Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1727 Deep brain stimulation for treatment-refractory obsessive-compulsive disorder

Applicant: **Dr Philip Mosley**

Date of MSAC consideration: **23-24 November 2023**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

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

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported public funding of deep brain stimulation (DBS) for treatment-refractory obsessive-compulsive disorder (OCD) but considered that MBS listing of this procedure may not be the best means of public funding. MSAC considered that a public funding arrangement alternative to the MBS should be sought, following consultation with stakeholders. MSAC considered the safety of DBS was inferior to the standard of care but acceptable given the high unmet need for a small group of patients who had severe disease and for whom multiple previous treatment options had not been effective. MSAC noted the low certainty evidence for the superior clinical effectiveness of DBS but considered that better clinical evidence was unlikely to be forthcoming. MSAC noted the very high incremental cost effectiveness ratio (ICER) estimated for DBS was unreliable for decision making with regard to the cost effectiveness of DBS. MSAC considered that the ICER was overestimated, although it would likely still be high. MSAC considered the financial impact to the MBS would be low and the risk of leakage low due to the small tightly defined population group. MSAC considered that public funding of DBS was warranted noting the high clinical need for DBS as a treatment of last resort for a small number of patients with severe OCD, the low total financial cost of funding and the low risk of leakage if treatment was confined to highly specialised settings. MSAC also recognised the safety concerns, low certainty evidence for effectiveness and uncertain cost-effectiveness and for this reason proposed public funding outside a listing on the MBS.

Consumer summary
This is an application from psychiatrist, Dr Philip Mosley, requesting Medicare Benefits Schedule (MBS) listing of deep brain stimulation (DBS) for treatment-refractory obsessive-compulsive disorder (OCD). OCD is a psychiatric condition where people experience obsessive thoughts, images or impulses that provoke anxiety. These anxieties lead to people performing compulsions (such

Consumer summary

as repetitive handwashing, checking door locks, saying prayers) to soothe their anxiety. OCD can take over people's lives and affect their ability to work, socialise and form relationships. This has flow-on effects to the lives of patients' families, carers and communities.

OCD is usually treated with medication and psychotherapy. However, for some people with OCD, they may continue to have debilitating symptoms despite trying many different medications and psychotherapy (known as treatment-refractory OCD). For these patients, DBS may be a suitable treatment option. In DBS, a neurosurgeon implants electrical leads into the brain. The leads provide electrical stimulation to specific parts of the brain that are thought to be involved in OCD. When these parts of the brain are stimulated, this can help to decrease OCD symptoms. The electrical leads are connected to a device that generates the electrical impulses. This device is called a pulse generator and is about the size of a matchbox. It is placed under the skin in the chest. DBS is an established therapy for other conditions involving the brain such as Parkinson's disease.

MSAC noted that the number of people eligible for DBS would be small because the group is tightly defined. They are defined as people who have severe OCD and have exhausted all treatment options. MSAC felt that the studies researching DBS in OCD were low in quality mainly because the number of people in each study was quite small and long-term data was not available. However, MSAC acknowledged that this was because the number of people with treatment refractory OCD is small, and there will likely be few opportunities to collect more data in the future.

MSAC noted that the estimated ratio of cost in relation to effectiveness for this treatment is high and there was a lot of uncertainty around this estimate, making it difficult to calculate the value for money of this treatment. Even if it were re-calculated, the ratio of cost to effectiveness was still likely to be high. However, the small number of patients means that the total budget impact is small.

Therefore, MSAC agreed that DBS should be publicly funded for treatment-refractory OCD. However, MSAC was not certain whether the MBS was the best system to fund it particularly because patients undergoing DBS for treatment-refractory OCD were likely to need a lot of support services from a variety of different healthcare professionals working together. Therefore, MSAC proposed that providing DBS for treatment-refractory OCD in a setting alternative to the MBS (e.g., as an extension of a public hospital program instead) may be more appropriate for this treatment. MSAC recommended that there should be further consultation to determine if another funding program should be found.

MSAC's advice to the Commonwealth Minister for Health and Aged Care

MSAC supported the public funding of DBS for treatment-refractory OCD, because it is a small, tightly defined group of patients with severe disease and no other treatment options. However, MSAC considered that another funding mechanism may be more appropriate than the MBS.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this is an application from Dr Philip Mosley requesting Medicare Benefits Schedule (MBS) listing of DBS for treatment-refractory OCD.

MSAC noted that DBS is an established therapy for neurological conditions such as Parkinson's disease. The applicant proposed an amendment to the patient population under existing MBS items for DBS (items 40851, 40852, 40854, 40856, 40858, 40860, 40862), to include the treatment of people with 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. However, MSAC considered that utilisation should be carefully monitored and hence it was not advisable to use existing MBS item numbers for the treatment of severe treatment refractory OCD by DBS.

MSAC noted that there was public consultation input from one professional organisation, one medical device manufacturer and four state and territory offices of the chief psychiatrist. The consultation feedback received was all supportive of public funding for DBS for treatment-refractory OCD. MSAC noted that among the benefits of supporting the funding of DBS for OCD cited in the consultation feedback was that it provided an option for those who had failed standard of care and it could incentivise the development of additional centres of excellence where this procedure could be performed. MSAC noted that a small group of patients had severe OCD and were so debilitated that they could not participate in daily life. These patients had failed standard interventions and thus DBS would provide a treatment option which could improve the quality of life for the patients and their families. MSAC however noted disadvantages of supporting funding of DBS for OCD. The consultation feedback cited risks in terms of adverse events, lengthy post-operative programming of the devices was required and there was a limited evidence base.

MSAC noted that the clinical claim of superior effectiveness and inferior safety was supported by very low-certainty evidence due to very small sample sizes, lack of long-term comparative data, too few events and long recruitment periods. However, MSAC noted that due to the invasive nature of the DBS treatment and the limited prospects of future high-quality RCTs or comparative non-RCTs for a highly invasive surgical therapy (such as DBS), the current low certainty evidence may need to be viewed as the highest level of evidence likely to be available or forthcoming.

MSAC noted that no comparative safety data were available; all studies reported only adverse events related to DBS treatment. Serious and non-serious adverse events associated with the DBS surgery were reported in nine studies (total *n* = 157), device-related adverse events were reported in seven studies (total *n* = 151) and stimulation-related adverse events were reported in 12 studies (*n* = 214).

MSAC noted that the 15 studies presented reported changes in symptoms of OCD as assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). Overall, there appeared some improvement in Y-BOCS scores in patients who received DBS compared to patients who received sham or no treatment. An improvement in Y-BOCs scores was also observed over baseline scores when DBS was administered long term. The evidence also suggested a possible reduction in depression and anxiety, but this did not translate into a change in the rates of suicide attempts or deaths, suicidal thoughts and/or ideation. However, there were very few suicide events observed in the studies and therefore it was difficult to draw a robust conclusion regarding the effects of DBS on suicide events.

In the randomised-control trials (RCTs), active DBS stimulation was not more effective in achieving a ≥35% reduction in Y-BOCS scores (the minimal clinically important difference, MCID, across the studies) compared to sham stimulation (four RCTs; very low-certainty evidence). However, this finding may be limited by the short RCT phases of the studies (ranging from 2 weeks to 3 months). Active DBS stimulation, however, showed a statistically significant difference in mean change in Y-BOCS scores at the last follow-up compared to sham stimulation (six RCTs; very low-certainty evidence).

Data from studies with long-term DBS all indicated that Y-BOCS scores decreased after DBS stimulation compared to baseline. However, the response rate (where response is defined as the MCID of ≥35% Y-BOCS reduction) varied across studies, ranging from 7% to 78%.

MSAC noted that this procedure is limited to facilities with specialist neurosurgeons and neurologists experienced in DBS. Currently there are only three facilities in Australia where DBS procedures for psychiatric conditions are carried out, located in Victoria and Queensland. Currently, psychosurgery is prohibited in NSW under the *NSW Mental Health Act 2007*. Consultation with the states/territories clarified that in the ACT, under the *Mental Health Act 2015*, the performance of psychiatric surgery is permitted if certain approvals and conditions are met, although an application for psychiatric surgery has never been made in the ACT. In SA, the *Mental Health Act 2009* does not prohibit DBS, but there are a number of safeguarding requirements that must be fulfilled prior to a patient accessing this treatment. MSAC considered that it is likely that only a small number of DBS centres will ever specialise in OCD treatment due to the multidisciplinary expertise required.

MSAC noted that the economic evaluation was developed using a Markov model with four health states: DBS with a rechargeable implantable pulse generator, DBS with a non-rechargeable implantable pulse generator, survival and background mortality. The primary outcome calculated in the model was cost per Quality Adjusted Life Years (QALY) which, based on clinical advice and time to realise all health outcomes, was estimated over a 10-year time horizon, and sourced from the main economic study (Moon et al. 2017)[1]. The costs of standard of care (pharmacotherapy and psychotherapy) were not considered in the model as these costs are realised in both the intervention and comparator arms and are therefore offset. Instead, the standard of care arm only considered QALY gains.

