NICE National Institute for Health and Care Excellence

HEALTHTECH ASSESSMENT PROGRAMME

Digital therapy for chronic tic disorders and Tourette syndrome
Draft guidance – Comments

Committee date: 20 February 2025

THEME: Evidence for Orbit

Comment number	Name and organisation	Section number	Comment	NICE Response
1	Consultee 1 University of Nottingham NIHR MindTech HealthTech Research Centre (HRC)- ORBIT team.	Has all of the relevant evidence been taken into account?	Response from ORBIT developers: NIHR MindTech HealthTech Research Centre (HRC) EFFECTIVENESS: We respectfully disagree with the committee's view that impact of ORBIT on people's symptoms and health-related quality of life is uncertain and represents an evidence gap. In our view, where uncertainty lies is not in the ORBIT trial data where the evidence of long-term clinical and cost-effectiveness is clear and compelling, but in the transferability of these benefits and level of engagement with the intervention when ORBIT is delivered within routine NHS care. This should be the focus of a RWE study and data collection. The results of the HTA-funded ORBIT trial published in Lancet Psychiatry doi: 10.1016/S2215-0366(21)00235-2 (primary outcome and 6-month follow-up) and Journal of Child Psychology and Psychiatry doi: 10.1111/jcpp.12921 (18-month follow-up) provides clear evidence of clinically meaningful reduction in tic severity and improvement in quality of life for the ERP intervention compared to a strong active comparator of psychoeducation, which were sustained up to 18-months follow-up. Specifically, we found evidence of greater improvement in the ERP group	Thank you for your comment. The EAG stated that the main concern is with uncertainty around long-term quality-adjusted life year (QALY) benefits beyond 18 months and the transition probabilities in the economic modelling were only available at two time points, which created uncertainty about whether the effect of the severity of tic has plateaued. The committee considered the consultation comments with the clinical and economic evidence for ORBIT, external assessment group (EAG) report and input from clinical experts and patients. The committee

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			for young person-reported tic-specific quality of life (C&A-GTS-QoL) at both time points (12 months = −5.79; 95% CI: −10.28 to −1.30: 18 months = −9.00; 95% CI: −13.98 to −4.01). After adjustment for tic severity at baseline and site, the analysis revealed that the ERP intervention reduced YGTSS-TTSS (tic symptom severity) by 2.64 points (95% CI: −4.48 to −0.79) with an effect size of −0.36 (95% CI: −0.61 to −0.11) after 12-month follow-up and by 2.01 points (95% CI: −3.86 to −0.15) with an effect size of −0.27 (95% CI -0.52 to −0.02) after 18-month follow-up, compared with the psychoeducation group. The ORBIT trial represents both the largest and longest follow-up of ERP behavioural tic therapy in the literature to date. The extended naturalistic follow-up to 18-months can be regarded as essentially a per-protocol parallel group analysis as very few participants in either arm received other active interventions. The committee recommended an extended follow-up of 24 months in a self-controlled RWE study. The value of this approach is unclear given the likely low retention, existing evidence of stability of effects between 6- and 18-month follow-up and proposed lack of a comparison group – which would make it impossible to draw conclusions in a RWE study about clinical or cost-effectiveness where it is not possible to isolate the impact of the study intervention from other influences. With regards to health-economic related measure of quality of life (CHU9D) the data from the ORBIT trial identified that there is a significant relationship between the YGTSS (tic severity reduction) and preference-based health related quality of life as measured using the CHU9D – there is a disutility of –0.003 (95% CI –0.003 to –0.002) for every 1 point change on the YGTSS [Hollis et al. 2023; doi.org/10.1111/jcpp.13756]. Given these published findings from the within-trial health economic	acknowledged that it would be costly to collect data at 24 months. The committee concluded further analyses of data collected in the ORBIT-UK trial is sufficient to reduce the uncertainty. The impact that ORBIT has on people's symptoms should be measure using the Yale Global Tic Severity Scale, the Clinical Global Impression Score – Improvement, and ideally the Goal Based Outcomes sale. Details are noted in section 2.1 of the evidence generation plan for ORBIT.

