

## **Application 1727**

**Deep Brain Stimulation for Treatment-  
Refractory Obsessive-Compulsive Disorder**

## **PICO Confirmation**

**Summary of PICO/PPICO criteria to define question(s) to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)**

**Table 1 PICO for deep brain stimulation for treatment-refractory obsessive-compulsive disorder: PICO Set 1**

Component	Description
Population	Persons with severe, treatment-refractory obsessive-compulsive disorder (OCD), i.e. OCD that has not been adequately controlled despite treatment for at least 12 weeks with maximum tolerated doses of at least three selective serotonin reuptake inhibitors (SSRI), clomipramine, and at least one attempt at OCD specific psychotherapy
Intervention	Deep brain stimulation (DBS) of the subcortex in combination with continued pharmacotherapy and/or psychotherapy
Comparator	Continued high dose pharmacotherapy combined with repeated courses of psychotherapy (Standard of Care)
Outcomes	<ul style="list-style-type: none"> <li>• Safety               <ul style="list-style-type: none"> <li>○ Serious adverse events (neurologic &amp; physical)</li> <li>○ Procedure-related adverse events, e.g., haemorrhage, implantation site infection</li> <li>○ Adverse events/complications</li> </ul> </li> <li>• Clinical effectiveness               <ul style="list-style-type: none"> <li>Primary outcomes:                   <ul style="list-style-type: none"> <li>○ Reduction in symptoms of OCD, as assessed by the Yale Brown Obsessive-Compulsive Scale (established MCID: 35% reduction of score)</li> <li>○ Proportion of patients showing an MCID of 35% reduction of score</li> </ul> </li> <li>Secondary Outcomes:                   <ul style="list-style-type: none"> <li>○ Reduction in depression and anxiety symptoms</li> <li>○ Reduced rate of suicide</li> <li>○ Improved quality of life</li> <li>○ Reduction in medication requirement and psychotherapy requirement over time</li> <li>○ Increased rate of employment</li> </ul> </li> </ul> </li> <li>• Cost-effectiveness               <ul style="list-style-type: none"> <li>○ Cost per life-year gained</li> <li>○ Cost per quality-adjusted life-year (QALY) gained</li> </ul> </li> <li>• Healthcare resources               <ul style="list-style-type: none"> <li>○ Cost of intervention delivery</li> <li>○ Cost associated with changes in clinical management (e.g., follow-up)</li> </ul> </li> <li>• Total Australian Government healthcare costs:               <ul style="list-style-type: none"> <li>○ Total cost to the Medicare Benefits Schedule (MBS)</li> <li>○ Total cost to other healthcare services.</li> </ul> </li> </ul>
Assessment questions	What is the safety, effectiveness and cost-effectiveness of DBS of the subcortex <i>versus</i> pharmacotherapy and psychotherapy for treatment of severe refractory OCD?

## Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of deep brain stimulation (DBS) of the subcortex for treatment of severe refractory obsessive-compulsive disorder (OCD) was received from Dr Philip Mosley by the Department of Health and Aged Care.

The applicant expects that compared to pharmacotherapy combined with psychotherapy, DBS of the subcortex for the treatment of severe treatment-refractory OCD will have:

- Superior clinical effectiveness in selected patients
- Non-inferior safety.

The overall aim of DBS therapy is to reduce the symptoms of OCD as assessed by the Yale Brown Obsessive-Compulsive Scale (Y-BOCS), reduce the rate of suicide and increase the quality of life in persons with severe, treatment-refractory OCD who have not responded to sequential trials of medication and psychotherapy.

## PICO criteria

### *Population*

The intervention is intended for patients with severe obsessive-compulsive disorder who continue to experience highly disabling symptoms despite being treated with a combination of pharmacotherapy and psychotherapy. Eligible patients would meet the DSM-5 criteria to have a confirmed diagnosis of severe, treatment-refractory OCD made by a specialist psychiatrist. The minimum duration of the illness would be at least 5 years, which is in line with current practice in Australia.[1, 2]

### *Defining obsessive-compulsive disorder*

OCD is a psychiatric condition characterised by the intrusion of ego-dystonic, anxiety-provoking thoughts, urges or images (obsessions), generally accompanied by repetitive mental acts or behaviours (compulsions), which are carried out to neutralise the obsessions, or to mitigate anxiety associated with them. The phenomenology of these obsessions is broad. People with OCD may be excessively concerned with germs, preoccupied with symmetry or disturbed by intrusive violent, sexual or religious thoughts. Compulsions such as cleaning, ordering, checking and repeating may consume waking hours.

Secondary anxiety and depressive disorders are common. OCD typically develops in childhood and young adulthood and is highly impairing. The World Health Organisation rates OCD as a leading global cause of disability, and the rate of suicide in OCD is increased by a factor of 10 over the general population.[3, 4] Social and occupational functioning is severely impaired in all domains in individuals with severe OCD [5], with an estimated annual cost to Australian society associated with OCD of AUD 3.4 billion [6].

*PASC noted that the proposed population are patients with severe and treatment-refractory obsessive-compulsive disorder (OCD).*

### *Management*

The mainstay of treatment for OCD involves a combination of pharmacological (antidepressant) and psychological (cognitive behavioural therapy; CBT) approaches.[7, 8] However, an estimated 30% of patients still have clinically-significant symptoms despite appropriate treatment with an antidepressant and psychotherapy.[9-12]

The most effective psychological treatment for OCD involves deliberate exposure to anxiety-provoking situations with the expectation that this anxiety (and the need to maintain compulsive rituals) will habituate over time.[7, 8]

However, individuals with severe OCD commonly find this process intolerable and cannot engage fully in treatment or else do not habituate despite persistent exposure. The net result is that there exists a subgroup of people with OCD who are treatment-refractory, remain highly-disabled and who have limited therapeutic options available to them to improve their quality of life.