MSAC noted that an additional analysis was conducted following expert clinical advice regarding whether MBS items 40858 and 40860 should be applied once or twice during initial DBS surgery, given that these items are for unilateral procedures, but the DBS procedure is typically bilateral. The applicant confirmed that billing each of these items twice is more consistent with clinical practice. MBS item 40858 is the unilateral placement, removal or replacement of the extension lead, and MBS item 40860 is the unilateral DBS target localisation for the insertion of a single neurostimulation wire. MSAC noted the sensitivity analyses conducted by the assessment group, which corrected the cost of surgical items required for MBS items 40858 and 40860 (using bilateral costings), generated an incremental cost-effectiveness ratio (ICER) of $912,489 per quality-adjusted life year (QALY). MSAC noted that the utility values were a key driver of the model, and that using a 0.21 utility improvement (rather than 0.16 used in the base case) resulted in an ICER of $483,716/QALY. MSAC noted that the Moon et al. (2017) study had used a lower incremental cost of US$31,000 and a higher incremental QALY of 0.9, which produced an ICER of US$34,462/QALY (~A$54,000) in the UK.

MSAC noted that ESC considered that the different ICERs were probably driven by the difference in mortality applied. The model did not capture any differences in health outcomes or costs when an individual in the model transitions from severe to not severe OCD; however, it is plausible that this would improve the utility of the intervention for responders. ESC noted the assessment found no comparative evidence of difference in suicide or suicidal thoughts and/or ideation due to DBS treatment. However, there may be evidence for utility changes due to the reduced risk of suicide or suicidal thoughts and/or ideation based on OCD severity in the literature for the general population versus the target population of this intervention. Given these considerations, MSAC considered that the reported ICER of the economic evaluation was unreliable for decision making. However, MSAC considered that any further modelling would be unlikely to be decisive

[1] Moon et al., 2017. The cost-effectiveness of deep brain stimulation for patients with treatment-resistant obsessive-compulsive disorder. *Medicine (Baltimore). 1*(27), e7397.

as the ICER per QALY would be likely to remain high even if it is not as high as the $912,489 estimated.

MSAC noted that the Department Commissioned Assessment Report (DCAR) and public consultation feedback cited potential gains to the productivity of the patient population and carers from public funding of the procedure though no evidence (quantitative or otherwise) was provided to support this claim. MSAC considered that a relevant question was whether productivity gains and losses and carer benefits would be more relevant here than in other interventions and populations considered by MSAC.

When including MBS items 40858 and 40860 twice during the initial DBS surgery, the overall additional cost to the MBS is $67,619 in year 1 (assumed utilisation by 5 people) to $425,608 in year 6 (30 people) or just under $1.5 million over 6 years. The majority of this cost is attributable to the index DBS surgery which would include the pre-operative assessment ($119,673), the implantation ($897,570) and follow-up after initial surgery ($370,834).

MSAC noted that the total cost to the Australian health budget is calculated to be approximately $6.7 million over six years. Of the various healthcare budgets included in the total cost, the maximum cost is attributed to cost of the prostheses (approximately $3.6 million), the cost to the MBS (approximately $1.5 million) and then to the hospitals (approximately $1.6 million).

MSAC considered there was limited scope for service leakage or inappropriate patient selection, given that this treatment is typically undertaken in a centre of excellence with a high level of support and due attention to safety considerations. The group of patients eligible is tightly defined and patients are highly informed about the treatment. MSAC noted that ongoing multi-disciplinary support for patients following the DBS procedure is essential for optimal patient care and should be included in the MBS item descriptor if listed.

MSAC noted that although a patient's OCD symptoms may improve following DBS, they may continue to have functional limitations and therefore DBS does not constitute a definitive 'cure' for OCD. However, improving patients' OCD symptoms from the very severe to less severe range is likely to have a positive impact on patients and their carers. It is uncertain if smaller improvements in Y-BOCS scores might also improve quality of life. MSAC noted that 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, to refine the efficacy and safety profile of this therapy. However, as this registry will be conducted at a later date, the planned registry was not considered as a component of the clinical and economic evaluation. MSAC considered that a pre-condition of implementation for the public funding of this procedure should be the establishment of the data registry and that the registry should also collect health related quality of life outcome measures.

MSAC acknowledged that cost is currently a significant barrier to DBS treatment of refractory OCD in the private system and providing MBS funding for this service may serve to reduce the barrier to access to treatment for a vulnerable population, and as the consultation feedback noted, also stimulate additional supply, hence increasing equity of treatment. However, MSAC considered that the additional supply of DBS in the private system stimulated by MBS funding may have risks as well as benefits. It is likely that patients accessing DBS will require additional multidisciplinary team (MDT) and support services both pre and post-operatively to support their mental health and wellbeing. MSAC considered that these services could be better co-ordinated and integrated with DBS treatment services in a public setting. Overall, MSAC supported public funding of DBS for treatment refractory OCD but considered that MBS listing of this procedure may not be the best means of public funding. MSAC noted the department considers that given the service is estimated to be of low volume and is for patients with severe OCD, it may be better

suited to provide DBS in the public system where associated multidisciplinary team (MDT) and support services can provide integrated care.

Therefore, MSAC supported public funding of DBS for severe treatment-refractory OCD but considered it may not be appropriate for funding through the MBS and requested the department seek alternative public funding arrangements, following consultation with stakeholders.

4. Background

MSAC has not previously considered DBS for treatment-refractory OCD.

DBS is an established therapy for neurological conditions such as Parkinson's disease. The application seeks an amendment to the patient population under the following existing MBS items: 40851; 40852; 40854; 40856; 40858; 40860; 40862.

5. Prerequisites to implementation of any funding advice

DBS requires a deep brain stimulation system for the implantation of the device (ARTG ID 351630): The Medtronic Model B35200 Percept™ PC Neurostimulator with BrainSense™ is part of an active implantable device system for deep brain stimulation and sensing.

In addition, the Medtronic Model 3391 DBS Lead (ARTG ID 174469) is an implantable component of the multiprogrammable system-Reclaim DBS Therapy for OCD and is designed to electrically stimulate specific areas of the brain. It 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.

6. Proposal for public funding

The applicant is proposing 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 (as considered by PASC) are marked in blue and are identical in the descriptors, as described in Table 1 below.

Table 1: Presentation of amended MBS items

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40851 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: 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.) (Assist.)
Fee: $4,189.60 Benefit: 75% = $3,142.20

Abbreviations: MBS= Medicare Benefits Scheme

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

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40852 DEEP BRAIN STIMULATION (unilateral) subcutaneous placement of neurostimulator receiver or 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.) (Assist.)
Fee: $360.05 Benefit: 75% = $270.05

Abbreviations: MBS= Medicare Benefits Scheme

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

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40854 DEEP BRAIN STIMULATION (unilateral) revision or removal of brain electrode 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: $556.45 Benefit: 75% = $417.35

Abbreviations: MBS= Medicare Benefits Scheme

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

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40856 DEEP BRAIN STIMULATION (unilateral) removal or replacement of neurostimulator receiver or 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: $270.05 Benefit: 75% = $202.55

Abbreviations: MBS= Medicare Benefits Scheme

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

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40858 DEEP BRAIN STIMULATION (unilateral) placement, removal or replacement of extension lead 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: $556.45 Benefit: 75% = $417.35

Abbreviations: MBS= Medicare Benefits Scheme

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

Category 3 – THERAPEUTIC PROCEDURES
MBS item 40860 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: 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: $2,138.30 Benefit: 75% = $1,603.75

Abbreviations: MBS= Medicare Benefits Scheme

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

Abbreviations: MBS= Medicare Benefits Scheme
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. The intervention would only be provided in a hospital inpatient setting (public or private hospitals).

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, MBS items for unilateral procedures may be required for revision and replacement procedures. The explanatory notes of the MBS item descriptors could clarify this.

The intervention 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.

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.

The device is programmed 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.

Rarely (in approximately 2-5% of cases) an infection of the device necessitates hardware ex-plantation, treatment with antibiotics and reimplantation at a later date (Bernstein et al., 2019; Fytagoridis et al., 2016).

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 and non-rechargeable Medtronic battery is presently AUD $17,283 and AUD $13,592, respectively. 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 five patients will utilise DBS for OCD in the first year.

An overall breakdown of delivery of DBS is presented in Table 2.

