouse or partner?
29.	Lacked support in the ways you need from your family or friends?
COGNITION	
30.	Unexpectedly fallen asleep during the day?
31.	Had problems with your concentration, e.g. when reading or watching TV?
32.	Felt your memory was bad?
33.	Had distressing dreams or hallucinations?
COMMUNICATION	
34.	Had difficulty with your speech?

35. Felt unable to communicate with people properly?
36. Felt ignored by people?
BODILY DISCOMFORT
37. Had painful muscle cramps or spasms?
38. Had aches and pains in your joints or body?
39. Felt unpleasantly hot or cold?

Source: (34)

APPENDIX V FINANCIAL PROXIES

Valuing outcomes involves the monetisation of non-financial outcomes by assigning them appropriate financial proxies. Financial proxies should reflect the value of the change in the outcome from the perspective of the stakeholder experiencing the outcome. Given that many outcomes are non-financial in nature, this process requires the judgement of the authors to decide – based on an understanding of the stakeholders and their experience of the outcomes – what values are appropriate. To ensure the perspective of all stakeholders were accurately captured, assumptions were validated with secondary research.

Three main techniques have been used to value outcomes:

- Economic valuation – for economic outcomes, the financial value represents the actual savings/cost to the stakeholder. For example, reduced out-of-pocket costs for aids and modifications was valued based on the average amount of money patients can avoid paying for aids such as walkers, wheelchairs, grab bars, and railings per year if access to levodopa-based DATs became more readily available.
- Willingness to pay/accept – a willingness to pay study explicitly asks stakeholders how much value they place on a certain outcome. For example, the average annual cost of a family holiday represents the value partners of people living with PD are willing to pay for increased hope for the future as during consultation, partners of people living with PD spoke of how their ability to plan for the future and hopes for retirement were impacted by their partner's PD diagnosis. After their partner commenced treatment with a levodopa-based DAT, people felt that they were more able to partake in leisure activities with their partner and their hopes for their future retirement increased.
- Replacement valuation – the cost of another service(s) and/or good(s) that would achieve the same amount of change. For example, reduced worrying from children with parents living with PD was valued using the cost of a nursing home. During stakeholder consolation, people living with PD noted that their children "told us to go to a retirement village" as they were worried about their ability to take care of themselves Whilst living at home. Aged care homes provide support and accommodation for people who are unable to continue living independently in their own homes, who need ongoing help with everyday tasks, and who require regular medical care. As such, people living with aPD often transition to aged care homes as their symptoms progress and/or they are no longer able to safely remain at home.

The financial proxies, valuation approach and rationale for each outcome are outlined in Table 24.

Table 24 Financial Proxies

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	Economic valuation	$1,539.80	As PD advances, people experience worsening symptoms affecting their mobility. This increases their dependence on aids and modifications (including walkers, wheelchairs, grab bars, railings) and so too increases associated costs. The average annual costs associated with such aids and modifications are detailed in the Deloitte Access Economics *Living with Parkinson's Disease* report (Table 7.2), stratified by Hoehn and Yahr PD stages (32). The M15-736 clinical trial data demonstrated that upon commencing treatment with a levodopa-based DAT, people living with aPD experience an improvement in their motor symptoms, improving their mobility and reducing reliance on aids and modifications (35). If access to levodopa-based DATs became more readily available, people living with PD may commence treatment from the earlier stages of PD, thereby reducing their experience of worsening PD symptoms. The difference in average annual out-of-pocket cost between Hoehn and Yahr Stage II (when patients commence treatment) and Hoehn and Yahr Stage III-V was used to represent this avoided cost. This value was then adjusted to consider inflation from 2011.
	Increased connection to family and friends	Willingness to pay/accept	$9,625.48	The average weekly household spending for people aged 45 years and above for recreation was used as the proxy for increased social connection. This reflects how much people are willing to pay to maintain their social connection by spending on recreation (including leisure and social activities such as dining out) (36). To determine the average annual household spending on recreation, the average weekly household expenditure was multiplied by the number of weeks per year and adjusted to account for inflation from 2015-16.
	Increased independence	Replacement valuation	$53,268.10	In the absence of treatment with a levodopa-based DAT, people may experience worsening symptoms as their PD advances, affecting their ability to perform activities of daily living independently. In some cases, people living with aPD may require additional support within their home, including tasks relating to hygiene, food preparation, and nursing. The purpose of formal care programs such as Home Care Packages (HCP) is to help older Australians receive access to such supports within their own homes. As such, these programs facilitate maintained independence as they aim to provide people the support needed to remain living at home. It is expected that people living with aPD will require a high level of care. High Care Needs (Level 4) packages include 12-14 hours of care per week, or up to 2 hours per day (37). As such, the annual cost of a Level 4 HCP was used to represent the value of increased independence.

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
	Increased ability to remain in the workforce	Economic valuation	$42,354.00	Whilst many people living with PD continue to work for many years after their diagnosis, for some their condition makes it difficult to continue working at the same capacity. As such, it was assumed that people living with aPD who are of working age would continue to work part-time. During stakeholder consultation, people living with aPD spoke of the importance of a maintained income stream so they could remain financially supported and not worry about treatment costs etc. This was supported during consultation with nurses and patient advocacy organisations. As such, the median annual wage in Australia was used as the financial proxy for this outcome to represent the value of remaining in the workforce. To calculate the part-time equivalence, it was assumed that 50% of people living with aPD would move from full-time to part-time work. Assuming majority of people living with aPD who are of working age are between 45-64 years, the median weekly wage for this age group in Australia was calculated based on census data (38). The median weekly wage for people aged 45-64 years in Australia was then multiplied by the number of weeks in a year to determine the median annual wage.
	Increased hope for the future	Willingness to pay/accept	$5,702.00	During consultation, people living with aPD spoke of how their ability to plan for the future and hopes for retirement were impacted by their PD diagnosis. This was supported by secondary research. After commencing treatment with a levodopa-based DAT, people living with aPD felt that they were able to continue making travel plans, as they felt more in control of their disease and were less worried about their future disease status. A family holiday represents this hope for their future and retirement plans, and as such the average annual cost of a family holiday was used as the proxy for this outcome (39).
	Increased burden of discomfort	Willingness to pay/accept	-$2,186.02	Upon commencing treatment with levodopa-based DATs, people living with aPD experience increased discomfort because of the infusion site, pump, and tube. This results in a need to adjust attire to carry and/or conceal the infusion site, pump, and tube. During consultation, people living with aPD explained they purchased new clothing to accommodate the infusion site, pump, and tube. As such, the average household spending on clothing and footwear was used as the proxy for increased discomfort. Weekly data extracted from the Household Expenditure Summary (2015) was first multiplied by 52 and adjusted to account for inflation to calculate the average annual household spending on clothing and footwear for people aged 45 years and above (36). This valuation is negative to account for the fact this this is a negative outcome for stakeholders.