Psychologists administering exposure-oriented CBT in Australia must be at the level of “Clinical Psychologist” (i.e. have a clinical masters degree or PhD in psychology) and must be specifically trained in the delivery of exposure and response prevention. [13]

#### *OCD severity and defining treatment-refractory OCD*

The severity of the illness is assessed using the Y-BOCS, which is a clinician-administered semi-structured interview and is the gold standard instrument for assessing people with OCD.[14, 15] A score of greater than 24/40 is clinically accepted to denote a severe level of OCD symptoms, and patients are required to score above this threshold on 2 separate occasions at least 2 weeks apart to be eligible for DBS. Cut-off values of 26/40 have also been reported.[16]

The applicant suggested that treatment-refractory OCD would be confirmed with a corroborated history of treatment defined by insufficient response to at least:

- two trials of selective serotonin reuptake inhibitors (SSRI) at maximum tolerated dose for at least 12 weeks, plus
- one trial of clomipramine at maximum tolerated dosage for at least 12 weeks, plus
- one augmentation trial with an antipsychotic for at least eight weeks in combination with one of the aforementioned drugs, plus
- one complete trial of exposure-based psychotherapy confirmed by a psychotherapist.

*PASC discussed the number of SSRIs that patients would need to have trialled before DBS is considered. The RANZCP suggested that 4 SSRIs should be trialled beforehand. While the FDA recommends that 3 SSRIs should be trialled before considering DBS. PASC discussed whether the requirement to trial treatment with at least three separate medications (SSRIs - selective serotonin reuptake inhibitors) and concurrent OCD specific psychotherapy (exposure therapy) may be too strict, given some patients may experience adverse drug reactions or may be unable to tolerate a complete course of exposure therapy. In addition, the applicant stated that access to exposure therapy is limited and associated with high out of pocket costs for patients.*

*PASC considered the requirement to trial three SSRIs, clomipramine and at least one attempt at psychotherapy was appropriate. PASC considered that patients do not need to complete full courses serotonergic antidepressants if these are not tolerated.*

### *Burden of disease*

The lifetime prevalence of obsessive-compulsive disorder is estimated to be 1-2% in the general population.[17] After appropriate treatment with an antidepressant and psychotherapy, the number of persons with residual symptoms has been estimated at 30% [9-12] and following failed response to three consecutive pharmacotherapies and psychotherapy this number falls to 10% [18].

In an American naturalistic sample, 1% of cases with OCD met the accepted eligibility criteria for deep brain stimulation – i.e. severe residual symptoms despite appropriate and adequate consecutive trials of pharmacotherapy and psychotherapy.[19]

### *Utilisation estimates*

The number of individuals with very severe and highly treatment-refractory OCD qualifying for deep brain stimulation is likely to be low [6], with a projected number of five patients utilising the service for the first full year.

The applicant anticipates the limited uptake of this therapy in Australia for two reasons. First, deep brain stimulation is only intended to be used in this psychiatric population amongst those who are severely ill and highly treatment-refractory. Most people do not wish to consider neurosurgery unless they are highly disabled by their symptoms. Second, at present there are only a handful of multidisciplinary teams with the expertise to conduct this procedure. Individuals identified by their treating psychiatrist as potentially suitable for deep brain stimulation (DBS) would be referred to a deep brain stimulation centre, a dedicated, experienced unit with strong affiliations with multidisciplinary research teams. Currently, there are three such centres in Australia: i) Royal Melbourne Hospital, Melbourne, ii) St Vincents Hospital, Melbourne and iii) St Andrews Hospital, Brisbane. At this unit the patient would be evaluated by a neurosurgeon, neurologist and neuropsychiatrist experienced in DBS. A report would be prepared for review by the Mental Health Review Tribunal (note, legislative requirements differ between states in Australia as regards neurosurgery for psychiatric disorders). The purpose of the tribunal is to convene an independent panel of experts to ensure that the treatment is appropriate and the patient has the capacity to voluntarily consent to the procedure. Once this is accomplished and approved by the tribunal, implantation of the DBS device can proceed.

Note that the Mental Health Review Tribunal is in the state where the patient is having the procedure (not necessarily their home state). Due to differing state legislative requirements not all states will have the same access to DBS for this patient group. Consultation with the states is underway (no feedback has been provided by NSW to date).

It is conceivable that the existing groups will have a role in training other centres (for example in South Australia and Western Australia), but any new centres will be required to develop their teams and workflow, which will take time.

### ***Intervention***

The proposed health technology, DBS of the subcortex, is a therapeutic medical service. DBS is a surgical treatment that involves the implantation of permanent stimulating electrodes within the brain, targeted to a specific region in the subcortex (the inner region of the brain). These electrodes are connected to a small battery that typically sits under the skin of the chest wall. Each electrode delivers a very small field of targeted electricity that changes the activity of neurons (brain cells) in that region. The DBS device can be adjusted post-operatively without the need for further surgery, to vary the size, shape and position of the stimulation field. DBS is an established therapy for neurological conditions such as Parkinson's disease and has been used extensively in Australia and overseas with an estimated >150,000 devices implanted.

The implantation of the DBS device is delivered in an inpatient hospital setting. It involves neurosurgery, neurology, psychiatry, radiology, anaesthetic and intensive care physicians. The targeting and implantation

of the DBS system is delivered by a neurosurgeon and neurologist working in tandem. The follow up of the patients and programming of the device is delivered by a psychiatrist experienced in neurostimulation.

#### *Pre-operative planning*

The patient is admitted to the DBS unit and undertakes a magnetic resonance imaging (MRI) scan of the brain. The DBS neurologist and neurosurgeon visualise the subcortical structures that are to be targeted by the DBS electrodes. Using planning software, the target is mapped using the patient's brain anatomy to define a trajectory for each electrode to pass safely through the skull and into the brain to reach the defined target.