Table 2: Approximate cost profile of DBS for treatment-refractory OCD

Item	Cost
MBS Item 40851 – Insertion of deep brain stimulation device by neurosurgeon	$4,340.45
MBS Item 40852 – Subcutaneous placement of pulse generator	$373.0
MBS Item 40858 – Placement of extension lead*	$576.50
MBS Item 40860 – Target localisation*	$2,215.30
MBS Item 40862 – Programming of DBS device = $207.75 (estimate 20 programming sessions to optimise stimulation settings	$4,155.00
Cost of DBS hardware estimated: • Neurostimulator IPG non-rechargeable x 50% patients = $6,796.00 ($13,592 each) • Neurostimulator IPG rechargeable x 50% patients= $9,927.50 ($19,855 each) • Recharger for the rechargeable IPGx 50% patients = $891.0 ($1,782.00 each) • Percept patient programmer= $1,264.00 • Sensight 0.5 mm Permanent Lead x 2= $8,240.00 • Sensight lead extensions x 2= $3,790.00 • Electrodes= $1,240.00 • Burr hole cover= $497.00 • Sterile MER Connectors and cables= $181.00 • Intraoperative accessories- Insertion tube= $158.00	$32,984.50
Total cost	$44,644.75[1]

Abbreviations: DBS= deep brain stimulation; IPG= implantable pulse generator; MBS= Medical Benefits Scheme

*MBS items 40858 and 40860 have each been billed once in this cost profile, resulting in a total cost of $44,644.75. However, these MBS items are for unilateral procedures and the proposed intervention is a bilateral procedure. The applicant has suggested that billing items 40858 and 40860 twice is more reflective of clinical practice. The implications of these revised costings have been explored in a supplementary analysis for the economic evaluation and are reported in

the financials section. 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. Although this cut-off value is not evidence based 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.

7. Population

One PICO set was used for the assessment of DBS for treatment-refractory OCD.

DBS for treatment-refractory OCD is proposed to be available for patients with 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.

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 (Malhi et al., 2022; Mosley et al., 2022).

DBS is considered an add-on technology for the small number of persons who remain highly treatment-refractory. The aim of DBS is to enhance OCD treatment, and patients are likely to require ongoing treatment with medication and psychotherapy.

DBS 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.

8. 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 (SSRIs and the tricyclic antidepressant clomipramine). These may be augmented with an atypical antipsychotic medication. According to the ratified PICO, 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 include items 300, 302, 304, 306, 308 (provision of outpatient care by a psychiatrist) and item 80100 (provision of focussed psychological care by a psychologist).

Patients who require more than 50 psychiatry attendance services in a calendar year, for example, in the case of intensive psychotherapy, would move to items 310, 312, 314, 316 or 318, which are items with a lowered rebate.

9. Summary of public consultation input

Consultation input was received from one professional organisation, two medical device manufacturers, and four State and Territory offices of the chief psychiatrist:

- Royal Australian and New Zealand College of Psychiatrists (RANZCP)
- Medtronic Australasia Pty Ltd (Medtronic)
- Abbott Medical (Abbott)
- 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.
    - The RANZCP stated that costs for DBS for OCD would align with the currently available item numbers for DBS in neurological disorders.
    - 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 to 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.

10. Characteristics of the evidence base

A total of 15 studies (total n = 286) met the inclusion criteria for assessing the safety and effectiveness of DBS of the subcortex plus standard care in patients with severe treatment-refractory OCD. All studies were small with sample size ranging from 4 to 70 participants. Seven studies included a short RCT component where active DBS stimulation was compared to sham stimulation, in addition to a longer phase where all study patients received long-term active DBS stimulation. The evidence also included two prospective cohort studies (n = 58), one retrospective cohort study (n = 15), and five (n = 131) case-series of patients receiving DBS as part of their care. They key features of the included evidence are summarised in Table 3.

There were numerous studies identified that did not meet the pre-specified PICO definition of severe treatment- refractory OCD, specifically patients failing a trial of at least three different selective serotonin reuptake inhibitors (SSRIs) plus clomipramine. From 15 studies included in the evidence base, 5 were from studies were patients failed a trail of at least 3 SSRIs + clomipramine, and 10 were from studies where patients failed a trail of at least 2 SSRIs + clomipramine. It was judged that the studies in the latter group were still applicable to the assessment due to illness severity. All studies were in adults aged 18 years or over with the mean age of participants in the included studies ranging from 36 to 48 years.

Table 3: Key features of the included evidence for deep brain stimulation of the subcortex standard of care vs. standard of care

References	N	Design/duration	Risk of bias	Outcome(s)*	Use in modelled evaluation~
3 SSRIs + clomipramine					
Abelson 2005	4	RCT, crossover DB (3 weeks on/off) + open phase	*High*[a] *Moderate*[b]	Adverse events OCD severity, depression, anxiety	Not used
Barcia 2019	7	RCT, crossover DB (3 months on/off)	*High*[a]	OCD severity	Not used

References	N	Design/duration	Risk of bias	Outcome(s)*	Use in modelled evaluation~
Goodman 2010	6	RCT (delayed start, 1 month) + open phase	*High*[a] *Moderate*[b]	Adverse events OCD severity, depression, anxiety, QoL	Not used
Mar-Barruita 2022	50	Cohort (prospective)	*Poor*[c]	Adverse events OCD severity, depression	Not used
Islam 2015	8	Case series	*Acceptable*[d]	Adverse events OCD severity	Not used
2 SSRIs + clomipramine					
Denys 2010	16	Open phase + RCT, DB (2 weeks on/off) + open phase	*High*[a]	Adverse events OCD severity, depression, Anxiety	Not used
Luyten 2016	24	RCT, crossover DB (3 months on/off) + open phase	*High*[a] *Serious*[b]	Adverse events OCD severity	Not used
Mallet 2008	16	RCT, crossover DB (3 months on/off)	*High*[a]	Adverse events OCD severity, depression	Not used
Mosley 2021	9	RCT, DB + open phase	*High*[a] *Serious*[b]	Adverse events OCD severity, depression	Not used
Charbades 2020	15 (new)	Prospective cohort, no control	*Poor*[c]	Adverse events OCD severity	Not used
Van der Vlis 2021	8	Retrospective cohort, no control	*Poor*[c]	Adverse events OCD severity, depression, anxiety, QoL	Not used
Denys 2020 (Graat 2021)	70	Case series	*Acceptable*[d]	Adverse events OCD severity, depression, anxiety, QoL, medication use, employment status	Not used
Farrand 2018	7	Case series	*Acceptable*[d]	Adverse events OCD severity, depression, anxiety	Not used
Greenberg 2010 (Greenberg 2006)	26	Case series	*Acceptable*[d]	Adverse events OCD severity, depression, anxiety	Not used
Huys 2019	20	Case series	*Acceptable*[d]	Adverse events OCD severity, depression, anxiety	Not used

Abbreviations: DB= double blind; HAM-A/D= Hamilton Scale for Anxiety/Depression; RCT= randomised controlled trial: SSRI= selective serotonin reuptake inhibitor; QoL= quality of life.

* Outcomes listed here are only outcomes of interest to the PICO for this clinical evaluation. The full list of outcomes reported by each study are described in Appendix B.

~ The Gadot et al. 2019 systematic review article was used.

[a] ROB 1.0 Cochrane Risk of Bias tool is rated per domain: low, unclear, high.

[b] ROBINS-I Tool assessment is out of: low, moderate, serious, critical, no information.

[c] Newcastle-Ottawa Scale (NOS) assessment is out of: good, fair, poor.

[d] The Canada Institute of Health Economics (IHE) Quality Appraisal Tool for Case Series (Interventional) assessment is out of: acceptable, high risk.

11. Comparative safety

No comparative safety data was available. All studies reported adverse events related to DBS treatment only. For clarity purposes adverse events were classified as surgery related, device related, or stimulation related in this report.

Surgery related adverse events

Serious and non-serious adverse events associated with the DBS surgery were reported in nine studies (total n = 157). Serious adverse events related to surgery included intracerebral haemorrhage, seizure, malposition of electrodes, malposition of pulse generator and infection. Haemorrhages were reported at an equal rate in two studies (Greenberg 2010, Mallet 2008): 1/13 (7.7%) and 2/26 (7.7%), respectively. Generalised tonic-clonic seizure occurred in 1/26 (3.8%) participants in one study Greenberg et al. (2010). Malposition of electrode was reported in two studies at rates of 6/70 (8.6%) in one (Denys et al., 2020; Mosley et al., 2021) and 1/9 patients (1.1%) in the other (Mosley et al., 2021). Malposition of pulse generator was observed in 2/70 (2.6%) patients in one study (Denys et al., 2020). Commonly reported non-serious adverse events included headaches, delirium and wound infection.

Device related adverse events

Device related adverse events were reported in seven studies (total n = 151). Breaking of the electrode or extension wire was reported in two studies and observed in 5/25 (25%) in Mar-Barrutia et al. (2022) and 2/13 (15.4%) in Greenberg et al. (2010). Other adverse events observed include feeling the pulse generator on the chest, infection of the pulse generator, as well as pulling or tightening of extension leads.