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			analysis – we are unclear why the committee has interpreted these findings as uncertain, and the justification and purpose of collecting the CHU9D in a self-controlled RWE study. In conclusion, we believe the trial results do not support the committee's interpretation of an evidence gap, on the contrary they provide robust evidence regarding the positive impact of the ORBIT ERP intervention on both tic severity and quality of life. Hence, our focus in the RWE study will be to benchmark clinical outcomes (YGYSS and C&A-GTS-QoL), intervention engagement and user experience against the trial results at 3 and 6 months where greatest change is expected to occur. SUB-GROUPS: The committee requested further analysis of clinical and cost-effectiveness in different sub-groups. 1.Co-morbidities: First, regarding the potential impact of clinical co-morbidity on intervention outcomes - we have already explored this within the ORBIT trial with respect to co-morbid ADHD and anxiety where the greatest clinical uncertainty lies about potential moderating effects. Specifically, we conducted unplanned post hoc analysis to investigate whether the ERP intervention had a differential effect on participants with or without comorbid anxiety or ADHD. The analysis reported in Hollis et al (2021 Lancet Psychiatry) shows that there was no evidence to support co-morbidity moderating outcomes. We also explored this further in our process evaluation which explored possible moderators for the effectiveness of ORBIT. These findings also showed that co-morbidity did not have any impact on outcome. The committee raised the potential impact of co-morbid mood disorders, OCD and ASD. First, from our clinical experience and the literature – there is no a priori reason to expect effect moderation with these co-	The committee noted that there is limited evidence for children and young people with diagnosed comorbidities, people from different ethnic backgrounds, adult population and people with severe tic disorders. More information is needed on the efficacy of ORBIT in these different subgroups to further support committee decision making.

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			morbidities. We would be interested in the evidence the committee is drawing on to make these predictions of potential moderation. One of the advantages of providing an e-coach in ORBIT is that it supports motivation and engagement, which we agree can be challenging in young people with low mood. Second, from a practical standpoint, a much larger trial (i.e. 1000s of participants), or comparative RWE study would be needed for an adequately powered analysis of interactions (moderator) effects. Third, regarding clinical representativeness of the ORBIT trial population, it was a pragmatic trial with no exclusions of any of the co-morbidities of interest to the committee. Finally, regarding engagement and uptake, we also know that generally children with ASD are likely to engage well with digital therapies (Scarcella et al, 2023)., and in our clinical practice young people with ASD and tics engage well with a structured ERP intervention. 2. Ethnicity: Turning to the question of the ethnic/ demographic diversity of the ORBIT sample – we have explored this and found it broadly to be in line with the UK population [Hollis et al. Health Technol Assess 2023;27(18). https://doi.org/10.3310/CPMS3211]. Data from NHS Digital shows that 13% of the UK population belongs to an ethnic minority group (ONS, 2023): https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity /articles/changeovertimeinadminbasedethnicitystatisticsengland2016to2020/2022-05-23 Data from the ORBIT trial broadly reflects this, with 12% of participants from an ethnic minority group. In the survey NICE commissioned as part of this review the sample was: 1,508 people of whom 83% had received	