#### *Surgical implantation*

On the day of the surgery the patient is anaesthetised and a metal stereotactic frame is attached to the patient's skull. A Computed Tomography (CT) brain scan (with the frame attached) is fused to the existing MRI scan with medical software. This fused image is used to calculate the precise three-dimensional intracranial coordinates of the surgical target. Still under general anaesthesia the neurosurgeon drills a small burr hole on each side of the patient's skull and passes a recording electrode along a pre-determined trajectory to the target structure. Accurate placement in the target is confirmed using intra-operative microelectrode recording of local field potentials, and later by briefly rousing the patient from anaesthesia. At this time, the neurologist can assess the effect of intra-operative stimulation on the patient and screen for any unwanted motor or sensory effects (such as facial pulling, gaze deviation or paraesthesia). Once accurate placement is verified, permanent stimulating electrodes are inserted and their final position is verified using another CT brain scan. In DBS for OCD, one electrode is placed in each hemisphere of the brain.

The implanted stimulating electrodes are routed subcutaneously and connected to a pulse generator sited in the pectoral or abdominal fascia. Each electrode comprises between four to eight contacts, any number of which can be activated to deliver a small, focussed and continuous field of electricity in the local neural tissue. In the electrical circuit, the charge is delivered by means of at least one positive (anodal) and one negative (cathodal) terminal. Initially, the device is programmed with one contact as the cathode and the pulse generator as the anode, a configuration known as '*monopolar*'.

The DBS device is activated at a low level intra-operatively and the patient is moved to the intensive care unit for twenty-four hours, before returning to the surgical ward. Although an optimal contact has been identified in theatre, the lead neurologist reviews the patient several times per day during this time to corroborate the tolerability of therapy and to trial alternative contacts if necessary. Recovery from functional neurosurgery is relatively swift and persons with OCD are typically discharged home within 2-3 days of DBS device implantation.

*PASC noted that the target for DBS for treatment-refractory OCD are the subcortical regions of the brain. The four principal targets include the ventral anterior limb of the internal capsule (ALIC), nucleus accumbens, bed nucleus of the stria terminalis, and subthalamic nucleus. The applicant explained that all of these areas are very close together in the sub cortex and are part of a unified circuit. Stimulation at any point in this circuit has been shown to reduce symptoms of OCD. The applicant noted that the specific region targeted was often associated with clinician expertise and only a single region would be targeted per patient however the target and intervention is complex and highly individual.*

#### *Post-operative care*

Patients return to the outpatient clinic weekly to fortnightly during the initial postoperative months and are reviewed by the DBS clinicians including the unit psychiatrist. The DBS device is programmed to give greater stimulation amplitude at the chosen contact. This occurs non-invasively through a computer that communicates with the pulse generator in the patient's chest wall. Increases in stimulation are guided by

the patient's level of symptom relief and the emergence of side effects. It may take six to twelve months to find the optimal stimulation parameters, with the slow accrual of benefits during this time.

The continuation of the patient's usual psychotropic medication and/or psychotherapy is considered on an individual basis based upon the relative benefit for that person. The full response to DBS may take more than 12 months to accrue. At this point, if there has been a substantive response to DBS, a slow reduction of medication may be considered. A further trial of psychotherapy should be attempted in all patients, as there is evidence that people who have benefitted from DBS can now tolerate the distress of exposure therapy and accrue additional benefits.[20]

Note that patients who have travelled from interstate will be required to stay close to the outpatient clinic for a certain period of time post-operatively.

*PASC noted that the aim of the intervention is to enhance OCD treatment and patients are likely to require ongoing treatment with medication and psychotherapy.*

*PASC noted that the intervention is a complex process involving many steps and specialised multi-disciplinary care. Following clinical assessment and the DBS procedure, patients require post-operative care, frequent follow-up post-discharge from hospital and frequent monitoring and adjustment of stimulation parameters.*

*PASC noted that given the highly specialised nature of the intervention and the expertise required, there are very few centres available in Australia offering DBS for OCD. There is a trade off between the need for specialised centres with expertise in performing the intervention and the need for travel for rural patients. The applicant explained that DBS needs to be performed in a specialised centre, due to the high level of expertise required. To improve access, follow-up appointments can be offered to rural and remote patients through telehealth. PASC noted that remote monitoring and programming of DBS devices for the Parkinson's disease population has recently been introduced and may become possible for DBS devices targeting OCD in the future, which will further improve access for patients not residing close to a DBS centre.*

*PASC noted the Medtronic lead/electrode kit (ARTG 174469) is the only DBS lead kit currently registered on the ARTG with an indication for OCD. The applicant confirmed that other DBS leads have been used for OCD both in the research setting and in current clinical practice.*

## **Comparator**

The appropriate comparator for DBS in patients with treatment-refractory OCD is pharmacotherapy combined with psychological therapy.

Pharmacological therapy for OCD comprises antidepressant therapy with serotonergic agents (selective serotonin reuptake inhibitors or the tricyclic antidepressant clomipramine). These may be augmented with an atypical antipsychotic. Clomipramine is regarded as the most effective drug treatment for OCD. It is often not used first line as it has anticholinergic properties that cause side effects such as dry mouth, constipation and urinary retention.

Effective psychological therapy comprises 'exposure and response prevention'. In this style of therapy, the patient learns to gradually and deliberately place themselves in situations that trigger their obsessive fears, but without performing a neutralising compulsion. For example, a patient with contamination fears may progress over the course of therapy from being able to touch a chair and not wash their hands to being able to touch a toilet and not wash their hands. The principle is that the fear response central to OCD 'habituates' as the patient challenges themselves.