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
Partners of people living with Parkinson's disease	Reduced worry about partner's health	Replacement valuation	$48,535.77	Aged care homes provide support and accommodation for people who are unable to continue living independently in their own homes, who need ongoing help with everyday tasks, and who require regular medical care. They provide accommodation and personal care 24 hours a day, as well as access to nursing and general health care services. People living with aPD often require such care in the later stages of their disease due to functional impairment, drug complications, dementia, and incontinence. For their partners and primary caregivers, these symptoms make it so that they are no longer able to safely care for the person living with aPD at home. As such, care provided by aged care homes may be required to reduce their burden of care and worry about their partner's health (40). During consultation, a partner of a person who had passed away due to aPD validated this, explaining they needed the support of aged care homes to safely care for their partner and reduce their worry about management of their partner's PD. Therefore, the average cost of an aged care home was used as a financial proxy for reduced worry about partner's health. The average aged care home costs and fees in Australia was calculated by adding the average of the Daily Accommodation Payment (DAP) and Basic Daily Fee and multiplying by the number of days per year. A Refundable Accommodation Deposit (RAD) is a lump sum payment to secure a room in an aged care home. The average RAD across Australia is $440,000.00. The RAD is fully refundable once an individual leaves the aged care facility. If an individual is not able to pay a RAD, they instead pay a DAP (41). The Multiple Permissible Interest Rate (MPIR) is a Government-set interest rate used to calculate the DAP. The DAP is based on the price to secure a room in an aged care facility. It is used to determine equivalence between a daily payment and a refundable lump sum payment. The current MPIR is 6.31% (28). The average DAP was calculated by multiplying the average RAD by the current MPIR and dividing by the number of days per year. The Basic Daily Fee is paid by every individual living in aged care homes for the day-to-day services they will receive such as food and beverage, cleaning services, and facilities management. The Basic Daily Fee is set at 85% of the single person rate of the basic age pension. Based on current rates, the Basic Daily Fee is $56.87 per day (42).

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
	Increased social connection	Willingness to pay/accept	$9,625.48	During consultation with stakeholders, it was clear that people living with aPD are "*more dependent on* [their partner] *than they usually would be*" due to their PD symptoms. However, with access to treatment with a levodopa-based DAT, partners of people living with aPD experienced reduced carer burden, increasing their personal time, and time spent with family and friends. In turn, this provides partners of people living with aPD the freedom to maintain their social connections including participating in recreational activities. As such, household spending for people aged 45 years and above on recreation was used as a financial proxy for increased social connection for partners of people living with aPD (36). To determine the average annual household spending on recreation, the average weekly household expenditure was multiplied by the number of weeks per year (52) and adjusted to account for inflation from 2015-16.
	Increased carer wellbeing	Replacement valuation	$22,330.35	The symptoms of advancing PD pose a significant challenge to partners of people living with aPD, resulting in a substantial impact on an individual's physical, emotional, and mental wellbeing. Survey responses from partners of people living with PD evidenced this, explaining that "*everyday feels like Groundhog Day*" and "*it's really hard to live out of the* [PD] *sphere*". Acknowledging these challenges, the financial proxy for increased wellbeing for partners of people living with aPD was access to respite care. Respite care provides temporary care for people living with aPD, relieving carers from their caring responsibilities for short periods of time and providing support where possible. The Australian Government provides access to up to 63 days of respite care per year. Whilst this limit is based on residential respite care, it is assumed that a similar level of care would be required for community-based care (43). Assuming that a day of respite care provided in the community would cover a full working day, the hourly cost of a Mable support worker who can provide respite care was used to estimate the cost of 63 days of respite care (44). This is considered a conservative estimate, as one partner of a person living with aPD noted *"she came for three hours, twice a week. If she could have stayed a night, it would have been wonderful... six hours isn't a lot when it's 24/7."*

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
	Increased hope for the future	Willingness to pay/accept	$5,072.00	During consultation and supported by secondary research, partners of people living with aPD spoke of how their ability to plan for the future and hopes for retirement were impacted by their partner's PD diagnosis. After their partner commenced treatment with a levodopa-based DAT, people felt that they were more able to partake in leisure activities with their partner and their hopes for their future retirement increased. People noted the ability to travel with their partner as something they looked forward to. A family holiday represents this hope for their future and retirement plans, and as such the average annual cost of a family holiday was used as a proxy for this outcome (39).
	Increased ability to remain in the workforce	Economic valuation	$84,708.00	When people living with aPD have access to treatment with a DAT, their partner would be able to remain at work full-time, as their need for care is reduced. As such, it was assumed that partners of people living with aPD who are of working age would continue to work full-time and therefore receive a consistent income stream During stakeholder consultation, partners of people living with aPD spoke of the importance of a maintained income stream so they could remain financially supported and not worry about treatment costs etc. As such, the median annual wage in Australia was used as the financial proxy for this outcome to represent the value of remaining in the workforce. To calculate the median annual wage for partners of people living with aPD, it was assumed that the majority of those who are of working age would be aged between 45-64 years. As such, the median weekly wage for this age group in Australia was calculated based on census data (38). This weekly wage was multiplied by the number of weeks in a year to determine the annual wage.
Children of people living with Parkinson's disease	Increased connection to parent	Economic valuation	$972.00	During stakeholder consultation, people living with aPD explained the importance of being able to communicate over the phone as a way to remain connected to their family and friends, including their children. As such, the average cost of a monthly phone-on-a-plan mobile phone contract in Australia was used as the proxy for increased connection to parent (45).