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			a diagnosis of tic disorders had 88.6% from White British backgrounds, 4.9% other White and 2.8% White mixed. Other backgrounds were in very small percentage (under 1% each). Hence, to explore clinical- and cost-effectiveness of the intervention in non-white populations with tic disorders (prevalence 1%-3%) would require a sample size of at least 10,000 which is neither feasible nor fundable. From our experience, the main question regarding ethnicity and digital interventions is whether the design and content is culturally appropriate and acceptable and supports engagement. We believe this is best explored qualitatively in ethnically diverse focus groups of young people, however, we still note that access to these groups will take time. 3. Severity: The committee questioned the differential efficacy of the ORBIT ERP intervention in young people with more severe tics. We respectfully disagree with the committee that this represents an evidence gap. ORBIT trial inclusion criteria did not exclude participants with severe tics. Hence, the ORBIT trial recruited a moderately severe symptomatic sample with a mean YGTSS-TTSS of 28.4 (SD 7.7). This level of baseline tic severity is higher than reported in other trials of tic behavioural therapy and is similar to that found in our specialist tic clinic in Nottingham. Crucially, in response to the committee's concerns, our analysis showed that tic severity did not impact the efficacy of ORBIT [Khan et al. 2022: Journal of Behavioral and Cognitive Therapy; doi.org/10.1016/j.jbct.2022.02.005]. QUALITATIVE WORK: Our existing research involved 20 in-depth interviews of young people and their carers who participated in the ORBIT trial, the findings of which are reported in Khan et at al. (2022). Our plan is to conduct further qualitative interviews (n=20) to assess the	The committee welcomes the additional studies from the ORBIT-UK trials. More information on how using the technology would affect

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			user experience of the new ORBIT platform rolled out in a NHS clinical service in the current i4i Product Development Award (PDA) study. HEALTH ECONOMICS: The ORBIT trial provided in depth evidence on the impact of on resource use [Hollis et al. Health Technol Assess 2023;27(18)]. There was no significant impact of the ORBIT intervention on resource use. Lower YGTSS scores though are associated with lower levels of resource use, but only for specialist CAMHS services. Tic severity had no significant relationship with any other resource use. We have also recently published a paper looking at this in greater detail which may not have been available to the committee [Hall et al; BMJ Ment Health 2024;27:1–6.https://mentalhealth.bmj.com/content/27/1/e301241.abstract]. We respectfully disagree with the committee's interpretation that there is an evidence gap here to be filled. We have no reason to believe that any further evidence collected on this domain would generate useful data that differs, or adds value, from that collected in our trial and would be likely to be less robust. We would ask the committee to clarify more specifically what they feel is missing or remove this recommendation. We are unclear what the value of adding more information on healthcare use would add over the data we already have – please see the point raised above and the papers: Hollis et al. 2023; [https://doi.org/10.1111/jcpp.13756] and Hall et al. 2024 [https://doi.org/10.1136/bmjment-2024-301241]. In ORBIT, we saw no difference in the use of other resources by tic severity, this is in line with what you might expect, it is unlikely that tics	resource use in the NHS, during and after implementation, is needed to help the committee understand the technology's cost effectiveness.

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			would result in hospital inpatient admissions and that tics themselves are unlikely to result in A&E attendance, except in the odd case.	
2	Consultee 1 University of Nottingham NIHR MindTech HealthTech Research Centre (HRC)- ORBIT team.	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	We have highlighted above areas where we disagree with the committee's interpretation of evidence gaps with respect to our published clinical trial and qualitative data on clinical and cost-effectiveness of the ORBIT intervention. We believe that the summaries should more closely reflect the published data.	Thank you for your comment. Please see the response to comment 1 above.
3	Consultee 1 University of Nottingham NIHR MindTech HealthTech Research Centre (HRC)- ORBIT team.	Are the recommendations sound and a suitable basis for guidance to the NHS?	WITH REFERENCE TO DIAGNOSIS: We will be collecting routine clinical data on diagnoses, both in our n=20 i4i PDA and any future RWE. However, we believe that outside a clinical study (in RWE) requiring patients to have received a formal tic disorder diagnosis would acts a major barrier to accessing ORBIT given the extremely long waits and current lack of capacity in the NHS for specialist tic diagnostic assessments. As clinical specialists we are aware that CAMHS and Paediatric sites are often not providing a formal diagnosis (which is also common practice across other neurodevelopmental disorders) but are able to identify impairing tic symptoms. ORBIT is not a diagnostic intervention and cannot be used to confirm diagnosis. To limit ORBIT to only patients who have a confirmed diagnosis would be to withhold the intervention to many young people. We ask that the committee consider modifying this request to align more with the proposed intended use for ORBIT which is: "patients who have been referred with clinically significant primary tic symptoms requesting	Thank you for your comment. The committee noted that ORBIT is not a diagnostic intervention and cannot be used to confirm diagnosis and diagnosis criteria for tic disorder in real world evidence will limit intervention to formally diagnosed cases excludes many young people due to NHS capacity constraints. However, experts addressed that expanding the criteria to include clinically significant tic symptoms could result in misdiagnosis and potential harm