The currently used MBS item numbers for the treatment of patients with OCD (provision of outpatient care by a psychiatrist – items 300, 302, 304, 306, 308; provision of focussed psychological care by a psychologist – item 80100) are listed below.

It should be noted that patients who require more than 50 psychiatry attendance services in a calendar year in the case with intensive psychotherapy would move to items 310, 312, 314, 316 or 318, which are items with a lowered rebate.

*PASC noted that the comparator should be optimised pharmacological plus psychological therapy, which constitutes the best treatment currently available for OCD.*

Category 1 - PROFESSIONAL ATTENDANCES
MBS item 300 Professional attendance by a consultant physician in the practice of the consultant physician's specialty of psychiatry following referral of the patient to him or her by a referring practitioner-an attendance of not more than 15 minutes in duration at consulting rooms, if that attendance and another attendance to which item 296 or any of items 300 to 308 applies have not exceeded 50 attendances in a calendar year for the patient
Fee: \$46.50 Benefit: 75% = \$34.90 85% = \$39.55

Category 1 - PROFESSIONAL ATTENDANCES
MBS item 302 Professional attendance by a consultant physician in the practice of the consultant physician's specialty of psychiatry following referral of the patient to him or her by a referring practitioner-an attendance of more than 15 minutes, but not more than 30 minutes, in duration at consulting rooms, if that attendance and another attendance to which item 296 or any of items 300 to 308 applies have not exceeded 50 attendances in a calendar year for the patient
Fee: \$92.75 Benefit: 75% = \$69.60 85% = \$78.85

Category 1 - PROFESSIONAL ATTENDANCES
MBS item 304 Professional attendance by a consultant physician in the practice of the consultant physician's specialty of psychiatry following referral of the patient to him or her by a referring practitioner-an attendance of more than 30 minutes, but not more than 45 minutes, in duration at consulting rooms), if that attendance and another attendance to which item 296 or any of items 300 to 308 applies have not exceeded 50 attendances in a calendar year for the patient
Fee: \$142.80 Benefit: 75% = \$107.10 85% = \$121.40

Category 1 - PROFESSIONAL ATTENDANCES
MBS item 306 Professional attendance by a consultant physician in the practice of the consultant physician's specialty of psychiatry following referral of the patient to him or her by a referring practitioner-an attendance of more than 45 minutes, but not more than 75 minutes, in duration at consulting rooms, if that attendance and another attendance to which item 296 or any of items 300 to 308 applies have not exceeded 50 attendances in a calendar year for the patient
Fee: \$197.10 Benefit: 75% = \$147.85 85% = \$167.55

Category 1 - PROFESSIONAL ATTENDANCES
MBS item 308 Professional attendance by a consultant physician in the practice of the consultant physician's specialty of psychiatry following referral of the patient to him or her by a referring practitioner-an attendance of more than 75 minutes in duration at consulting rooms), if that attendance and another attendance to which item 296 or any of items 300 to 308 applies have not exceeded 50 attendances in a calendar year for the patient
Fee: \$228.70 Benefit: 75% = \$171.55 85% = \$194.40



## Category 8 - MISCELLANEOUS SERVICES

### MBS item 80100

Professional attendance for the purpose of providing focussed psychological strategies services for an assessed mental disorder by a psychologist registered with Medicare Australia as meeting the credentialing requirements for provision of this service - lasting more than 20 minutes, but not more than 50 minutes - where the patient is referred by a medical practitioner, as part of a GP Mental Health Treatment Plan or as part of a shared care plan; or referred by a medical practitioner (including a general practitioner, but not a specialist or consultant physician) who is managing the patient under a referred psychiatrist assessment and management plan; or referred by a specialist or consultant physician in the practice of his or her field of psychiatry or paediatrics.

These therapies are time limited, being deliverable in up to ten planned sessions in a calendar year (including services to which items 283 to 287; 2721 to 2727; 80000 to 80015; 80100 to 80115; 80125 to 80140; 80150 to 80165 apply).

(Professional attendance at consulting rooms)

Fee: \$74.75 Benefit: 85% = \$63.55

## Outcomes

### Safety

- Serious adverse events (neurologic & physical)
- Procedure-related adverse events, e.g., haemorrhage, implantation site infection
- Adverse events/complications related to the surgery, device or other cause

### Clinical effectiveness

#### Primary outcomes:

- Reduction in symptoms of OCD, as assessed by the Yale Brown Obsessive-Compulsive Scale (established MCID: 35% reduction of score)[21, 22]
- Proportions of patients showing an MCID of 35% reduction of score

#### Secondary Outcomes:

- Reduction in depression and anxiety symptoms (e.g. using the Montgomery Åsberg Depression Rating Scale or the Hamilton Depression Rating Scale)
- Improved quality of life
- Reduction in medication requirement and psychotherapy requirement over time
- Reduced rate of suicide (e.g. using the Montgomery Åsberg Depression Rating Scale or the Hamilton Depression Rating Scale)
- Increased rate of employment

*PASC noted the importance of the secondary outcomes (eg. reduction in depression and anxiety symptoms, improved quality of life). However, given the small number of patients undergoing DBS for OCD, it will be difficult to accurately measure the secondary outcomes until a significant number of patients have been included in a registry.*