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
	Reduced worry about parent	Replacement valuation	$48,535.77	Aged care homes provide support and accommodation for people who are unable to continue living independently in their own homes, who need ongoing help with everyday tasks, and who require regular medical care. They provide accommodation and personal care 24 hours a day, as well as access to nursing and general health care services. As such, people living with aPD often transition to aged care homes as their symptoms progress and/or they are no longer able to safely remain at home (40). During stakeholder consultation, people living with aPD noted their children "*told us to go to a retirement village*" as they were worried about their ability to care for themselves whilst living with aPD at home. Stakeholders explained much of their children's worry was related to their aPD symptoms, including a decreased ability to perform ADL and an increased risk of falls. To reduce this worry, children encouraged their parents living with aPD to consider aged care homes, where appropriate care and support would be provided. As such, the cost of a aged care homes is used as the proxy for reduced worry about parent's health. The average aged care home costs and fees in Australia was calculated by adding the average of the Daily Accommodation Payment (DAP) and Basic Daily Fee and multiplying by the number of days per year. A Refundable Accommodation Deposit (RAD) is a lump sum payment to secure a room in an aged care home. The average RAD across Australia is $440,000.00. The RAD is fully refundable once an individual leaves the aged care facility. If an individual is not able to pay a RAD, they instead pay a DAP (41). The Multiple Permissible Interest Rate (MPIR) is a Government-set interest rate used to calculate the DAP. The DAP is based on the price to secure a room in an aged care facility. It is used to determine equivalence between a daily payment and a refundable lump sum payment. The current MPIR is 6.31% (28)The average DAP was calculated by multiplying the average RAD by the current MPIR and dividing by the number of days per year. The Basic Daily Fee is paid by every individual living in aged care homes for the day-to-day services they will receive such as food and beverage, cleaning services, and facilities management. The Basic Daily Fee is set at 85% of the single person rate of the basic age pension. Based on current rates, the Basic Daily Fee is $56.87 per day (42).

Stakeholders	Outcome	Valuation approach	Value of financial proxy (annual)	Rationale
Australian Government	Avoided cost of healthcare services	Economic valuation	$26,102,780.40	The average health resource utilisation costs related to both mild PD (Hoehn and Yahr Stage I - II) and moderate PD (Hoehn and Yahr Stage III – IV) from a health system perspective was calculated by adding the PD-related costs, including hospitalisations, hospital transport, medical services, and allied health (31). The cost of pharmaceuticals was excluded from this calculation to avoid double counting. Upon commencing treatment with a levodopa-based DAT, people living with aPD experience an improvement in their overall PD symptoms, reducing their likelihood of requiring hospitalisation. By investing in improved access to levodopa-based DATs, people with aPD will commence treatment in the earlier stages of PD (corresponding to Hoehn and Yahr Stage II at baseline) (31). Based on data from the M15-736 clinical trial, 69% of people living with aPD will experience an improvement in their overall PD symptoms, thereby reducing their health resource utilisation associated with hospitalisation and other costs (35). The difference in average costs of healthcare services and utilisation between mild and moderate-severe PD was used to calculate the avoided cost. This total was then multiplied by the proportion of people living with PD receiving treatment with a levodopa-based DAT expected to experience an overall improvement in PD symptoms and adjusted to account for inflation.
	Avoided cost of welfare services and support payments	Economic valuation	$4,464,415.61	With an increased ability to remain in the workforce, both people living with aPD and their partners have a lesser need for welfare services and support payments, reducing the cost of welfare services and support payments (46). Payment rates for the Disability Support Pension (DSP) for people living with aPD are currently set at $706.20 per fortnight. Payment rates for the Carer Payment are currently set at $706.20 (47). Based on M15-736 clinical trial data and calculations of effect size, 12% of people living with aPD who receive treatment with a levodopa-based DAT are of working age (45-64 years) and are expected to experience an improvement in overall PD symptoms, increasing their ability to remain in the workforce (35). Similarly, it was expected that the proportion of partners of people living with aPD able to remain in the workforce is equal to the proportion of working aged people living with aPD who experience an improvement in their overall symptoms. As such, the avoided cost of welfare services and support payments was calculated as the yearly cost of a DSP for the number of people living with aPD that are able to remain in the workforce plus the annual cost of a Carer Payment for partners of people living with aPD who are able to remain in the workforce.

APPENDIX VI PROPORTION OF STAKEHOLDERS IMPACTED

It is not assumed that all stakeholders included in the model experience every outcome, nor experience outcomes in a similar way. For example, not every person living with aPD will experience increased independence when they commence treatment with a levodopa-based DAT. However, it is not expected that people living with aPD will experience *reduced* independence (i.e. the negative opposing outcome) as a result of treatment with a levodopa-based DAT. Analysis of the M15-736 clinical trial data found that although some people in the trial did experience declines in their quality of life as measured by the PDQ-39, these declines were greater in the participants who remained on oral therapy. As such, this analysis conservatively considers that those who did not experience an improvement in an outcome experienced no change.

For this SROI, the proportion of people living with aPD experiencing an outcome was calculated using M15-736 clinical trial data (35) and calculations of effect size (Cohen's *d*).

For stakeholders who were not directly engaged in the clinical trial (partners and children of people living with aPD), a specific assumption was made regarding the proportion of stakeholders impacted, reflecting the calculations based on M15-736 clinical trial data. These assumptions are outlined for each outcome in Table 25 below.

As each PD journey is unique, variation in the proportion of stakeholder experiencing each outcome is expected. To ensure the results accurately capture the true experience of stakeholders, inputs were verified in follow up interviews with people living with aPD, their partners, and nurses.

The proportion of stakeholders impacted and rationale for each outcome are outlined in Table 25.

Table 25 Proportion of stakeholders impacted

Stakeholders	Outcome	Proportion	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	69%	Based on the M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 69% of participants who receive treatment with a DAT are expected to experience an improvement in their mobility compared to patients who remain on oral medication.
	Increased connection to family and friends	73	Based on M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 73% of participants who receive treatment with a levodopa-based DAT are expected to experience an increased social connection, compared to patients who remain on oral medication.
	Increased independence	62%	Based on M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 62% of participants who receive treatment with a levodopa-based DAT are expected to experience an improvement in their ability to perform ADL, compared to patients who remain on oral medication.