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			behavioural intervention tics". WITH REFERENCE TO CO-MORBIDITIES: We have developed a clinician referral form that will be part of the ORBIT platform, this collects information on possible/diagnosed co-morbidities. We will deploy this in any future RWE study. However, it should be acknowledged that co-morbid diagnoses associated with tic presentations are often under-reported by clinicians and thus the diagnostic sensitivity of a RWE study is unlikely to match that of the trial, where we employed structured research diagnostic assessments (e.g. DAWBA) to determine the likely presence of these conditions. As already noted, we have already explored (and excluded) the potential moderating effects of co-morbid anxiety disorder and ADHD in the ORBIT trial. WITH REFERENCE TO ADULTS: The ORBIT ERP intervention has been specifically developed for children and young people and the evidence-base applies only to this population. While it may appear attractive to extend use to adults- we believe this would be premature as the priority should be adoption and roll-out for children and young people in the NHS. Adaptation and testing in adults would require separate funding and would distract from the proposed RWE in children and young people, to support early intervention at the age when tics typically first present. We would welcome a future funding call to explore this further, but this would not be achievable in the 2-year time frame or without further research and funding. We would ask that the committee remove the request to extend RWE to adults within the current ORBIT evidence generation plan. WITH REFERENCE TO 24MTH FOLLOW-UP: As mentioned, we have a planned n=20 clinical study to assess usability of the new platform and	to patients. So, the committee concluded that the digital therapy should be targeted at individuals with a formal diagnosis of tic disorder or Tourette's syndrome. Please see the response to comment 1 above.

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			benchmark real-world engagement and clinical outcomes against the trial data. In this study, we are following patients up to 3 months post baseline. We believe it is critical to undertake our planned n=20 study to ascertain the usability of the platform before moving to extended real-world roll-out. We would not anticipate increasing the length of follow-up in this study as this would delay our ability to move to a larger RWE study in more sites. However, we would plan our RWE study to follow participants up to 6 months after the intervention. Given that the greatest clinical change occurs during the first 6-months and that there is a plateauing of effects from 12-months to 18-months, it is not clear what extra value (with considerable extra cost) follow-up to 24-months will add (see Figure 7 in Hollis et al.2023 https://doi.org/10.3310/CPMS3211). As the effect remains the same over the longer time horizon this means that the ICER will also remain the same as the key clinical impact has already happened. The 18-month trial data was largely per-protocol (i.e. the majority of participants did not access other behavioural therapies or start new tic medications during this time) and the trial data has the benefit of having a control group. Following participants up to 24 months in a RWE is likely to result in significant data loss and bias in responders. It also adds significant burdens onto clinical sites and patients. We would request that the committee remove the request to follow up to 24 months as the costs outweigh any benefits. WITH REFERENCE TO QUALITATIVE DATA: While we agree with the committee that further qualitative work would be useful – it needs to answer specific questions and provide new insights to support adoption. Our n=20 clinical study (commencing 2025) will aim to interview all participants (parents/young people) and thus be able to gather a	