Stimulation related adverse events

Stimulation related adverse events were reported in 12 studies (n = 214). Adverse events associated with DBS stimulation were the most frequently reported adverse events but also most likely to be reversed through adjusting of the stimulation parameters. Frequently reported serious adverse events related to stimulation included hypomania, increased depression, suicide attempts or suicidal thoughts/ideations. Mallet et al. (2008) and Greenberg et al. (2010) reported severe hypomania in 3/13 (23%) and 1/26 (3.8%) patients, respectively. Hypomania was also a commonly reported non-serious stimulation associated adverse event observed in nine separate studies with rate ranging from 1/13 (7.7%) in Mallet et al. (2008) to 11/25 (44.0%) in Mar-Barrutia et al. (2022) and 4/8 (50%) in van der Vlis et al. (2021). Abelson et al. (2005); Goodman et al. (2010); Islam et al. (2015); Mar-Barrutia et al. (2022)

12. Comparative effectiveness

Fifteen studies reported changes in symptoms of OCD as assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). Overall, there appeared some improvement in Y-BOCS scores in patients who received DBS, compared to patients who received sham or no treatment (Table 4). An improvement in Y-BOCs scores was also observed over baseline scores when DBS was administered long-term.

In the RCTs, active DBS stimulation was not more effective in achieving a ≥ 35% reduction in Y-BOCS scores, compared to sham stimulation (RR 1.36 (95% CI 0.66, 2.08); p = 0.41; I^2 = 0%; 46 participants; 4 RCTs; very low certainty evidence). This finding may be limited by the short treatment duration (range 2 weeks to 3 months). Active DBS stimulation however, showed a difference in mean change in Y-BOCS scores at last follow-up, compared to sham stimulation

(MD -6.01 (95% CI -8.79, -3.22); p < 0.0001; I^2 = 27%; 103 participants; 6 RCTs; very low certainty evidence).

Data from studies with long-term DBS including the open phases of the RCTs (k = 4), cohort studies (k = 3) and case series (k = 5) all indicated that Y-BOCS scores decreased after DBS stimulation compared to baseline. Number of responders (≥ 35% Y-BOCS reduction) varied across studies, range: 7% to 78%.

The GRADE certainty of the evidence is *very low*, due to low-quality of the studies (high risk of bias, heterogeneity, too few events, very small sample sizes).

Summary of evidence for all outcomes is presented in Table 4.

Table 4: Summary of findings of DBS compared to standard of care or sham treatment in severe treatment-refractory OCD

Outcome	Participants Studies	Overall certainty of evidence	Risk of bias	Summary
Adverse events	N = 286 (7 RCTs, 3 cohort, 5 case series)	⨁⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c] *Acceptable*[d]	Surgery related SAEs included haemorrhages (7.7% in two studies), seizure (3.8% in one study), malposition of electrode or pulse generator (range from 2 studies: 1.1% to 8.6%). Common device related AE were breaking of electrode or extension wire, feeling pulse generator on the chest, infection of the pulse generator and tightening of leads. SAEs during stimulation included hypomania (3.8% and 23%, two studies), increased depression, suicide attempts or suicidal thought or ideations.
OCD severity (Y-BCOS)	N = 286 (7 RCTs, 3 cohort, 5 case series)	⨁⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c] *Acceptable*[d]	**6 trials from RCT phases:** • ≥ 35% reduction: little, non-significant difference favouring active DBS, RR 1.36 (95% CI 0.66, 2.08); p = 0.41; I^2 = 0%; 46 participants; 4 RCT) • Mean change at last follow-up: a difference favouring active DBS, MD -6.01 (95% CI -8.79, -3.22); p < 0.0001; I^2 = 27%; 103 participants; 6 RCT) **Remaining studies:** All studies indicated that OCD severity decreased after DBS stimulation compared to baseline. Number of responders (≥ 35% Y-BOCS reduction) varied across studies, range: 7% to 78%.

Outcome	Participants Studies	Overall certainty of evidence	Risk of bias	Summary
Depression	N = 162 (4 RCTs, 2 cohort, 4 case series)	⊕⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c] *Acceptable*[d]	All studies noted an improvement in the HAM-D, DASS-S, MADRS, and BDI scores for patients treated with active DBS compared to baseline.
Anxiety	N = 96 (2 RCTs, 1 cohort, 4 case series)	⊕⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c] *Acceptable*[d]	Small improvements in HAM-A. DASS-A, and STAI scores compared to baseline scores.
Suicide	N = 227 (5 RCTs, 2 cohort, 4 case series)	⊕⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c] *Acceptable*[d]	No obvious increase in suicide, suicidal thoughts and/or ideations because of DBS treatment.
Quality of life	N = 80 (2 RCTs, 2 cohort)	⊕⊙⊙⊙ Very low	*High*[a] *Serious*[b] *Poor*[c]	DBS showed a significant improvement in 'vitality' domain of SF-36, and showed some improvements in WHOQOL BREF and EQ-5D scales.
Medication and psychotherapy requirements	N = 120 (1 cohort, 1 case series)	⊕⊙⊙⊙ Very low	*Poor*[c] *Acceptable*[d]	No obvious differences between DBS and no DBS reported.
Employment	N = 26 (1 case series)	No judgement	*Acceptable*[d]	One study reported 60% had a positive change in school or work participation by 36 months.

Abbreviations: AE= adverse event; BDI= Beck Depression Inventory; CI= confidence interval; DASS-A/D= Depression/Anxiety Severity Scale; DBS= deep brain stimulation; EQ-5D= EuroQol-5Dimension Index; HAM-A/D= Hamilton Anxiety/Depression Scale; MADRS= Montgomery-Asberg Depression Rating Scale; MD= mean difference; N/n= number of participants; OCD= obsessive-compulsive disorder; RCT= randomised controlled trial; RR= risk ratio; SAE= serious adverse event; SF-36= short form survey for quality of life; STAI= State-Trait Anxiety Inventory; Y-BOCS= Yale-Brown Obsessive-Compulsive Scale; WHOWOL-BREF= World Health Organization; Quality of Life Scale.

⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect.
⊕⊕⊕⊙ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
⊕⊕⊙⊙ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
⊕⊙⊙⊙ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

[a] ROB 1.0 Cochrane risk of bias tool is rated per domain: low, unclear, high.
[b] ROBINS-I Tool assessment is out of: low, moderate, serious, critical, no information.
[c] Newcastle-Ottawa Scale (NOS) assessment is out of: good, fair, poor.
[d] The Canada Institute of Health Economics (IHE) Quality Appraisal Tool for Case Series (Interventional) assessment if out of: acceptable or high risk.

Clinical claim

The use of DBS to the subcortex results in superior effectiveness compared with continued standard of care in patients with severe treatment-refractory OCD.

The use of DBS to the subcortex results in inferior safety compared with continued standard of care in patients with severe treatment-refractory OCD.

The confidence of this conclusion is low. However due to the invasive nature of the DBS treatment and the limited prospects of future high quality RCTs or comparative non-RCTs for a

highly invasive surgical therapy (such as DBS), the evidence from lower certainty evidence may need to be viewed as the highest level of evidence that will be available for the assessment.

13. Economic evaluation

A clinical claim of superior effectiveness and inferior safety for DBS in combination with continued pharmacotherapy and psychotherapy compared to the standard of care for patients with treatment-refractory OCD was determined in Section 2, albeit on a weak evidence base. As one economic study identified in the literature search reported utilities for the target population related to the DBS procedure (Moon et al., 2017), a cost-utility analysis was conducted which was in line with the suggested economic evaluation in the PICO (1727 Final PICO, page 12). However, the clinical claim deviates from the PICO where a clinical claim of superior effectiveness and non-inferior safety was determined. It is noted that PASC considered a clinical claim of inferior safety to be more appropriate given the inherent risks of infection, device complications, and invasive nature of the surgery, compared to continued clinical management (1727 Final PICO, page 13).

The economic evaluation was developed using a Markov model with four health states including DBS with a rechargeable IPG, DBS with a non-rechargeable IPG, survive and background mortality. The primary outcome calculated in the model was cost per QALY which, based on Departmental clinical advice and time to realise all health outcomes, was estimated over a ten-year time horizon, and sourced from the main economic study (Moon et al., 2017). The costs of standard of care (pharmacotherapy and psychotherapy) are not considered in the model as these costs are realised in both the intervention and comparator arms and therefore are offset. Instead, the standard of care arm considered only QALY gains.

It is noted that utility improvement calculation in Moon et al., 2017 relies on the assumption that there is an approximate 45% reduction in the mean YBOCS score as defined by a meta-analysis. As such, it is implicitly assumed in the model that this assumption upholds. This is in line with the literature, such as Gadot et al., 2022 that reported a 47% reduction in YBOCS score post DBS at last follow up across 249 patients. Additionally, a meta-analysis of reduction in YBOCS scores from baseline to follow up post DBS from studies identified in the clinical evaluation reported an estimated overall 42% reduction in YBOCS score (Figure 11), which is approximately in line with the assumption in Moon et al., 2017. Additionally, the model assumed a 58% response to treatment based on pooled clinical results which is consistent with Moon et al., 2017. Therefore the assumptions behind the utility improvement calculation in Moon et al. 2017 (regarding response rate to treatment and reduction in YBOCS scores) used in the economic model can be regarded as in line with the avaliable literature on effectiveness of DBS for the treatment of OCD.