Stakeholders	Outcome	Proportion	Rationale
	Increased ability to remain in the workforce	12%	Based on clinical trial data and calculations of effect size (Cohen's *d*), 69% of participants who receive treatment with a levodopa-based DAT are expected to experience an improvement in their overall PD symptoms, increasing their ability to remain in the workforce. Additionally, 18% of people living with aPD are of working age. This rate has been multiplied by the proportion of people living with aPD who experience an improvement in their overall PD symptoms to account for the PD working age population to obtain the proportion of 12%.
	Increased hope for the future	69%	Based on M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 69% of participants who receive treatment with a levodopa-based DAT are expected to experience increased hope for the future, compared to patients who remain on oral medication.
	Increased burden of discomfort	100%	Based on interviews with N=4 people living with PD and N=2 nurses who care for people living with aPD, all patients who initiate treatment with a DAT will experience some level of discomfort associated with the pump at first.
Partners of people living with Parkinson's disease	Reduced worry about partner's health	62%	It is expected that people who experience reduced worry about their partner's health is expected to equal the proportion of people living with aPD who experience increased independence. Based on M15-736 clinical trial data and calculations of effect size (Cohen's d), 62% of people living with aPD who receive treatment with a levodopa-based DAT experience an increase in independence compared to people who remain on oral medication.
	Increased social connection	62%	It is expected that partners who experience increased social connection will be equal to the proportion of people living with aPD who experience increased independence as a result of treatment with levodopa-based DATs. Based on M15-736 clinical trial data and calculations of effect size (Cohen's d), 62% of people living with aPD who receive treatment with a levodopa-based DAT are expected to experience an increase in independence compared to people who remain on oral medication.
	Increased carer wellbeing	69%	As an increase in carer wellbeing is influenced by many aspects of PD, it is expected that the proportion of partners who experience improved wellbeing equals the proportion of people living with aPD who experience overall improvement in PD symptoms. Based on M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 69% of people living with aPD who receive treatment with a levodopa-based DAT are expected to experience an improvement in overall PD symptoms compared to people who remain on oral medication.

Stakeholders	Outcome	Proportion	Rationale
	Increased hope for the future	73%	It is expected that partners who experience increased hope for the future equals the proportion of people living with aPD who experience an increased social connection. Based on M15-736 clinical trial data and calculations of effect size (Cohen's d), 73% of people living with aPD who receive treatment with a levodopa-based DAT are expected to experience an increased desire and ability to participate in leisure and social activities compared to people who remain on oral medication.
	Increased ability to remain in the workforce	12%	It is expected that partners who experience an increased ability to remain in the workforce equals the proportion of working aged people living with aPD who experience an improvement in their overall PD symptoms. Based on clinical trial data and calculations of effect size (Cohen's *d*), 69% of people living with aPD who receive treatment with a levodopa-based DAT are expected to experience an improvement in overall PD symptoms, increasing their ability to remain in the workforce. Additionally, 18% of people living with aPD are of working age and it is assumed that the same rate would apply to their partners. The proportion of partners who would be of working age has been multiplied by the proportion of people living with aPD who experience an improvement in their overall PD symptoms to calculate the proportion of partners who would be able to remain in the workforce.
Children of people living with Parkinson's disease	Increased connection to parent	62%	It is expected that children of people living with aPD who experience an increased connection to their parent equals the proportion of people living with aPD who experience an increased connection to family. Based on M15-736 clinical trial data and calculations of effect size (Cohen's *d*), 62% of people living with aPD who receive treatment with a levodopa-based DAT are expected to experience an increased connection to family compared to people who remain on oral medication.
	Reduced worry about parent	69%	It is expected that children who experience reduced worry about their parent's health as a result of treatment with levodopa-based DATs is expected to equal the proportion of people living with aPD who experience an overall improvement in PD symptoms. Based on M15-736 clinical trial and calculations of effect size (Cohen's *d*), 69% of people living with aPD receive who receive a treatment with a levodopa-based DAT experience an improvement in overall PD symptoms compared to people who remain on oral medication.
Australian Government	Avoided cost of healthcare services	100%	The Australian Government represents one stakeholder and is always impacted by financial outcomes, therefore the proportion is assumed to be 100%.
	Avoided cost of welfare services and support payments	100%	The Australian Government represents one stakeholder and is always impacted by financial outcomes, therefore the proportion is assumed to be 100%.

APPENDIX VII IMPORTANCE

A weight representing importance was applied to each valuation to account for the degree to which the outcome matters to the stakeholder. Each financial proxy is weighted by importance determined based on the stakeholder consultation including surveys.

For each outcome (excluding children of people living with PD outcomes and the Australian Government), stakeholders were asked to rank the treatment outcomes most important to them. Rankings for each outcome were then ordered and allocated an importance weighting. The weighted average importance of outcomes was then calculated.

The importance weighting and rationale for each outcome is outlined in Table 26.

Table 26 Importance weighting

Stakeholders	Outcome	Importance	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	100%	As the outcome is already financial in nature, the importance is 100%.
	Increased connection to family and friends	81%	Based on survey data (N=57 people living with PD). The weighted average importance of outcomes linked to increased social connection, including ability to connect with others in social settings and ability to participate in leisure activities without worrying about PD symptoms was calculated.
	Increased independence	93%	Based on survey data (N=57 people living with PD). The weighted average importance of outcomes linked to increased independence, including reduced tremors, rigidity, and risk of falls and ability to perform ADL was calculated.
	Increased ability to remain in the workforce	100%	As the outcome is already financial in nature, the importance is 100%.
	Increased hope for the future	73%	Based on survey data (N=57 people living with PD). The weighted average importance of outcomes linked to increased hope for the future, including feeling more in control of disease and reduced worry about future health was calculated.
	Increased burden of discomfort	30%	Based on secondary research into insulin pumps and continuous glucose monitors for patients with diabetes. "*Do not like diabetes devices on my body*" was reported as a barrier for 30% of people. In the absence of data specific to people living with aPD, this 30% was used as the importance of discomfort. It is expected that discomfort will be significantly less important than the improvement in overall PD symptoms. During stakeholder consultation, one nurse noted "*the benefits outweigh having to wear a device*".
Partners of people living with Parkinson's disease	Reduced worry about partner's health	90%	Based on survey data (N=26 partners of people living with PD). The weighted average importance of outcomes linked to reduced worry about partner's health, including reduced carer burden and worry about whether their partner has taken their medication was calculated.