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			reasonable data set on the usability and acceptability of the new ORBIT platform. We will ensure that our interview topic guide is guided by the questions/points the NICE report raises. However, we have concerns about the feasibility/practicality of continuing to collect qualitative data in a larger RWE study at different NHS sites. We would anticipate that our further RWE would be in the form of service evaluation rather than research. To ask participating sites to interview families would add significant burden to them. An alternative would be for our research team to conduct the interviews, but this would then require REC/HRA approval and add significant costs/time to our team, without funding to deliver this. We would like to ask the committee whether the additional qualitative work we have planned in our n=20 clinical study would be sufficient or whether this would require continuing in our RWE with additional unfunded costs/burden to local sites. WITH REFERENCE TO FURTHER HEALTH ECONOMIC DATA: We agree with the study design proposed by NICE for evaluating the intervention implementation. However, we would not consider this necessary or sufficient for health economic analysis, as we know we can see an improvement at 6 months regardless. We would ask the committee to reflect that our existing trial health economic data is very robust and superior to what might be gained if we continued to collect similar health economic data using a self-controlled RWE study design. Finally, we would like to highlight our recent paper (which the committee may not have seen) that provides additional data on the health economic benefits of ORBIT that may address some of the points raised in the report: Hall et al. 2024 [https://doi.org/10.1136/bmjment-2024-301241]	

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			WITH REFERENCE TO A SELF-CONTROLLED STUDY DESIGN: we do not feel this is an appropriate study design for evaluating the independent effects of an intervention for tic disorders using a measure such as the YGTSS without a comparator condition. Tic disorders are often characterised by natural fluctuations in tic severity over time causing significant variation in YGTSS scores over time. These fluctuations might be independent and unrelated to the intervention and could confound the results. However, in a RWE a within subject self-controlled design could used to benchmark clinical change against pre-existing ORBIT trial data at a group level and also allow the addition of self-reported real-world outcomes such as the CORC Goal Based Outcome (GBO) measure and clinician-rated measures of improvement such as the Clinical Global Impressions -improvement (CGI-I) scale which was used in the ORBIT trial.	
4	Consultee 1 University of Nottingham NIHR MindTech HealthTech Research Centre (HRC)-ORBIT team.	Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?	SEVERITY: The ORBIT trial inclusion criteria did not exclude participants with severe tics. We consider the ORBIT use case to be as first line widely accessible behavioural treatment for tics in a stepped approach to care, regardless of tic severity. Hence, we would continue to include patients with severe tics in future RWE studies. We would ask the committee to revise their interpretation that there is an evidence gap regarding the impact of ORBIT on more severe tics. Firstly, the ORBIT trial reached a moderately severe symptomatic sample with a mean YGTSS-TTSS of 28.4 (SD 7.7), which is more severe than previous published studies and corresponds to tic severity seen in our Nottingham clinical service. Secondly, we would also ask that the committee acknowledge our trial data which demonstrated that tic severity did not impact the efficacy of	Thank you for your comment. Please see the response to the comment 1 above.

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			ORBIT: Khan et al. 2022: Journal of Behavioral and Cognitive Therapy; [doi.org/10.1016/j.jbct.2022.02.005]. https://www.sciencedirect.com/science/article/pii/S2589979122000142#sec0130 ETHNICITY: We acknowledge that patients presenting with tics being seen by CAMHS or Paediatric services are predominately White British. Data from our Tourette's clinic in Nottingham serving a population of >1m in Nottingham and Nottinghamshire) shows that 1% of the patients identify as Black and 2% as Asian. On a national scale, we also acknowledge that this data is extremely hard to gather, data from NHS Digital (obtained by our study team) showed between January 2021-January 2022, ethnicity was not recorded in 80% cases. ONS data shows that 13% of the UK population belongs to an ethnic minority group (www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity/articles/changeovertimeinadminbasedethnicitystatisticsengland2016to2020/2022-05-23). Our data from ORBIT broadly reflects this. In ORBIT our ethnicity was: 88% White, 6% mixed, 3% Asian. In the survey NICE commissioned as part of this review the sample was: 1,508 people of whom 83% had received a diagnosis of tic disorders had 88.6% from White British backgrounds, 4.9% other White and 2.8% White mixed. Other backgrounds were in very small percentage (under 1% each). We suggest this adds further evidence that the ORBIT trial population is in line with NICE survey and is representative of people being seen by	