Due to a lack of available data for the Australian severe treatment-refractory OCD population who undergo DBS, transition probabilities and resource use was determined using a range of literature sources, Departmental clinical advice and past MSAC submissions with DBS as the intervention. Cost components considered in the model include MBS, prothesis and hospital costs which were sourced from MBS online, the Prothesis List and AR-DRG hospital data.

It is noted that 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, as this registry will be conducted post the completion of the assessment, the planned registry is not considered as a component of the economic evaluation.

A summary of the key components of the economic model is detailed in the table below.

Table 5: Summary of the economic evaluation

Component	Description
Perspective	Health care system perspective
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
Prior testing	NA[a]
Comparator	Continued high dose pharmacotherapy combined with repeated courses of psychotherapy (Standard of Care)
Type(s) of analysis	Cost-utility analysis (CUA)
Outcomes	Outcomes: - Quality-adjusted life years (QALYs)
Time horizon	10 years
Computational method	Markov model
Generation of the base case	Modelled: - Identify clinical pathway from clinical evidence. - Conduct a systematic review of other economic evaluations. - Identify inputs including costs, transition probabilities and utilities. - Verify inputs with clinical experts. - Develop, run and review TreeAge model.
Health states	Health states: - DBS surgery (non-rechargeable) - DBS surgery (rechargeable) - Survive - Background mortality
Cycle length	Annual
Transition probabilities	A range of sources were used to inform the transition probabilities in the model, with the majority being sourced from the main economic model (Moon et al., 2017). All sources are outlined in Table 36.
Discount rate	5% for both costs and utilities as per MSAC Guidelines
Software	TreeAge Pro and Microsoft Excel

Abbreviations: CUA= Cost-utility analysis DBS = Deep Brain Stimulation; OCD = Obsessive Compulsive Disorder; QALY = Quality-adjusted Life Year; SOC = Standard of Care; SSRI= selective serotonin reuptake inhibitors; Y-BOCS = Yale-Brown Obsessive Compulsive Scale

[a] Prior testing includes an assessment prepared by the DBS psychiatrist for the mental health tribunal. The tribunal reviews the suitability of the candidate for DBS and their capacity to consent voluntarily to DBS. As clinical experts note that no agreed cost is attached to this assessment, prior testing is not considered as a cost in the intervention arm.

The cost impacts of expanding the current MBS items for DBS to include patients with severe treatment-refractory OCD are presented below as disaggregated and aggregated results by health state and cost component, including MBS, State and Territory (hospital costs) and prothesis item costs.

The results demonstrate that the overall costs of DBS are higher than standard of care, which is evident as procedural, hospital and prothesis costs associated with this procedure are substantial. It is noted that whilst the rechargeable IPG health state absorbs the majority of costs (60%), the long-term benefits from fewer IPG revision or replacement procedures in this health state is likely to result in less complications and long-term costs.

A summary of disaggregated and aggregated cost impacts of DBS for severe treatment-refractory OCD patients over ten years are detailed the table below.

Table 6: Health care resource items: disaggregated summary of cost impacts in the economic evaluation

Type of resource item	Subtype of resource item	DBS arm	SOC arm	Incremental cost	% of total incremental cost
MBS costs	Rechargeable	$18,251	$0	$18,251	15%
	Non-rechargeable	$11,375	$0	$11,375	10%
	Total cost	**$29,626**	**$0**	**$29,626**	**25%**
Hospital costs	Rechargeable	$13,258	$0	$13,258	11%
	Non-rechargeable	$10,348	$0	$10,348	9%
	Total cost	**$23,606**	**$0**	**$23,606**	**20%**
Prothesis costs	Rechargeable	$40,069	$0	$40,069	34%
	Non-rechargeable	$25,340	$0	$25,340	21%
	Total cost	**$65,409**	**$0**	**$65,409**	**55%**
Total costs	Rechargeable	$71,577	$0	$71,577	60%
	Non-rechargeable	$47,063	$0	$47,063	40%
	Total cost	**$118,641**	**$0**	**$118,641**	**100%**

Abbreviations DBS= Deep brain stimulation; MBS= Medicare Benefits Schedule; SOC= Standard of care.

In conclusion DBS is a costly, yet effective solution for patients with severe treatment-refractory OCD. It is evident that the costs for DBS are significant compared to the standard of care, with an ICER of $891,509 per QALY gained. However, as previously stated, severe treatment-refractory OCD is associated with significant societal costs such as productivity loss, which have not been assessed in the DCAR model. Therefore, it is important to consider these costs in decision making (see Other relevant information for further detail).

The incremental cost per QALY is presented in the table below.

Table 7: Results of the economic evaluation

Parameter	DBS	SOC	Increment
Costs	$118,641	$0	$118,641
QALYS	5.85	5.72	0.13
Incremental cost per QALY gained			**$891,509**

Abbreviations DBS= Deep brain stimulation; QALY= quality-adjusted life year; SOC= standard of care.

The model was most sensitive to changes in the proportion of patients that respond to DBS, complication rates, years to battery replacement and utility improvements post DBS response. A summary of the key drivers of the economic are detailed below.

Table 8: Key drivers of the model

Description	Method/Value	Impact Base case: $891,509 /QALY gained
Proportion of responders to DBS	The proportion of responders was identified through a pooled analysis of literature conducted in the clinical evaluation section of the submission. This input relied on study data with high degree of bias and therefore was tested in a sensitivity analysis. The base case input (58%) was varied by ±12%. The lower limit tested (46%) had the largest impact on the incremental utilities gained from DBS, with a reduction of incremental 0.03 QALYs, resulting in an overall increase in the ICER by 30%. It is noted that as only the responder arm in the DBS patient pathway gains utilities post DBS surgery, it is expected that the higher proportion of people who respond to DBS is associated with greater QALYs gained.	*Medium, favours the comparator (SOC)* *Decreasing the proportion of responders increased the ICER to $1,182,469/QALY gained.*
Complication rates	Complication rates post DBS implantation and battery replacement were tested as these inputs were sourced from the main economic study which was based on Korean and UK populations. Both inputs were varied by ±20% from the base case. The upper limit for complications post DBS implantation and lower limit for complications post battery change resulted in the largest amendments from the base case results in terms of cost and QALYs gained, however the maximum change to the results was only 11%	*Minor, favours the comparator (SOC)* *Increasing the complication rate post initial DBS implantation increased the ICER to $979,619/QALY gained.* *Minor, favours the intervention (DBS)* *Decreasing the complication rate post battery change decreased the ICER to $839,732/QALY gained.*
Years to battery replacement	Multiple reports for years to battery change for non-rechargeable IPGs were identified through literature and clinical opinion. As such two inputs were tested in scenario analyses; the first using the average time to replacement identified by the literature (2 years), and the second identified in the PICO (5 years). Overall, there was a maximum change to base case results of 10% where replacement occurs after two years. This is because battery replacement is associated with high costs, including additional prothesis costs, and additional complications.	*Medium, favours the comparator (SOC)* *Decreasing the average years to battery replacement for non-rechargeable IPGs increased the ICER to $982,650/QALY gained.*
Utilities	The utility values sourced from the main economic study are highly uncertain as they apply to a Korean-based population. Additionally, the utilities calculated were based on YBOCS scores reported in a 2015 meta-analysis. As the calculations used to estimate the base case and post DBS utilities were not provided, it is difficult to validate this method. As such a range of utility values were tested based on updated meta-analysis and a pooled analysis from studies identified in the clinical evaluation. Three out of four scenarios used the base case utility and all scenarios had varied post DBS response utilities as per the literature. The maximum change to base case results was identified where there was an increase in the utility improvements of responders and non-responders post DBS by 0.22 and 0.06 QALYs.	*High, favours the intervention (DBS)* *Increasing the utility gained post DBS procedure for responders and non-responders by 0.22 and 0.06 utilities, respectively, decreased the ICER to $483,716/QALY gained.*

Abbreviations: DBS= Deep brain stimulation; IPG= implantable pulse generator; ICER = incremental cost-effectiveness ratio; PICO= population, intervention, comparator and outcome; QALY = quality-adjusted life year; SOC= standard of care.

The results of the univariate sensitivity analyses for inputs that had a greater than 10% impact on the ICER are summarised below. These include response rates, base case utility for DBS patients and QALYs improvements after DBS. An additional analysis was conducted following expert clinical advice regarding whether MBS items 40858 and MBS item 40860 should be applied once or twice during initial DBS surgery. The applicant confirmed that billing each of these items twice is more consistent with clinical practice. MBS item 40858 is the unilateral placement, removal or replacement of the extension lead, and MBS item 40860 is the unilateral DBS target localisation for the insertion of a single neurostimulation wire. When including these items twice during the initial DBS surgery, the ICER increases by 2.4%.