# Clinical management algorithms

## *Current clinical management*

The diagram in

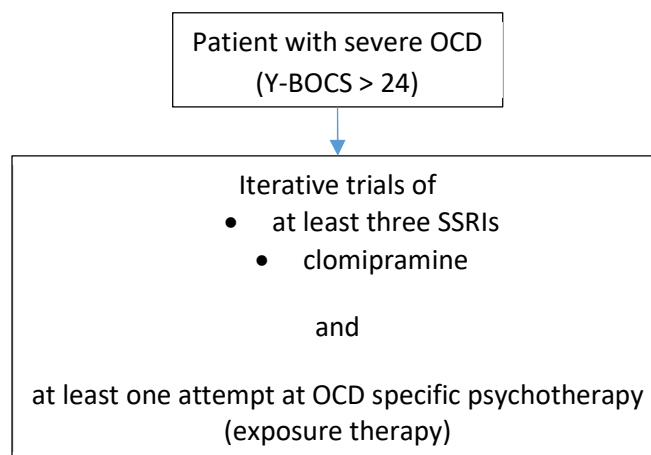
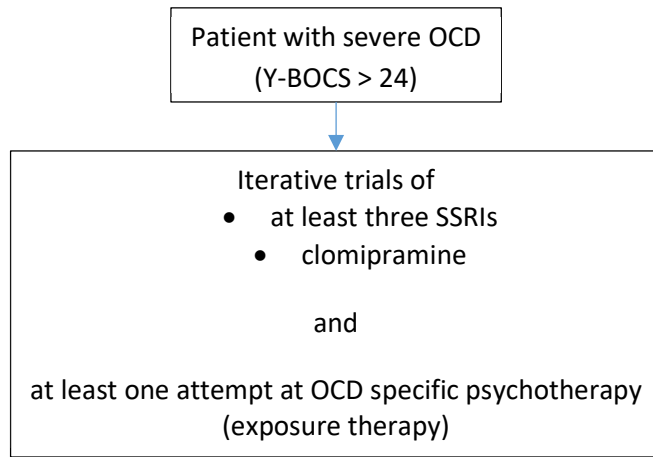


Figure 1 summarises the current clinical management pathway for people diagnosed with severe treatment-refractory obsessive-compulsive disorder.

Patients with severe OCD undergo the following sequence of treatments:

1. Pharmacological therapy is introduced and titrated to the maximum tolerated dose. First line medications include serotonergic antidepressants (selective serotonin reuptake inhibitors).
2. If the patient has residual symptoms the antidepressant is switched to another agent, or an atypical antipsychotic is combined with the antidepressant as an augmentation strategy.
3. If the patient has residual symptoms the tricyclic antidepressant clomipramine is trialled. Serum levels of clomipramine and its metabolites are used to define the appropriate therapeutic dose.
4. Alongside trials of medication, psychotherapy is instituted using the principles of exposure and response prevention. This is typically carried out by a clinical psychologist.
5. If the patient fails to respond and continues to exhibit severe symptoms, iterative trials of antidepressants, antipsychotics and psychotherapies are continued, often with diminishing benefits.



**Figure 1 Current clinical management algorithm**

OCD=obsessive-compulsive disorder; SSRI=selective serotonin reuptake inhibitors; Y-BOCS=Yale Brown Obsessive Compulsive Scale

## Proposed clinical management

The proposed medical service (DBS) is meant to only be available if people with OCD *continue* to have severe and disabling symptoms *despite* adequate trials of these therapies. There are some individuals who, despite high dose pharmacotherapy and repeated courses of psychotherapy, are unable to habituate their fear responses and cannot attenuate their compulsive behaviour. As such, DBS is not considered a substitution but an add-on for the small number of persons who remain highly treatment-refractory. In fact, DBS has been shown to be synergistic with ongoing psychotherapy, through allowing patients to make gains with exposure and response prevention when previously their fear response did not habituate.[20]

The diagram in

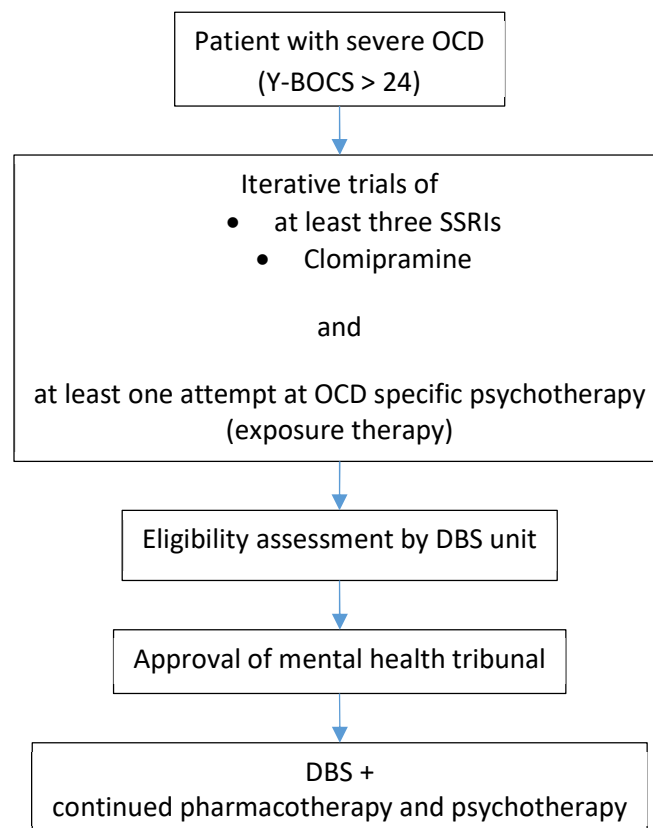
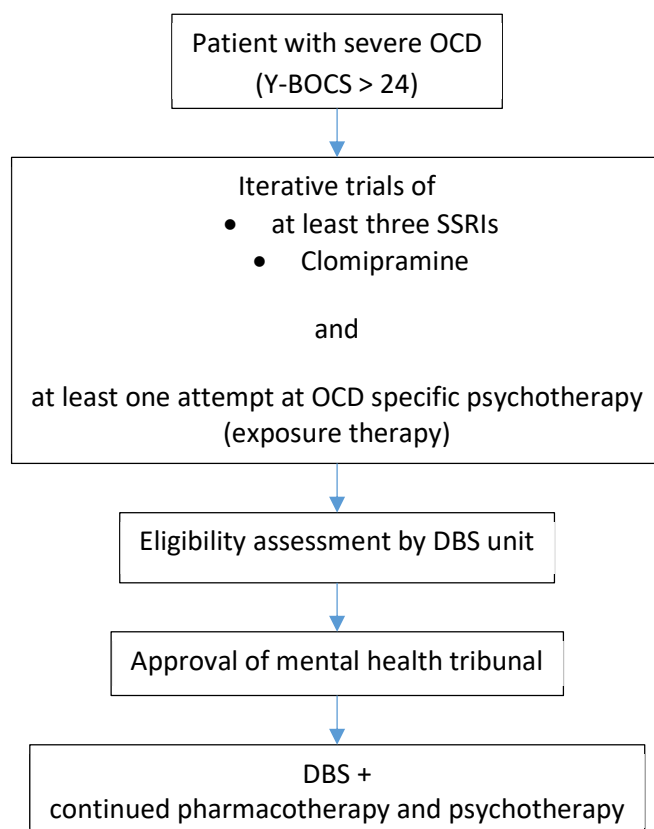