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			clinical services. We would ask the committee to acknowledge the clinically representative nature of the ORBIT trial sample within a UK context. We will continue to record ethnicity in any RWE study. However, we do not believe it is practicable or meaningful to collect a sufficiently large sample to explore with adequate statistical power comparative clinical and cost-effectiveness in different ethnic groups. We would ask that the committee modify their recommendations in light of this.	
5	Consultee 1 University of Nottingham NIHR MindTech HealthTech Research Centre (HRC)-ORBIT team.	Are there any other relevant ongoing studies that address the evidence gaps?	Our n=20 clinical study and NIHR i4i PDA award will address some of these gaps, but others will require a separate RWE study. As part of our NIHR i4i PDA we are planning a small scale (n=20) clinical study to test the usability of the new platform commencing mid/late 2025. This platform has embedded measures that we anticipate using in our wide scale roll-out, including the YGTSS, C&A-GTS QoL and the generic Goal Based Outcomes (GBO) measure. The clinical study evaluates tests the usability/acceptability of the platform and adherence to the intervention in real-world clinically referred population as well as the acceptability of these measures and be used in our future real-world evaluation (RWE) study. ADDITIONAL POINTS: We would like to ask when the committee proposes the 2-year time frame for RWE should commence? We respectfully ask the committee to acknowledge that we are currently in the first year of an NIHR i4i PDA award to support the production of an NHS-ready and compliant ORBIT product. At present, we do not have the ORBIT platform “live” and available for real world roll-out and evaluation. We anticipate the platform being ready by June/July 2025. We had	Thank you for your comment. The committee noted that existing research for ORBIT involved 20 in-depth interviews of young people and their carers in the ORBIT trial. The committee welcomes the company conducting further qualitative interviews (n=20) to assess the user experience of the new ORBIT platform rolled out in an NHS clinical service in the current i4i Product Development Award (PDA) study by mid-2025.

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			initially proposed in our PDA that the n=20 clinical study to explore the usability of the platform would not commence until Nov 2025. However, we would be willing to bring this forward to as close to when the platform is ready as feasible. We have already been proactive in writing the clinical study protocol to ensure this is possible. The clinical study is required in order to understand the usability of the platform (beta testing). We would not be willing to go to RWE before establishing the usability of this platform first and removing any 'bugs'. We ask that our time frame for starting the two-year evidence generation plan commences after the end of clinical study and when we have an appropriate RWE generation plan designed and funded (we would anticipate this starting in 2027).	

THEME: Evidence for Neupulse

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6	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Has all of the relevant evidence been taken into account?	Partially - Psychoeducation is not widely available. Processes are being developed as Neupulse expands and prepares for launch to support uses through set up and use. This is a requirement within ISO 13485. Our clinical trial showed that the device is effective without a formal diagnosis Stephen Jackson's research group at the University of Nottingham were	Thank you for your comment. The committee noted that the anticipated use of Neupulse is not restricted to people with a clinical diagnosis of tic disorders or Tourette syndromes. However, the committee

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			funded by the MRC to directly investigate the effects of Neupulse stimulation on the most common conditions that co-occur with Tourette syndrome, i.e., OCD, ADHD, and generalised anxiety disorder (GAD). These studies demonstrated that Neupulse stimulation significantly reduced the symptoms of OCD (Cohen's D = 0.76, t-value = 2.73, p-value < 0.02) and GAD (Cohen's D = 0.52, t-value = 2.2, p-value < 0.05). Data available on request.	emphasised that the use of Neupulse should involve supervision from healthcare professional and be used following a formal diagnosis of tic disorder or Tourette's syndrome. Further evidence is needed about the clinical impact and potential adverse effects of the technology in people without a clinical diagnosis. NICE encourages the company to submit relevant studies for future consideration.
7	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	No. Limited information available on cost to the NHS. Clinical effectives - see our comments on documents.	Thank you for your comment. The EAG stated that there is good evidence relating to NHS costs for specific tic severity health states available from the ORBIT study. The EAG would have preferred to have access to all resource use and costs (not just CAMHS) by health state for the economic modelling. Costs of the Neupulse intervention are commercial in confidence and have been incorporated within