Table 9: Sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	Source
Proportion of patients that respond to DBS (base case value 58%)				
Lower limit: 46%	$118,641	0.10	$1,182,469	Calculated
Upper limit: 70%	$118,641	0.17	$715,462	Calculated
Utility improvements post-DBS response (base case value 0.16)				
Utility improvements after response (0.21)	$118,641	0.18	$648,659	(Alonso et al., 2015)
Utility improvements after response (0.22)	$118,641	0.25	$483,716	(Gadot et al., 2022)
Base case utility and utility improvement (base case 0.71, 0.16)				
Base case utility and utility improvement for OCD patients (0.28, 0.22)*	$118,641	0.19	$616,434	(Ooms et al., 2017)
Corrected MBS surgical items (utilisation of two instances each for MBS items 40858 and 40860 for initial surgery)				
Corrected MBS surgical items	*$121,433*	*0.13*	*$912,489*	*Calculated*

ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year.
*The starting utility estimate is updated to 0.28 and the utility improvement estimate is updated to 0.22 as defined by Ooms et al., 2017

14. Financial/budgetary impacts

Net financial impact to the MBS

Following the applicant advice regarding whether MBS item 40858 and MBS item 40860 were applied once or twice during initial DBS surgery, the cost of the initial surgery used in the financial estimates varies from that used in the economic modelling. While the economic estimates included the impact of applying MBS item 40858 and 40860 twice each as a sensitivity analysis, the financial model has included this as the corrected base case. For transparency the original base case estimates and corrected base case can be found in the main body of this report. MBS item 40858 is the unilateral placement, removal or replacement of the extension lead, and MBS item 40860 is the unilateral DBS target localisation for the insertion of a single neurostimulation wire. When including these items twice during the initial DBS surgery, the financial impact to the MBS increases by 5.3% over six years compared to the scenario where these items are only used once each during the initial surgery.

The assessment found that the overall additional cost to the MBS over six years would amount to approximately $1. million (Table 10). The majority of this cost is attributable to the index DBS surgery which would include the pre-operative assessment ($119,673), the implantation ($897,570) and follow-up ($370,834).

Table 10 Impact to the MBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
Base case: No. of people receiving the initial surgery	5	10	15	20	25	30	105
Cost to MBS							
DBS eligibility & Pre-operative Assessment	$5,699	$11,397	$17,096	$22,795	$28,494	$34,192	$119,673
Initial DBS surgery*	$42,741	$85,483	$128,224	$170,966	$213,707	$256,449	$897,570
Follow up after initial surgery	$17,659	$35,318	$52,976	$70,635	$88,294	$105,953	$370,834
Post-surgical revision of electrodes#	$827	$1,655	$2,482	$3,310	$4,137	$4,964	$17,375
Post-surgical revision of Leads#	$337	$673	$1,010	$1,347	$1,683	$2,020	$7,070
Replacement of IPG#	$0	$0	$0	$6,631	$13,263	$19,894	$39,788
Removal of IPG#	$356	$712	$1,068	$1,424	$1,780	$2,136	$7,476
Total Cost to MBS	$67,619	$135,238	$202,857	$277,107	$351,357	$425,608	$1,459,786

Abbreviations: DBS= deep brain stimulation; IPG= implantable pulse generator; MBS= Medicare Benefits Schedule

* Calculated using the corrected base case, applying MBS items 40858 and 40860 twice each for the initial DBS surgical procedure.

Note that applying MBS items 40858, 40860 and 40854 (unilateral revision or removal of brain electrode) twice in a proportion of patients may also be required for the revision, replacement and removal procedures. This has not been applied yet to the base case. Currently these MBS items 40858, 40860 and 40854 have been applied once each.

The financial implications to the Australian healthcare budget resulting from the proposed listing of deep brain stimulation (DBS) for severe treatment-refractory obsessive-compulsive disorder (OCD) are summarised in Table 11. The total cost of providing DBS to treatment-refractory OCD population to the Australian health budget (inclusive of costs to the MBS, Prescribed List of Medical Devices and Human Tissue Products and State/Territory hospitals) is approximately $6.7 million over six years. The maximum cost is attributable to the index DBS surgery of $6.2 million.

Of the various healthcare budgets included in the total cost, the maximum cost is attributed to cost of prostheses— $3.6 million, followed by the cost to the MBS — $1.5 million and finally to the hospitals— $1.6 million.

It should be noted an epidemiological approach was not adopted as this method derived unrealistically high estimates of utilisation, and as such the utilisation reported in the PICO Confirmation was used, however this source is also uncertain.

Table 11 Total costs of all DBS services to healthcare budgets

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
Cost of Index DBS procedure*#	**$294,713**	**$589,425**	**$884,138**	**$1,178,851**	**$1,473,564**	**$1,768,276**	**$6,188,967**
Cost of surgery for revision of electrodes	$4,161	$8,321	$12,482	$16,642	$20,803	$24,964	$87,372
Cost of surgery for revision of leads	$6,738	$13,475	$20,213	$26,951	$33,689	$40,426	$141,492
Cost of surgery for IPG replacement	$0	$0	$0	$36,638	$73,277	$109,915	$219,830
Cost of surgery for IPG removal	$1,298	$2,597	$3,895	$5,193	$6,491	$7,790	$27,263
Total costs of all DBS services	$306,909	$613,819	$920,728	$1,264,275	$1,607,823	$1,951,371	$6,664,925
Total costs of all DBS services- by healthcare budget							
Cost to MBS	$67,619	$135,238	$202,857	$277,107	$351,357	$425,608	$1,459,786
Cost to prostheses list	$168,606	$337,212	$505,818	$691,414	$877,011	$1,062,607	$3,642,668
Cost to hospital	$70,684	$141,369	$212,053	$295,754	$379,455	$463,156	$1,562,471
Total cost of DBS	$306,909	$613,819	$920,728	$1,264,275	$1,607,823	$1,951,371	$6,664,925

Abbreviations: DBS= deep brain stimulation; IPG= implantable pulse generator; MBS= Medicare Benefits Schedule

* Calculated using the corrected base case, applying MBS item 40858 and 40860 twice each for the initial DBS surgical procedure.

Note that applying MBS items 40858, 40860 and 40854 (unilateral revision or removal of brain electrode) twice in a proportion of patients may also be required for the revision, replacement and removal procedures. This has not been applied yet to the base case. Please see Section 3.2.12 for details of costings.

This assessment is based on estimating total cost of DBS, which equates to the net financial impact on the Australian Government Health budget. The usual standard of care is pharmacotherapy and psychotherapy. Therefore, given that the intervention is a surgical procedure, the financial model includes the costs of items and services that would otherwise not be utilised in the absence of DBS. The overall costs described in this section indicate the net incremental costs to the MBS, the hospitals and the prostheses list, compared with the total cost of standard of care.

Net financial impact to other health budgets

The assessment also accounted for the financial impact on the Prescribed List of Medical Devices and Human Tissue Products – costs that will be borne by private health insurance or patient (out-of-pocket expenses), and impact on hospital budgets through hospital stays. The total cost to the Prescribed List of Medical Devices and Human Tissue Products over 6 years is estimated to be approximately $3.6 million, while that to the hospitals is estimated to be approximately $1.6 million (Table 80). Notably the highest costs to both the prostheses list as well as the hospitals are attributable to the index DBS surgery (prostheses costs $3.5 million and hospital costs $1.3 million). This high cost is expected given the initial surgery will be associated with a whole array of prostheses not required for the follow-up surgeries, which will be very few in any case.

Table 12:Cost to the prostheses list and the hospitals, associated with DBS procedure for treatment-refractory OCD

Procedures	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
COST TO PROSTHESES LIST							
Initial/ index DBS surgery	$164,923	$329,845	$494,768	$659,690	$824,613	$989,535	$3,463,373
Post-surgical revision of electrodes	$467	$934	$1,401	$1,868	$2,336	$2,803	$9,809
Post-surgical revision of leads	$3,217	$6,433	$9,650	$12,866	$16,083	$19,299	$67,547
Replacement of IPG	$0	$0	$0	$16,990	$33,980	$50,970	$101,940
Removal of IPG	$0	$0	$0	$0	$0	$0	$0
Total cost to prostheses list	**$168,606**	**$337,212**	**$505,818**	**$691,414**	**$877,011**	**$1,062,607**	**$3,642,668**
COST TO HOSPITALS							
Initial DBS surgery	$63,691	$127,383	$191,074	$254,765	$318,457	$382,148	$1,337,517
Post-surgical revision of electrodes	$2,866	$5,732	$8,598	$11,464	$14,331	$17,197	$60,188
Post-surgical revision of leads	$3,185	$6,369	$9,554	$12,738	$15,923	$19,107	$66,876
Replacement of IPG	$0	$0	$0	$13,017	$26,034	$39,051	$78,102
Removal of IPG	$942	$1,885	$2,827	$3,769	$4,711	$5,654	$19,788
Total cost to hospitals	**$70,684**	**$141,369**	**$212,053**	**$295,754**	**$379,455**	**$463,156**	**$1,562,471**

Abbreviations: DBS= deep brain stimulation; IPG= implantable pulse generator; OCD= obsessive-compulsive disorder

The scenario analyses indicated that the overall health budget was the most sensitive to change in utilisation estimates, i.e., the uptake of DBS procedure (Table 13). It is noted that the current estimate of utilisation of 5 people in the first year, is uncertain, but these were considered conservative given the status of DBS availability in Australia for OCD patients. The sensitivity analyses found that increasing the annual uptake of DBS by 25% would increase the overall expenditure by approximately $1.7 million, while employing the epidemiological approach would lead to a cost increase of greater than $10 million. Notably, the steep increase in the costs associated with increased utilisation of DBS, are associated with the cost of prostheses. The impact on MBS costs and hospital costs were affected to a lesser extent.