Stakeholders	Outcome	Importance	Rationale
	Increased social connection	80%	Based on survey data (N=26 partners of people living with PD). The weighted average importance of outcomes linked to increased social connection, including reduced carer burden, increase in personal time, and time spent with family and friends was calculated.
	Increased carer wellbeing	82%	Based on survey data (N=26 partners of people living with PD). The weight average importance of outcomes linked to increased carer wellbeing, including fewer sleep disturbances, and increased personal time as a result of reduced carer burden was calculated.
	Increased hope for the future	88%	Based on survey data (N=26 partners of people living with PD). The weighted average importance of outcomes linked to an increased hope for the future, including an increased ability to participate in leisure activities with their partner was calculated.
	Increased ability to remain in the workforce	100%	As the outcome is already financial in nature, the importance is 100%.
Children of people living with Parkinson's disease	Increased connection to parent	65%	Based on survey data (N=57 people living with PD). The weighted average importance of outcomes linked to increased connection to family, including ability to communicate and ability to connect with others was calculated. During stakeholder consultation, people living with aPD provided examples of how they were able to connect to family as a result of access to levodopa-based DATs. They explained they were able to communicate with their children over the phone as their speech improved and had a greater ability to spend time with their children as a result of reduced tremors, rigidity, and risk of falls. As such, it is assumed the importance of an increased connection to a parent living with aPD is equal to the importance of an increased connection to family for people living with aPD.
	Reduced worry about parent	90%	Based on survey data (N=26 partners of people living with PD). The weight average importance of outcomes linked to reduced worry about partner's health, including reduced carer burden and worry about whether their partner has taken their medication was calculated. As immediate family members, children of people living with aPD would value reduced worry about a parent's health. It is assumed that the importance of this outcome to children is equal to the importance of reduced worry for partners of people living with aPD.
Australian Government	Avoided cost of healthcare services	100%	As the outcome is financial in nature, the importance is assumed to be 100%.
	Avoided cost of welfare services and support payments	100%	As the outcome is financial in nature, the importance is assumed to be 100%.

APPENDIX VIII DURATION

Duration details the length of time the outcome is expected to last (in years). During initial consultation with AbbVie Pty Ltd, it was decided that the SROI would be a forecast analysis with a time horizon of three years. A three-year time period limits uncertainty associated with reduced clinical effectiveness over time as for each stakeholder, the duration of the outcomes are expected to continue past the three years. It also captures the short- and medium-term changes in health and social impacts expected to result from treatment with a levodopa-based DAT.

For each stakeholder outcome (except "Increased discomfort for people living with aPD"), it is assumed that the outcome will be experienced by at least some people (or partners/children of people) with aPD for the duration of the forecast. Whilst not all people living with aPD will experience the specified outcome for the entire duration, this is accounted for by the drop off rate.

As many of the stakeholders consulted during this SROI did not have direct experience with a levodopa-based DAT, they were unable to inform estimates of duration. Of those stakeholders who did have experience, most had been receiving treatment for a relatively short period of time, as many were receiving treatment as part of a clinical trial for Vyalev®. As such, secondary research was used to inform estimates of duration. Outcomes from a prospective, real-world study of Duodopa® (the DUOGLOBE study) found that people receiving treatment with levodopa-based DAT continue to experience statistically significant improvements in "Off" time and QoL up to 36 months after commencing treatment (20). As such, the assumption that outcomes will last for at least 3 years for some participants is considered reasonable.

The duration and rationale for each outcome is outlined in Table 27.

Table 27 Duration

Stakeholders	Outcome	Duration	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	3 years	It is assumed that this outcome will be experienced by at least some people with aPD for the duration of the forecast. Whilst not all people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased connection to family and friends	3 years	It is assumed that this outcome will be experienced by at least some people with aPD for the duration of the forecast. Whilst not all people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased independence	3 years	It is assumed that this outcome will be experienced by at least some people with aPD for the duration of the forecast. Whilst not all people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased ability to remain in the workforce	3 years	It is assumed that this outcome will be experienced by at least some people with aPD for the duration of the forecast. Whilst not all people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased hope for the future	3 years	It is assumed that this outcome will be experienced by at least some people with aPD for the duration of the forecast. Whilst not all people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.

Stakeholders	Outcome	Duration	Rationale
	Increased burden of discomfort	1 year	Based on interviews with N=4 people living with PD and N=2 nurses who care for people living with PD, discomfort associated with the pump is temporary. People living with aPD adapt to the new infusion site, pump, and tube by purchasing different clothes or a bag in which to carry the device. Eventually, the infusion site, pump, and tube simply become part of their usual routine. This is supported by secondary research, where people stated that they "*got used to carrying the pump*". As such, it was assumed that increased discomfort would not last the entire three-year time horizon.
Partners of people living with Parkinson's disease	Reduced worry about partner's health	3 years	It is assumed that this outcome will be experienced by at least some partners of people living with aPD for the duration of the forecast. Whilst not all partners of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased social connection	3 years	It is assumed that this outcome will be experienced by at least some partners of people living with aPD for the duration of the forecast. Whilst not all partners of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased carer wellbeing	3 years	It is assumed that this outcome will be experienced by at least some partners of people living with aPD for the duration of the forecast. Whilst not all partners of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased hope for the future	3 years	It is assumed that this outcome will be experienced by at least some partners of people living with aPD for the duration of the forecast. Whilst not all partners of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Increased ability to remain in the workforce	3 years	It is assumed that this outcome will be experienced by at least some partners of people living with aPD for the duration of the forecast. Whilst not all partners of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
Children of people living with Parkinson's disease	Increased connection to parent	3 years	It is assumed that this outcome will be experienced by at least some children of people living with aPD for the duration of the forecast. Whilst not all children of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.
	Reduced worry about parent	3 years	It is assumed that this outcome will be experienced by at least some children of people living with aPD for the duration of the forecast. Whilst not all children of people living with aPD will experience this outcome for the entire duration, this is accounted for by the drop off rate.

Stakeholders	Outcome	Duration	Rationale
Australian Government	Avoided cost of healthcare services	3 years	Whilst not all people living with aPD will experience an improvement in overall PD symptoms for the duration of the forecast, this is accounted for by the drop off rate. As such, it is assumed that the reduction in healthcare resource utilisation will last for the duration of the forecast.
	Avoided cost of welfare services and support payments	3 years	Whilst not all people living with aPD will experience an improvement in overall PD symptoms for the duration of the forecast, this is accounted for by the drop off rate. As such, it is assumed that the reduction in welfare services and support payments will last for the duration of the forecast.

APPENDIX IX ATTRIBUTION

Attribution accounts for contribution of external factors to the outcome in addition to levodopa-based DATs.