Figure 2 represents the clinical management algorithm that patients would follow after the proposed service/technology is introduced. After the introduction of the new therapy (DBS), patients with treatment-refractory OCD would have an additional MBS-approved treatment option:

1. Persons with severe obsessive-compulsive disorder (OCD) who had not responded to trials of at least three selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempt to complete a course of psychotherapy would be referred to a deep brain stimulation (DBS) unit for evaluation.
2. The psychiatrist at the DBS centre will confirm that the potential patient has indeed fulfilled the criteria for treatment-refractory OCD and this will involve liaison with the usual treating psychiatrist and psychologist. The DBS psychiatrist will also screen for other psychiatric exclusion criteria such as substance use disorder, severe personality disorder, high-risk suicidal behaviour (not an exhaustive list). The DBS psychiatrist will use this information to prepare a report for the mental health review tribunal. The multidisciplinary team including the neurologist and neurosurgeon will assess general suitability for neurosurgery including co-morbid medical conditions.

3. The mental health tribunal would review the suitability of the candidate for DBS and their capacity to consent voluntarily.
4. With approval of the tribunal, the patient would undertake DBS device implantation and initial follow up would be conducted by the psychiatrist at the DBS centre, who would program the device.
5. Pharmacological therapy and psychotherapy would continue even after DBS device implantation. Published research has shown that one of the effects of DBS is to allow patients to accrue benefit from the psychotherapy – with a habituation of the fear response and ability to suppress compulsive rituals.



**Figure 2 Proposed clinical management algorithm**

DBS=deep brain stimulation; OCD=obsessive-compulsive disorder; SSRI=selective serotonin reuptake inhibitors; Y-BOCS=Yale Brown Obsessive Compulsive Scale

*PASC noted that DBS would be offered as an additional treatment for patients with OCD where the existing clinical management was unsuccessful.*

## Proposed economic evaluation

The overall clinical aim of DBS therapy is to reduce the symptoms of OCD, reduce the rate of suicide, improve the quality of life and increase the rate of employment in persons with severe, treatment-refractory OCD who have not responded to sequential trials of medication and psychotherapy.

Supportive evidence for the clinical claim includes four randomised controlled trials [23-26] and two non-randomised trials [27, 28], as well as a review of the existing trials [29]. In addition, a recent meta-analysis provides a comprehensive overview of the existing literature.[18]

The applicant plans to construct a data registry to collate all previous and prospective cases of DBS for OCD in Australia. Data will be collected on electrode placement, psychiatric outcomes and adverse events, in

order to refine the efficacy and safety profile of this therapy. However, the planned registry will not be a component of the assessment.

Based on this clinical claim of superior clinical effectiveness and non-inferior safety of DBS for treatment of medically refractory OCD compared to pharmacotherapy combined with psychotherapy, the appropriate economic evaluation is a cost-effectiveness or cost-utility analysis (Table 2).

**Table 2 Classification of comparative effectiveness and safety of the proposed intervention, compared with its main comparator, and guide to the suitable type of economic evaluation**

Comparative safety	Comparative effectiveness			
	Inferior	Uncertain <sup>a</sup>	Noninferior <sup>b</sup>	Superior
Inferior	Health forgone: need other supportive factors	Health forgone possible: need other supportive factors	Health forgone: need other supportive factors	? Likely CUA
Uncertain <sup>a</sup>	Health forgone possible: need other supportive factors	?	?	? Likely CEA/CUA
Noninferior <sup>b</sup>	Health forgone: need other supportive factors	?	CMA	CEA/CUA
Superior	? Likely CUA	? Likely CEA/CUA	CEA/CUA	CEA/CUA

CEA=cost-effectiveness analysis; CMA=cost-minimisation analysis; CUA=cost-utility analysis

? = reflect uncertainties and any identified health trade-offs in the economic evaluation, as a minimum in a cost-consequences analysis

<sup>a</sup> 'Uncertainty' covers concepts such as inadequate minimisation of important sources of bias, lack of statistical significance in an underpowered trial, detecting clinically unimportant therapeutic differences, inconsistent results across trials, and trade-offs within the comparative effectiveness and/or the comparative safety considerations

<sup>b</sup> An adequate assessment of 'noninferiority' is the preferred basis for demonstrating equivalence

*PASC noted that the appropriate economic evaluation for this application would be a cost-effective analysis or cost-utility analysis, However, PASC considered that a clinical claim of inferior safety may be more appropriate, given the inherent risks of infection, device complications, and invasive nature of the surgery, compared to continued clinical management.*

## Proposal for public funding

The applicant proposed an amendment to the patient population under existing MBS items for DBS (items 40851, 40852, 40854, 40856, 40858, 40860, 40862). The aim is to expand current MBS items for DBS to include the subgroup of people with OCD who have been reviewed by a panel of experts and approved by the mental health tribunal to undergo DBS for OCD. No changes have been proposed to the existing fees.