The budget impact analysis indicates that one-off costs associated with the initial DBS surgery comprise the maximum cost, most of which are attributable to the prostheses. Prostheses costs will be borne by the patient or the insurance company, and while these do not impact the Commonwealth government healthcare budget directly, it will have cost implications, should the prostheses be funded by the State/Territory. Further, in cases where a patient is unable to afford the considerable prostheses costs, they might not opt for the surgery at all. This high cost might result in inequity of access, which in turn could lead a decrease in the uptake over the years.

Table 13 Overall results of sensitivity analyses on overall financial impact on the Australian Government health budget

	Base case*		Sensitivity analysis*		
Sensitivity analysis	**Parameter**	**Cost to Australian health budget**	**Parameter**	**Cost to Australian health budget**	**Difference in total costs**
1. Utilisation projected using epidemiological approach	5 to 30 index DBS surgeries, total 105 over 6 years	$6,664,925	44 to 46 index DBS surgeries, total 268 over 6 years	$17,417,590	$10,752,665
2. Utilisation increased by 25% across the 6-year horizon	5 to 30 index DBS surgeries, total 105 over 6 years	$6,664,925	6 to 38 index DBS surgeries, total 131 over 6 years	$8,380,856	$1,715,931
3. Decreased IPG battery life#	3-8 users receive battery replacement, year 4 onwards, total 15 over 6 years	$6,664,925	3-10 users receive battery replacement, year 3 onwards, total 25 over 6 years	$6,826,134	$161,209
4. Higher proportion of users receive rechargeable battery#	50% users receive rechargeable battery, so 15 users receive battery replacement over 6 years	$6,664,925	85% receive IPG with rechargeable, and 15% receive IPG with non-rechargeable battery, so 5 users receive battery replacement over 6 years	$6,518,372	-$146,553
5. Higher number of pre-surgical psychiatric attendances	n=1 attendance pre-surgically for the index procedure	$6,664,925	n=5 attendances pre-surgically for the index procedure	$6,764,653	$99,728

Abbreviations: DBS= deep brain stimulation; IPG= implantable pulse generator; MBS= Medicare Benefits Schedule; OCD= obsessive-compulsive disorder.

* Calculated using the corrected base case, applying MBS item 40858 and 40860 twice each to the initial DBS surgical procedure.

Note that applying MBS items 40858, 40860 and 40854 (unilateral revision or removal of brain electrode) twice in a proportion of patients may also be required for the revision, replacement and removal procedures. This has not been applied to the base case. Please see Section 3.2.12 for details of costings.

15. Other relevant information

It is important to note DBS's impact on equity of access, and the ease of use of the equipment for patients receiving the surgery.

Given that only a few centres, located in metropolitan areas, in Australia offer DBS for severe treatment-refractory OCD, access to these centres may be a major barrier to receiving DBS for people living in rural or regional Australia. To improve access, follow-up appointments can be offered to rural and remote patients through telehealth—a feature not considered in the current assessment. In the absence of remote programming, the decision makers should consider the incidental costs to the patients. Secondly the implantable pulse generator (IPG) with rechargeable batteries, will be recharged at least once daily or weekly, manually. Such frequency for recharging may not be suitable for patients with disabilities, especially those with cognitive deficits. Even so studies have shown the cost effectiveness of rechargeable devices primarily due to fewer replacements of the IPG device. But the decision to fund the technology needs to also consider the ease of use and patients' attitudes towards the technology.

Overall, the societal perspective is notably important in this scenario. The proposed surgery could prove effective in significantly decreasing the symptoms of OCD and increasing productivity of patients with this condition. While DBS appears to be expensive, its advantages may outweigh the costs given the paucity of treatment options for severe treatment-refractory OCD.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- There is GRADE assessed low-quality evidence to support the superiority claim of DBS for the management of patients with severe treatment-refractory OCD.
- MSAC may wish to consider whether the cut-off Y-BOCS score to define serious OCD in the proposed item descriptor is necessary, given patients will be assessed by a DBS unit and an independent mental health review tribunal to qualify for consideration of the intervention.
- The safety of the intervention is inferior to its comparator due to the invasive nature of the treatment.

Economic issues:

- The ICER is higher than would normally be considered cost-effective; however, limited treatment options remain for this group of people who have failed conventional treatment.
- ESC noted that the utility values were a key driver of the model, and that using a 0.21 utility improvement (rather than 0.16 used in the base case) resulted in an ICER of $483,716/QALY.
- The ICER should be taken in context of factors not included in the model that may have a positive effect, such as improvements in productivity and potentially higher costs in the comparator arm for standard of care.

Financial issues:

- Severe treatment-refractory OCD is a rare disease and therefore the number of proposed treatments per year is likely to be low.
- The financial impact is uncertain but expected to be low given constraints on surgery and expertise. Most of the financial impact will be to the PL.

Other relevant information:

- Because of the limited centres offering this treatment, even if MBS funding is provided for this intervention, inequity of access to the intervention may remain.

ESC discussion

ESC noted that this application from Dr Philip Mosely requested Medicare Benefits Schedule (MBS) listing for deep brain stimulation (DBS) of the subcortex for the treatment of severe treatment-refractory obsessive–compulsive disorder (OCD).

ESC noted that this is a new application for this purpose. DBS is an established therapy for neurological conditions such as Parkinson's disease. The applicant is seeking an amendment to the patient population so that those with severe treatment-refractory OCD can access the therapy. It is considered an add-on therapy for persons within this population. The DBS therapy is aimed at enhancing the pre-existing treatment modalities, which will likely need to continue after the DBS treatment.

ESC noted some consultation feedback which suggested other therapies which could be potential comparators, namely repetitive transcranial magnetic stimulation (rTMS) and invasive ablative neurosurgical procedures. Some feedback noted the need for an option for people who have exhausted all other treatments because of the societal benefits associated with improving the quality of life for this group of patients. Feedback also noted that "severe treatment-refractory OCD" is not a defined medical condition, and that the limited data available highlights the need for more research in this area.

ESC noted that seven existing MBS items will need to be modified if this intervention is supported (40851, 40852, 40854, 40856, 40858, 40860, 40862). There are no proposed changes to the fee. However, ESC noted that some of the existing MBS items are for unilateral placement, but DBS for severe OCD requires bilateral placement and therefore some of the items will need to be billed twice for the initial procedure, using the Multiple Operation Rule (MOR). ESC noted the newly proposed bilateral reprogramming items proposed by the department. It is proposed that these items will have a fee equivalent to 150% of the unilateral items and could be used in either an inpatient or outpatient setting. Alternatively, the department also proposed a separate item could be placed in "Category 2- Diagnostic Procedures and Investigations" for use in the outpatient setting and would therefore avoid application of the MOR. ESC considered that creating a new parallel set of MBS item numbers for this condition would also allow for more accurate monitoring of utilisation, as would the registry proposed by the applicant.

ESC noted that the proposed changes to the MBS item descriptor includes reference to Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) threshold scores, which were cited in the literature. ESC noted the department's concern that including the Y-BOCS score in the item descriptors as potential cut-off points for treatment eligibility may subjectively restrict access to some patients who may benefit, given patients are also assessed for eligibility by a DBS unit and mental health tribunal. However, ESC considered that the inclusion of the Y-BOCS score provides some objectivity to the referral of patients to the DBS unit and mental health tribunal. ESC considered that MSAC may wish to consider whether the inclusion of specific medication and therapies that must be trialled prior to the intervention in the item descriptors would limit applicability to developments in the clinical care of severe OCD.

ESC noted that 10 of the studies included in the Department-Contracted Assessment Report (DCAR) included in their eligibility criteria that patients must have trialled at least 2 different selective serotonin reuptake inhibitors (SSRIs) plus clomipramine, which did not meet the definition of severe treatment-refractory OCD specified in the PICO (patients trialing at least 3 SSRIs plus clomipramine). ESC agreed with the assessment group that including these patients was acceptable due to the patients meeting the criterion for illness severity.