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				the economic model consistently with the information provided by the company.
8	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Are there any other relevant ongoing studies that address the evidence gaps?	Yes. See comments on Table 1 in Evidence Generation Plan.	Thank you for your comment.
9	Consultee 2 Neurotherapeutics Ltd (Neupulse)	1 1 Purpose of this document	NIHR or other funding would be required in order for Neupulse to generate the evidence requested in the plan.	Thank you for your comment. NICE acknowledges that further data collection requires additional funding, and that in some cases this will not be feasible.
10	Consultee 2 Neurotherapeutics Ltd (Neupulse)	1 1 Purpose of this document	Neupulse would welcome more discussion with NICE over the data collection and what data is essential.	Thank you for your comment. NICE's evidence generation team will contact all manufacturers included in the final guidance following publication. There will be an opportunity to discuss further details around evidence generation then.

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11	Consultee 2 Neurotherapeutics Ltd (Neupulse)	1 1 Purpose of this document	My understanding of this design would be a case-control study. Patients assigned to receive Neupulse or treatment as usual. Patients would be matched ideally for age, sex, tic severity, and maybe similar co-occurring condition profile.	Thank you for comment. The EAG stated that a case-control study is not the optimal design for assessing the effectiveness of Neupulse compared to treatment as usual. A longitudinal, prospective cohort study is proposed in the plan rather than a case-control study as it is minimising confounding factors. NICE's Real World Evidence framework describes the benefits of different study designs in the absence of a randomised control trial. It highlights that "Case-control studies conducted within existing database studies are generally not recommended because they use less information than cohort studies (Schuemie et al. 2019)."
12	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Clinical effectiveness compared with NHS standard care	YGTSS is not a suitable method for assessing the online effects of stimulation. This entirely fails to comprehend the rationale for the use of the Neupulse device.	Thank you for your comment. The committee agreed that information about the impact that the technology has on people's symptoms should be

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				recorded using the Yale Global Tic Severity Scale total scores, the Clinical Global Impression Score – Improvement, and ideally the Goal Based Outcomes scale. Please see details in section 2.1 of the evidence generation plan for Neupulse.
13	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Clinical impact of Neupulse in different subgroups	Our clinical trial data confirmed that there was no difference in tic severity between those participants with a formal diagnosis and those without a formal diagnosis of TD. This is entirely understandable given the difficulty that most people encounter in obtaining a diagnosis and accessing treatment. Our data indicate that there was no difference in the effectiveness of Neupulse stimulation between those with and those without a diagnosis.	Thank you for your comment. The committee agreed that further evidence is needed about the clinical impact and potential adverse effects of the technology in people without a diagnosis. However, the committee emphasised that the use of Neupulse should involve supervision from healthcare professional and be used following a formal diagnosis of tic disorder or Tourette's syndrome. There is limited evidence on the clinical efficacy of Neupulse in people with severe tic disorders. The committee was advised that tic severity may be more stable in adults than in children and

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				young people, enabling data analyses that could support future decisions around the user population. NICE encourages the company to submit relevant studies for future consideration.
14	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Clinical impact of Neupulse in different subgroups	Our data confirms that Neupulse stimulation significantly reduces anxiety in individuals with generalised anxiety disorder (Cohen D = -0.52, t = -2.2, $p < 0.05$).	Thank you for your comment. The EAG cannot find these data in the Maiquez et al. publication. NICE encourages the company to submit relevant studies for future consideration.
15	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Clinical impact of Neupulse in different subgroups	The participants in our clinical trial had moderate to severe tics. Furthermore, the more severe their tics at baseline the larger the reduction observed with Neupulse stimulation.	Thank you for your comment. NICE appreciate that the company's comment is aligned with the data provided. However, it should be noted that numbers are small and should be interpreted cautiously.
16	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Longer-term data on the clinical impact of Neupulse	The rationale for using the Neupulse device is that it delivers a significant reduction in tics on demand, at the push of a button. It is designed to reduce tic during stimulation. It was not intended to produce a cure or to have long lasting effects. Instead, it should be considered as a safe, non-invasive, analog of deep brain stimulation insofar as it reduces tics during stimulation.	Thank you for your comment. This aligns with EAG's approach to modelling Neupulse, which assumes that the intervention remains effective only while it is