The proposed changes to the current MBS item descriptors are marked in blue and are identical in the descriptors below.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40851</p> <p>DEEP BRAIN STIMULATION (bilateral) functional stereotactic procedure including computer assisted anatomical localisation, physiological localisation including twist drill, burr hole craniotomy or craniectomy and insertion of electrodes for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.) (Assist.)</p>
Fee: \$4,189.60 Benefit: 75% = \$3,142.20

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40852</p> <p>DEEP BRAIN STIMULATION (unilateral) subcutaneous placement of neurostimulator receiver or pulse generator for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.) (Assist.)</p>
Fee: \$360.05 Benefit: 75% = \$270.05

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40854</p> <p>DEEP BRAIN STIMULATION (unilateral) revision or removal of brain electrode for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.)</p>
Fee: \$556.45 Benefit: 75% = \$417.35

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40856</p> <p>DEEP BRAIN STIMULATION (unilateral) removal or replacement of neurostimulator receiver or pulse generator for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.)</p>
Fee: \$270.05 Benefit: 75% = \$202.55

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40858</p> <p>DEEP BRAIN STIMULATION (unilateral) placement, removal or replacement of extension lead for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.)</p>
Fee: \$556.45 Benefit: 75% = \$417.35

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS item 40860</p> <p>DEEP BRAIN STIMULATION (unilateral) target localisation incorporating anatomical and physiological techniques, including intra-operative clinical evaluation, for the insertion of a single neurostimulation wire for the treatment of:</p> <p>Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or</p> <p>Essential tremor or dystonia where the patient's symptoms cause severe disability.</p> <p><i>Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.</i></p> <p>Multiple Operation Rule (Anaes.)</p>
Fee: \$2,138.30 Benefit: 75% = \$1,603.75

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.



Category 3 – THERAPEUTIC PROCEDURES

MBS item 40862

DEEP BRAIN STIMULATION (unilateral) electronic analysis and programming of neurostimulator pulse generator for the treatment of:

Parkinson's disease where the patient's response to medical therapy is not sustained and is accompanied by unacceptable motor fluctuations; or

Essential tremor or dystonia where the patient's symptoms cause severe disability.

*Severe obsessive-compulsive disorder where the patient has a Yale-Brown Obsessive Compulsive Scale Score of greater than 24/40 despite three trials of selective serotonin reuptake inhibitors, one trial of clomipramine and at least one attempted course of psychotherapy incorporating exposure and response prevention.*

Multiple Operation Rule

(Anaes.)

Fee: \$200.55 Benefit: 75% = \$150.45 85% = \$170.50

Note: Proposed changes to the current MBS item descriptors are marked in blue italics.

DBS for treatment-refractory OCD would only be carried out by specialist neurosurgeons and specialist neurologists with relevant additional training and experience in functional neurosurgery.

DBS for treatment-refractory OCD would only be provided in a hospital inpatient setting (public or private hospitals).

Note that DBS for treatment-refractory OCD is a bilateral procedure in Australia, rather than a staged one as is common in other jurisdictions. Some of the MBS items (40851) are therefore for bilateral procedures. However, unilateral MBS items may need to be required for revision and replacement procedures. The explanatory notes of the MBS item descriptors could clarify this.

DBS surgery for treatment-refractory OCD would be performed once in the patient's lifetime. Therefore, a lifetime limit is suggested to be applied for MBS item 40851 (initial insertion/surgery), but not for items on revisions and re-insertions.

Rarely (in approximately 2-5% of cases) an infection of the device necessitates hardware explantation, treatment with antibiotics and reimplantation at a later date.[30, 31] The device is programmed quite intensively (every 1-2 weeks) at the commencement of treatment, but typically stable stimulation settings are obtained after 6-months and thereafter, device programming is generally not carried out at a greater frequency than 6-monthly.

The battery in the pulse generator depletes after 2-5 years and replacement is carried out as a day case procedure. In DBS for movement disorders such as Parkinson's disease, the hardware cost for battery replacement is covered by the private health fund. Most device manufacturers are now making rechargeable devices that have a much longer lifespan. The cost of a rechargeable Medtronic battery is presently AUD \$17,283.

The patient is admitted to hospital for a typical duration of 3-4 days. The surgical procedure itself takes 3-4 hours to perform in the hands of an experienced surgical team. Each subsequent programming session takes approximately 30-60 minutes to perform.

Note that the MBS item (40863) for remote programming of the DBS neurostimulator pulse generator has been confirmed as not appropriate for the DBS device used for OCD, however this could be amended in the future should this change.

It is estimated that approximately 5 patients will utilise DBS for OCD in the first year.

An overall breakdown of delivery of DBS is presented in Table 3.

**Table 3 Approximate cost profile of DBS for OCD**

Item	Cost
MBS Item 40851 – Insertion of deep brain stimulation device by neurosurgeon	\$4,123.60
MBS Item 40852 – Subcutaneous placement of pulse generator	\$354.40
MBS Item 40858 – Placement of extension lead	\$547.70
MBS Item 40860 – Target localisation (bilateral)	\$3,156.98
MBS Item 40862 – Programming of DBS device (bilateral) = \$295.50 (estimate 20 programming sessions to optimise stimulation settings)	\$5910.00
Cost of DBS hardware estimated: <ul style="list-style-type: none"> <li>• Percept PC neurostimulator = \$13,592</li> <li>• Percept patient programmer = \$1,264</li> <li>• Sensight Extension x 2 = \$3,790</li> <li>• Sensight 0.5mm lead x 2 = \$8,240</li> <li>• Sensight extension tunneler = \$158</li> <li>• Microtargeting electrode = \$1,354</li> <li>• Sterile MER cable = \$181</li> <li>• Insertion tube = \$158</li> </ul>	\$28,737.00
Total cost	\$42,829.68

DBS=deep brain stimulation; MBS=Medical Benefits Scheme

*PASC noted that DBS for OCD is a bilateral procedure.*

*PASC discussed the need for a specific cut-off value of the Yale Brown Obsessive-Compulsive scale (Y-BOCS) (24/40) to define severe OCD, given this cut-off value is not evidence based, however it is clinically accepted.*

The applicant explained that defining a cut-off value for the Y-BOCS and demonstrating that a patient's symptoms are above that cut-off value is helpful in justifying a patient's need for the intervention, particularly when the patient is presented to the Mental Health Review Tribunal for consideration of the intervention. It may also prevent a potential criticism that the intervention may be offered to patients who do not necessarily need it.