ESC noted that the clinical trial evidence comprised small numbers of patients and was overall of low quality. Seven small studies (total n = 82) included a blind randomised controlled trial (RCT) phase where active DBS was compared to sham DBS. ESC agreed with the pre-ESC response that it is difficult to obtain high-quality evidence for a rare condition and with such an invasive procedure. ESC noted the lack of patient numbers meant the evidence would always be considered low quality when using the GRADE assessment tool.

ESC noted that no comparative safety data against standard care were available. All studies reported adverse events (AEs) related to the DBS surgery and treatment only. The most commonly reported AEs were related to stimulation (hypomania, depression, suicide attempts or thoughts), while other AEs included surgery- and device-related complications. ESC considered the safety of DBS to be inferior to its comparator.

ESC noted that, overall, there appeared to be some improvement in Y-BOCS scores after DBS treatment, and that the scores appeared to improve from baseline in the long term.

ESC therefore considered that the clinical claim of superior effectiveness and inferior safety was supported by very low-certainty evidence due to small sample sizes, lack of long-term comparative data, too few events and long recruitment periods. ESC noted that while confidence in this safety and effectiveness claim is low, the invasive nature of the treatment alongside the limited prospects of high quality RCTs or comparative non RCTs may also temper this assessment, However, ESC recommended that the role of less-invasive procedures such as rTMS and the ability to gather more evidence for this comparator should be considered.

ESC noted that the economic model was a cost-utility analysis using a Markov model with four health states (DBS surgery [non-rechargeable], DBS surgery [rechargeable], survive and background mortality). A range of sources were used to inform the transition probabilities in the model, with most sourced from the main economic model[2]. The total cost of the procedure was $44,645 per patient, which generated an incremental cost-effectiveness ratio (ICER) of $891,509 per quality-adjusted life year (QALY) gained. ESC noted the sensitivity analyses conducted by the assessment group, which corrected the cost of surgical items required for MBS items 40858 and 40860 (using bilateral costings), generated an ICER of $912,489/QALY. ESC noted that the Moon et al. (2017) study had used a lower incremental cost of USD31,000 and a higher incremental QALY of 0.9, which produced an ICER of USD34,462/QALY (~AUD54,000) in the UK. ESC considered that, given that the same inputs were used for utilities and the same time horizon was used, the different ICERs were probably driven by the difference in mortality applied. ESC noted that the model did not capture any differences in health outcomes or costs when an individual in the model transitions from severe to not severe OCD, however ESC considered it plausible that this would improve the utility of the intervention for responders. ESC noted the assessment found no comparative evidence of difference in suicide or suicidal thoughts and/or ideation due to DBS treatment. However, ESC considered that there may be evidence for utility changes due to the reduced risk of attempted suicide based on OCD severity in the literature for the general population versus the target population of this intervention. ESC advised that additional modelling might be useful to provide an indication of $ICER/QALY based on plausible assumptions about the reduction in risk of attempted suicide due to the intervention, informed through the literature.

ESC noted that the utility values were a key driver of the model, and that using a 0.21 utility improvement (rather than 0.16 used in the base case) resulted in an ICER of $483,716/QALY.

Overall, ESC considered that the economic evaluation was based on uncertain inputs due to the low-quality trial evidence, but that DBS appeared to be effective but costly. ESC considered that additional costs in the standard of care arm that were not accounted for – such as losses in productivity of the patient population and the costs and reductions in quality of life to family and carers – could improve the ICER but were out of scope of the model. Thus, ESC considered that the ICER should be interpreted taking into account that there was no allowance for the wider societal impact of the intervention in the economic model.

ESC noted that the comparator arm cost was offset in the economic model which compared the costs of the intervention plus standard of care in the intervention arm and the costs of standard care only in the comparator arm (so that in practice the costs of the intervention in the intervention arm were compared to zero costs in the standard of care arm). However, ESC noted that costs in the standard of care arm could be higher if hospitalisation or other surgery was the outcome of standard of care – in which case the model would result in a lower net cost of the

[2] Moon et al., 2017. The cost-effectiveness of deep brain stimulation for patients with treatment-resistant obsessive-compulsive disorder. *Medicine (Baltimore). 1*(27), e7397

intervention than what has been assumed by simply offsetting the same standard of care cost in both arms.

ESC noted that as per the previous discussion, while taking account of reductions in risk of attempted suicide due to use of the intervention might also lead to a lower ICER, differences in risk of attempted suicide between patients in the intervention and standard of care arms were not statistically significant and were therefore not included.

ESC also noted that the technology used in the RCTs was older than that available now and used non-rechargeable batteries. Current updated technology uses rechargeable batteries, but with higher upfront costs. ESC noted that battery replacement is costly ($22,000 for non-rechargeable and $28,000 for rechargeable), and that these costs drive the ICERs as well. Moreover, ESC noted that the time horizon of 10 years in the model would have further increased the sensitivity of the ICER to these battery replacement costs. ESC considered the cost of complications post-surgery may have been overestimated in the DCAR.

ESC noted the financial implications of listing. Although the surgery is costly, the low utilisation keeps costs to the MBS to $67,619 in year 1 to $425,608 in year 6. ESC noted that main cost drivers are the pre-operative assessment, the implantation and the follow-up assessment. ESC also noted that there were significant costs to the Prescribed List of Medical Devices and Human Tissue Products and to hospitals – the total costs of DBS to all healthcare budgets were $306,909 in year 1 and $1,951,371 in year 6. ESC noted that severe treatment-refractory OCD is a rare disease and considered the number of proposed treatments per year likely to be low.

ESC noted that only three facilities in Australia (located in Brisbane and Melbourne) had the capacity to carry out DBS for psychiatric conditions. ESC noted that legislation in New South Wales and the Northern Territory prohibits brain surgery for mental illness, but patients could be referred to another state for treatment. However, ESC considered that these existing limitations on supply mean that even if this intervention were to be MBS funded there would still be highly limited access to the procedure.

ESC noted the pre-ESC response stated the latest DBS devices have the capacity for remote programming; however, the Department clarified the current MBS items do not apply to this technology.

17. Applicant comments on MSAC's Public Summary Document

We are pleased with the overall conclusion of the report, that public funding of deep brain stimulation (DBS) for treatment-refractory obsessive-compulsive disorder (OCD) is warranted. We would like to raise several issues in the context of the recommendation that the Commonwealth should create an alternative public funding mechanism to the Medicare Benefits Schedule (MBS) to fund the small number of eligible cases of DBS for OCD.

1. The MBS already funds DBS for other low-prevalence neurological conditions, such as dystonia and essential tremor, as well as higher prevalence conditions like Parkinson's disease. These patient groups are currently successfully treated in both the public and private settings. The suggestion that a different funding scheme will need to be created for the treatment of severe OCD appears discriminatory to those with a psychiatric illness.
2. There is a lack of clarity regarding the proposed alternative funding model, the process which would be followed and whether the responsibility for funding would lie with the Commonwealth or State Governments. It is difficult to envisage all state governments funding follow-up specialist services for this patient group given the small numbers. Equally, it is unlikely that one or two state governments would agree to fund public services which operate nationally. Finally, it should be noted that, to our knowledge. no state funded

specialist mental health service for obsessive compulsive disorder (at any level of severity) exists in Australia. People with obsessive compulsive disorder are rarely seen within public mental health services and even more rarely provided with ongoing treatment.

3. The report recommends that DBS be provided only as an extension of a public hospital program and that there are concerns regarding the ability of the private system to deliver such a program. Research by our group and others has shown that the most important factor determining a positive outcome after DBS for neurological and psychiatric disorders is accurate placement of the stimulating electrodes and skilled titration of electrical stimulation postoperatively. Accordingly, in the public summary document, the Royal College of Psychiatrists advises that surgery should occur in highly specialised centres, and the report acknowledges that only a small number of centres have the requisite skills to perform this treatment. Two world-class specialist teams exist in Australia (in Melbourne and Brisbane) and have been able to successfully treat patients from all states and territories in Australia. There remain significant resourcing and funding issues for both programs given the lack of State or MBS funding for this treatment. The availability of MBS item numbers would significantly help address this funding vacuum.

In summary, we believe that funding of neurological but not psychiatric conditions through the MBS, where evidence exists to support their effectiveness, is inequitable and unjust for those suffering with chronic, debilitating mental illnesses. Funding of this treatment through the MBS will benefit some of the sickest individuals in Australian society. Moreover, provision of this treatment in the private sector is no barrier to coordinating and receiving multidisciplinary allied health care, as demonstrated by Australian groups already providing this treatment.

Note, our previous responses to the DCAR and ESC reports can be found here:

https://qdocs.qimrberghofer.edu.au/mosley/

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website