As many of the stakeholders consulted during this SROI did not have direct experience with a levodopa-based DAT, they were unable to inform estimates of attribution. As the outcomes included in this SROI are measured based on randomised controlled clinical trial evidence, any external factors which may have contributed to each outcome are likely to be balanced between treatment groups. For example, whilst PD social support groups may also contribute to feelings of social connection to family and friends, this is likely to be balanced between those who received treatment with a levodopa-based DAT and those who remained on treatment with oral levodopa. As such, there is expected to be no incremental impact of these external factors.

As per a previously assured SROI by ExtraBanca (48), attribution was considered on a Likert scale according to the authors' judgement. This was equally applied to access to treatment with levodopa-based DATs as shown in Table 28 below.

Table 28 Attribution transformation scale

Likert scale	The change is completely the result of the intervention	The change is almost entirely the result of the intervention	The change is largely the result of the intervention	The change is partly the result of the intervention	The change is only marginally the result of the intervention	The intervention has nothing to with the change
Scoring	0%	20%	40%	60%	80%	100%

The attribution value and rationale for each outcome is outlined in Table 29.

Table 29 Attribution filters

Stakeholders	Outcome	Attribution	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	0%	Change in this outcome was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in this outcome are expected to be completely due to treatment with a levodopa-based DAT. Thus, a reduction in OOP costs for aids and modifications is completely the result of treatment with a levodopa-based DAT.
	Increased connection to family and friends	0%	Change in this outcome was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in this outcome are expected to be completely due to treatment with a levodopa-based DAT. Thus, an improvement in social connection is completely the result of treatment with a levodopa-based DAT.

Stakeholders	Outcome	Attribution	Rationale
	Increased independence	0%	Change in this outcome was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in this outcome are expected to be completely due to treatment with a levodopa-based DAT. Thus, an improvement in independence is completely the result of treatment with a DAT.
	Increased ability to remain in the workforce	0%	Change in this outcome was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in this outcome are expected to be completely due to treatment with a levodopa-based DAT. Thus, an increased ability to remain in the workforce is completely the result of treatment with a DAT.
	Increased hope for the future	0%	Change in this outcome was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in this outcome are expected to be completely due to treatment with a levodopa-based DAT. Thus, increased hope for the future is completely the result of treatment with a DAT.
	Increased burden of discomfort	0%	Burden of discomfort with the infusion site, pump, and tube is entirely due to treatment with a levodopa-based DAT. It is reasonable to assume that no other factor contributes to this outcome.
Partners of people living with Parkinson's disease	Reduced worry about partner's health	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As such, a reduced worry about health for partners of people living with aPD is also expected to be completely due to their partner's treatment with levodopa-based DATs.
	Increased social connection	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As such, the increase in social connection for partners of people living with aPD is also expected to be completely due to their partner's treatment with levodopa-based DATs.

Stakeholders	Outcome	Attribution	Rationale
	Increased carer wellbeing	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As such, the increase in carer wellbeing for partners of people living with aPD is also expected to be completely due to their partner's treatment with levodopa-based DATs.
	Increased hope for the future	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As such, an increase in hope for the future for partners of people living with aPD is also expected to be completely due to their partner's treatment with levodopa-based DATs.
	Increased ability to remain in the workforce	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As such, an increased ability to remain in the workforce for partners of people living with aPD is also expected to be completely due to their partner's treatment with levodopa-based DATs.
Children of people living with Parkinson's disease	Increased connection to parent	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As increased connection to a parent living with aPD is directly linked to that parent's ability and desire to maintain connection, the increase in connection to parents is also expected to be completely due to their parents treatment with levodopa-based DATs.

Stakeholders	Outcome	Attribution	Rationale
	Reduced worry about parent	0%	The proportion of people who experience a change in this outcome was measured using the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes for people living with aPD is expected to be completely due to treatment with a levodopa-based DAT. As reduced worry is directly linked to improved overall symptoms for people living with aPD, reduced worry about parents is also expected to be completely due to treatment with levodopa-based DATs.
Australian Government	Avoided cost of healthcare services	0%	Change in overall PD symptoms was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material changes in health status (and therefore health resource utilisation) are expected to be completely due to treatment with a levodopa-based DAT.
	Avoided cost of welfare services and support payments	0%	Change in overall PD symptoms was measured by the M15-736 clinical trial data, where people living with aPD either initiated treatment with a levodopa-based DAT or remained on oral medication (35). As the two groups were balanced by virtue of the randomisation process, any material change in outcomes is expected to be completely due to treatment with a levodopa-based DAT. Similarly, an increased ability to remain in the workforce for partners of people living with aPD is also expected to be completely due to treatment with levodopa-based DATs. As such, any avoided cost of welfare services and support payments is expected to be completely due to treatment with a levodopa-based DAT.

APPENDIX X DEADWEIGHT

Deadweight accounts for a degree of change in the outcomes that would have occurred without the intervention. Deadweight is used to measure the amount of change that could have happened regardless of intervention. Therefore, to identify this figure, it is needed to consider how likely it is that outcomes would have occurred if people living with Parkinson's disease did not have access to levodopa-based DATs. Deadweight is difficult metric to capture via stakeholder questionnaires as personal experience often distorts these estimates. In addition, stakeholders often do not have the experience of the counterfactual (i.e. what would have happened if they did not experience the intervention), and are therefore unable to accurately assess deadweight. Therefore, the author's judgement (validated by secondary research) was used to estimate a deadweight value for each outcome.

For each outcome a six-point scale, extracted from a previously assured SROI report by ExtraBanca (48) (Table 30) was used to measure deadweight.

Table 30 Deadweight transformation scale: 'The change would "…" have occurred'

Likert scale	Never	Very probably not	Might	Probably	Very probably	Certainly
Scoring	0%	20%	40%	60%	80%	100%

The deadweight filter applied and rationale for each outcome is outlined in Table 31.

Table 31 Deadweight filters

Stakeholders	Outcome	Deadweight	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to mobilise. This leads to a greater reliance on aids and home modifications. As such, a reduction in the need for aids and modifications would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased connection to family and friends	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to participate in leisure and social activities. As such, an improvement in social connection would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased independence	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to perform ADL. This leads to a reduction in independence. As such, an improvement in independence would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased ability to remain in the workforce	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms, in turn limiting their ability to remain at work. As such, an increased ability to remain at work would *very probably not* occur without access to treatment with a levodopa-based DAT.