*PASC considered whether a broader definition of the necessary previous treatments, prior to the intervention, would be more appropriate. The preferred agents could be detailed in the item descriptor's explanatory notes. PASC considered that the current population definition is acceptable, including the requirement to trial three SSRIs, clomipramine and at least one attempt at psychotherapy.*

*Additionally, PASC noted that some patients may be unable to 'complete' the course of psychotherapy because of the severity of their symptoms, and considered changing the descriptor to 'attempted a course' of psychotherapy to be appropriate.*

## Summary of public consultation input

PASC noted and welcomed consultation input from 1 professional organisation, 1 medical device manufacturer, and 4 state and territory offices of the chief psychiatrist:

- Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Medtronic Australasia Pty Ltd (Medtronic)
- Office of the Chief Psychiatrist WA (OCPWA)
- Office of the Chief Psychiatrist Tasmania (OCPTas)
- Office of the Chief Psychiatrist ACT (OCPACT)
- Office of the Chief Psychiatrist SA (OCPSA)

The consultation feedback received was all supportive of public funding for Deep Brain Stimulation for treatment-refractory OCD.

### **Clinical need and public health significance**

- The main benefits of public funding received in the consultation feedback included:
  - The need for an additional treatment for people who have exhausted other treatment options
  - Potential to incentivise the development of new centres of expertise in Australia
  - Improved quality of life for carers/family through reduced caring burden
  - Societal benefits such as improved productivity, more efficient use of healthcare resources and, potential savings to the healthcare sector
- The main disadvantages of public funding received in the consultation feedback included:
  - Limits to the evidence base, especially in respect of RCTs and long-term outcomes
  - Potentially lengthy programming time required postoperatively
  - Risks involved with surgical procedures and potential side effects
  - Relative risk of there being little or no significant improvement
- Other services identified in the consultation feedback as being needed to be delivered before or after the intervention included:
  - The RANZCP stated that DBS is not a substitution but an add-on therapy to psychological therapies or medications.
  - The RANZCP stated patients undertaking DBS usually require substantial psychological support, whether responding or not responding to the DBS.
  - Post-intervention management by a multidisciplinary team including a neurosurgeon, neurologist and, neuropsychiatrist experienced in DBS

### **Indication(s) for the proposed medical service and clinical claim**

- The consultation feedback agreed with the proposed population(s).
  - The RANZCP stated that clinical indications for DBS for OCD are set out with the RANZCP Clinical Memorandum. It states that DBS could be considered if all other treatment avenues have been exhausted, including trials of at least 4 SSRIs at maximum tolerated dose, one trial of clomipramine at maximum tolerated dose, one augmentation trial with an antipsychotic and one complete trial of exposure-based cognitive behavioural therapy. They added that, where available, other treatments with an evidence base supporting efficacy in OCD, such as deep repetitive Transcranial Magnetic Stimulation (rTMS), should also be provided prior to a consideration of a trial of DBS.
- The consultation feedback agreed with the proposed comparator(s).
  - Feedback from the RANZCP and Medtronic suggested other therapies could be potential comparators: rTMS and invasive ablative neurosurgical procedures (anterior capsulotomy, anterior cingulotomy).
- The consultation feedback agreed with the clinical claim.

### **Cost information for the proposed medical service**

- The consultation feedback agreed with the proposed service descriptor.
  - The RANZCP stated that the proposed item numbers are not clear in the definition of the professional groups able to claim the service.
- The consultation feedback agreed with the proposed service fee.

- o The RANZCP stated that costs for DBS for OCD would align with the currently available item numbers for DBS in neurological disorders.
- o The RANZCP added that the proposed costs reflect that the approved indication for OCD is for bilateral stimulation.

### **Additional comments**

The RANZCP stated legislative barriers affect access DBS to treat OCD. The offices of the chief psychiatrist in WA, Tasmania, the ACT and SA all stated that this service could be provided within their respective jurisdictions, provided that it was accessed through the relevant pathways in those jurisdictions. The RANZCP stated DBS to treat mental illness is currently prohibited in New South Wales and the Northern Territory. The ACT Chief Psychiatrist stated that DBS would fall within the definition of psychiatric surgery and that an application for psychiatric surgery has never been made under the ACT Mental Health Act 2015.

RANZCP stated that cautious provision of this therapy in highly specialised centres may be beneficial.

The RANZCP stated that they are supportive of developing a registry for all previous and prospective cases of DBS for OCD to ensure rigorous collection of outcome data.

*PASC noted the positive feedback from the Royal Australian and New Zealand College of Psychiatry (RANZCP) regarding the intervention and their support of the development of a registry.*

### **Next steps**

*PASC noted that the applicant wishes to proceed with a Department Contracted Assessment.*

## **Applicant Comments**

### ***Summary of Public Consultation Input***

The applicant stated that although the evidence for TMS for depression is robust, unfortunately the evidence for TMS for OCD is highly limited. They went on to state that the evidence base for DBS in OCD is much stronger.

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