Stakeholders	Outcome	Deadweight	Rationale
	Increased hope for the future	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their worry about their future health status. As such, an increased sense of hope for the future would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased burden of discomfort	0%	Discomfort with the pump and tube is entirely due to treatment with a levodopa-based DAT. It is reasonable to assume that no other factor contributes to this outcome.
Partners of people living with Parkinson's disease	Reduced worry about partner's health	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to remain independent and perform ADL including taking oral medication. This leads to increased carer burden and worry about health for partners of people living with aPD. As such, a reduced worry about partner's health for partners of people living with aPD would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased social connection	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to remain independent. This leads to increased carer burden for partners of people living with aPD, reducing personal time and time spent with family and friends. As such, an increase in social connection for partners of people living with aPD would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased carer wellbeing	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to remain independent. This leads to increased carer burden for partners of people living with aPD, increasing sleep disturbances and reducing personal time or time spent with family and friends. As such, an increase in carer wellbeing for partners of people living with aPD would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased hope for the future	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their desire and ability to participate in leisure and social activities. This reduces hope for the future for partners of people living with aPD, as they are unable to participate in social and leisure activities with their partner. As such, an increase in hope for the future for partners of people living with aPD *would very probably not* occur without access to treatment with a levodopa-based DAT.
	Increased ability to remain in the workforce	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms. This leads to increased carer burden for partners of people living with aPD and increased sleep disturbances, reducing the ability to remain in the workforce. As such, an increase in the ability to stay in the workforce for partners of people living with aPD would *very probably not* occur without access to treatment with a levodopa-based DAT.

Stakeholders	Outcome	Deadweight	Rationale
Children of people living with Parkinson's disease	Increased connection to parent	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms impacting their ability to connect with family, including their children. As improved connection to parents is directly linked to people living with aPD's ability and desire to maintain this family connection, it would *very probably not* occur without access to treatment with a levodopa-based DAT.
	Reduced worry about parent	20%	PD is a progressive neurodegenerative disease. As PD advances people may experience worsening symptoms. This leads to increased worry about parents living with aPD. As reduced worry is directly linked to improved overall symptoms for people living with aPD, it would *very probably not* occur without access to treatment with a levodopa-based DAT.
Australian Government	Avoided cost of healthcare services	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms increasing the likelihood of PD-related hospitalisations. This increases costs associated with healthcare services. As such, avoided costs of healthcare services would *very probably not* occur without access to treatment with levodopa-based DATs.
	Avoided cost of welfare services and support payments	20%	PD is a progressive neurodegenerative disease. As PD advances, people may experience worsening symptoms. This reduces the ability of people living with aPD and their partners to remain in the workforce, increasing the need for welfare services and support payments. As such, avoided costs of welfare and support payments would *very probably not* occur without access to treatment with levodopa-based DATs.

APPENDIX XI DISPLACEMENT

Displacement is a measure of how much the outcome displaced other outcomes. Displacement is not considered highly relevant for this SROI, as the outcomes being created are not displacing other outcomes (e.g. increasing hope for people living with aPD does not require reducing hope elsewhere).

Displacement is a difficult metric to capture via stakeholder questionnaires as personal experience often distorts these estimates. As such, displacement was defined by considering results from the M15-736 clinical trial data (35).

The displacement value and rationale for each outcome is outlined in Table 32.

Table 32 Displacement filters

Stakeholders	Outcome	Displacement	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased connection to family and friends	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased independence	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased ability to remain in the workforce	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased hope for the future	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased burden of discomfort	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
Partners of people living with Parkinson's disease	Reduced worry about partner's health	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased social connection	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.

Stakeholders	Outcome	Displacement	Rationale
	Increased carer wellbeing	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased hope for the future	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Increased ability to remain in the workforce	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
Children of people living with Parkinson's disease	Increased connection to parent	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Reduced worry about parent	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
Australian Government	Avoided cost of healthcare services	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.
	Avoided cost of welfare services and support payments	0%	Treatment with a levodopa-based DAT is displacing treatment with oral medication only. As the M15-736 clinical trial data accounts for the incremental change between treatments, displacement is assumed to be 0%.

APPENDIX XII DROP OFF

Drop off rate is the reduction in the magnitude of an outcome or in the influence that the intervention will have on the outcome over time.

As many of the stakeholders consulted during this SROI did not have direct experience with a levodopa-based DAT, they were unable to inform estimates of duration. Of those stakeholders who did have experience, many had been receiving treatment for a relatively short period of time, as they were receiving treatment as part of a clinical trial for Vyalev®. As such trial-based measures were used. For the majority of the outcomes, drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd (35), as it was thought that patients would discontinue treatment if they were no long experiencing an effect. Additionally, 36-month follow up data from a real-world observational study was used to validate the duration and drop off of outcomes for people living with aPD (20). This study found that significant improvements in PD symptoms were sustained through to 36-months for both motor and non-motor symptoms. This study was used to validate the assumption that outcomes would be maintained in the absence of treatment discontinuation.

The drop off value and associated rationale for each outcome is outlined in Table 33.

Table 33 Drop off filters

Stakeholders	Outcome	Drop off	Rationale
People living with Parkinson's disease	Reduced out-of-pocket costs for aids and modifications	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd.
	Increased connection to family and friends	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd.
	Increased independence	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd.
	Increased ability to remain in the workforce	20%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd. Additionally, 27% of people in the 45-64 age group who are currently working full-time intend to retire in the next five years. This rate has been added to the discontinuation rate to account for people organically leaving the workforce.
	Increased hope for the future	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study data, and PBS data provided by AbbVie Pty Ltd.
	Increased burden of discomfort	0%	Not applicable. As the rate of drop off is only applied after year one, it is not applicable or relevant for this outcome which has a duration of 1 year.

Stakeholders	Outcome	Drop off	Rationale
Partners of people living with Parkinson's disease	Reduced worry about partner's health	16%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd. Additionally, an estimated 1.5% of people aged 65 years and above will experience an admission into permanent residential aged care each year. This rate has been added to the discontinuation rate to account for people transitioning to permanent residential aged care based exclusively on age.
	Increased social connection	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd.
	Increased carer wellbeing	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd.
	Increased hope for the future	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd.
	Increased ability to remain in the workforce	20%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd. Additionally, 27% of people in the 45-64 age group who are currently working full-time intend to retire in the next five years. This rate has been added to the discontinuation rate to account for people organically leaving the workforce.
Children of people living with Parkinson's disease	Increased connection to parent	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd.
	Reduced worry about parent	16%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd. Additionally, an estimated 1.5% of people aged 65 years and above will have an admission to permanent residential aged care each year. This rate has been added to the discontinuation rate to account for people transitioning to permanent residential aged care based exclusively on age.
Australian Government	Avoided cost of healthcare services	14%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial data, open label study, and PBS data provided by AbbVie Pty Ltd.
	Avoided cost of welfare services and support payments	20%	Drop off was calculated using treatment discontinuation rates from the M15-736 clinical trial, open label study, and PBS data provided by AbbVie Pty Ltd. Additionally, 27% of people in the 45-64 age group who are currently working full-time intend to retire in the next five years. This rate has been added to the discontinuation rate to account for people organically leaving the workforce.

APPENDIX XIII COST INPUTS

Australia has a public healthcare system funded by a federal Government, which provides free or subsidised access to listed medicines (via the PBS), and healthcare services and medical procedures (via the Medicare Benefits Schedule (MBS)).

The drug costs of Duodopa® and Vyalev® were used as inputs for the cost of medicines. This cost was separated into PBS costs (paid by the Australian Government) (see Table 35) and the co-payment (paid by the patient) (see Table 34), based on the current price of Duodopa® on the PBS. The cost of medical services associated with commencing levodopa-based DATs was also included as an input, based on hospital costs and appointment costs with specialists including neurologists (see Table 35).

Table 34 Cost of medicines (paid by the patient) for people living with aPD

Input	Value	Source	Notes
Dudodopa®/Vyalev® cassettes per day	28	PBS item 11919H	The maximum quantity for Duodopa® per dispensed prescription is 28 units.
Average Duodopa® cassettes per day	1.10	Duodopa® Product Information	Provided by AbbVie Pty Ltd.
Average Vyalev® cassettes per day	1.32	Vyalev® Product Information	Provided by AbbVie Pty Ltd.
Duodopa® packs required per year	14.3	Calculated	The total number of Duodopa® packs required per year was calculated based on the number of cassettes per pack (28) and the number of cassettes required per day (1.1). This corresponds to the number of scripts to be dispensed per person per year.
Vyalev® packs required per year	17.2	Calculated	The total number of Vyalev® packs required per year was calculated based on the number of cassettes per pack (28) and the number of cassettes required per day (1.1). This corresponds to the number of scripts to be dispensed per person per year.
Average PBS co-payment	$8.33	PBS Co-payment, calculated	Weighted average co-payment amount based on PBS utilisation data for Duodopa®. General patients pay $30 per script, while concessional patients pay $7.30 per script. After reaching the safety net, general patients pay $7.30 per script and concessional patients pay $0. The majority of patients (78%) pay either the concessional co-payment or the concessional safety net amount ($0).
Average annual cost per patient	$133.17	Calculated	Weighted average annual cost per patient, based on the PBS co-payment amount and the number of scripts dispensed per patient per year. The average cost per patient is weighted between Duodopa® and Vyalev® patients.
Total cost for people living with advanced Parkinson's disease	**$163,538**	Calculated	

Table 35 Cost of medicines (paid by the Government) and medical services for people living with aPD

Input	Value	Source	Notes
Duodopa® PBS price	$5902.22	PBS item 11919H	Dispensed Price for Maximum Quantity (DPMQ) for Duodopa® on the PBS.
Duodopa® cassettes per pack	28	PBS item 11919H	The maximum quantity for Duodopa® per dispensed prescription is 28 units.
Duodopa® cassette per day	1.1	Duodopa® Product Information	Provided by AbbVie Pty Ltd.
Duodopa® cost per patient per year	$84,692	Calculated	Calculated based on the Duodopa® price per cassette and the average number of cassettes required per day.
Vyalev® cost per patient per year	$84,692	Assumption	It is assumed that Vyalev® and Duodopa® will have the same price on the PBS, if Vyalev® is listed based on a cost-minimisation approach.
Special Pricing Arrangement	22%	PBS_Expenditure_and_Prescriptions_Report_1-July-2020_to_30-June-2021.pdf	When a PBS-listed medicine has a Special Pricing Arrangement (SPA), the Australian Government recovers a percentage of expenditure (through a rebate). As such, the listed price does not reflect the price truly paid by the Government. Duodopa® currently has a SPA in place and it is assumed that Vyalev® will also have such an arrangement. The average rebate across all PBS-listed medicines was used, assuming that the rebate for Duodopa® and Vyalev® is similar to the average.
Total annual medication cost per patient	$66,059	Calculated	The rebate percentage above is applied to calculate the true cost to the PBS of Duodopa® and Vyalev® treatment.
Oral levodopa pack price	$302.62	PBS item 9292C	PBS price for levodopa 200 mg + carbidopa 50 mg + entacapone 200 mg (e.g. Stalevo®, TRIDOPA®). Each dispense includes 200 tablets.
Daily levodopa dose	1000 mg	M15-736 clinical trial data	At baseline, the average daily oral levodopa dose was 1,000 mg.
Levodopa doses per day	5	Calculated	Based on a daily dose of 1,000 mg and 200 mg per dose as per PBS item 9292C above.
Oral levodopa cost per year	$2,763.30	Calculated	Each script of levodopa/carbidopa/entacapone dispensed provides medication for an average of 40 days per patient (200 units/5 units daily). The total cost per dispense ($302.62) is divided by 40 to calculate the daily cost, and multiplied by the number of days per year to calculate the annual cost.
Incremental drug cost	$63,296	Calculated	The incremental drug cost of moving a patient from oral levodopa to a DAT. The co-payment amount per patient is assumed to be the same in both circumstances, and as such is not included in the incremental cost calculation.

Input	Value	Source	Notes
Total annual drug cost	$77,727,659	Calculated	Total incremental drug cost per patient, multiplied by the number of people receiving treatment.
Initiation cost Duodopa®	$16,123.05	National Hospital Cost Data Collection Cost Weights for AR-DRG v10, Round 24 (2019-20)	Weighted average cost for AR-DRG G05A and G05B (Minor small and large bowel interventions) which covers the insertion of PEG/J tube for Duodopa® treatment.
Specialist visits for initiation of Vyalev®	2.4	M15-736 clinical trial data	Provided by AbbVie Pty Ltd.
Cost per visit	$45.40	MBS item 105	Professional attendance by a specialist.
Initiation cost Vyalev®	$108.96	Calculated	
Total annual initiation cost	$1,550,437	Calculated	Calculated based on the initiation cost for each treatment and the number of people who will initiate each year.
Total cost for Australian Government	**$79,278,096**	Calculated	