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				actively in use. Committee noted that the Neupulse should be considered as safe as deep brain stimulation, but due to a lack of evidence showing this the committee could decide that further evidence was needed on the longer- term effects of the technology.
17	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.1 Longer-term data on the clinical impact of Neupulse	Does this mean follow-up with use of the device for 3 months?	Thank you for your comment. Section 2.1 of the evidence generation plan for Neupulse has been amended to clarify that “Follow ups should be recorded at 3 and 6 months after commencing or ongoing use of the intervention, and ideally at 12 and 18 months.”.
18	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.2 2.2 Evidence that further supports committee decision making	Our data shows that Neupulse stimulation significantly reduces ADHD symptoms (Cohen's D = -0.76, t = -2.73, $p < 0.02$) and OCD symptoms (Cohen's D = -0.76, t = -2.73, $p < 0.02$) and generalised anxiety (Cohen's D = -0.52, t = -2.02, $p < 0.05$)	Thank you for your comment. Please see the response to comment 14.
19	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.1 3.1 Evidence gaps and ongoing studies	No evidence is incorrect. Our clinical trial data confirmed that there was no difference in tic severity between those participants with a formal diagnosis and those without a formal diagnosis of TD. This is entirely understandable given the difficulty	Thank you for your comment. NICE has amended section 3.1 table 1 of the evidence

Comment number	Name and organisation	Section number	Comment	NICE Response
			that most people encounter in obtaining a diagnosis and accessing treatment. Our data indicate that there was no difference in the effectiveness of Neupulse stimulation between those with and those without a diagnosis. Our data show that Neupulse stimulation significantly reduces ADHD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and OCD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and generalised anxiety (Cohen's D = -0.52, t = -2.02, p < 0.05)	generation plan for Neupulse, the level of evidence available for the clinical impact of Neupulse has been changed from “no evidence” to “limited evidence”. The EAG cannot find these data in the Maiquez et al. publication. NICE encourages the company to submit relevant studies for future consideration.
20	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.1 3.1 Evidence gaps and ongoing studies	QOL data is available upon request but is not available in the public domain yet. clinicaltrials.gov results are pending publication.	Thank you for your comment. NICE will consider all newly available studies at the end of the evidence generation period.
21	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.1 3.1 Evidence gaps and ongoing studies	Our data show that Neupulse stimulation significantly reduces ADHD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and OCD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and generalised anxiety (Cohen's D = -0.52, t = -2.02, p < 0.05)	Thank you for your comment. Please see response to comment 14 above.
22	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.1 3.1 Evidence gaps and ongoing studies	We have limited information on the current NHS resources and costs	Thank you for your comment. NICE advice and NHS partnerships may be able to facilitate data collection for these utilities.
23	Consultee 2 Neurotherap	3.1 3.1 Evidence gaps	Do you mean people with and without a diagnosis or severity of tics?	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
	eutics Ltd (Neupulse)	and ongoing studies		Section 3.1 of the evidence generation plan for Neupulse regarding the evidence gaps and ongoing studies for clinical impact of Neupulse in different subgroups, refers to the subgroups specified in section 2.2 of the evidence generation plan for Neupulse. This includes people with and without a diagnosis, and people with severe tic disorders.
24	Consultee 2 Neurotherap eutics Ltd (Neupulse)	3.1 3.1 Evidence gaps and ongoing studies	Our data show that Neupulse stimulation significantly reduces ADHD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) OCD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and generalised anxiety (Cohen's D = -0.52, t = -2.02, p < 0.05)	Thank you for your response. Please see response to comment 14 above.
25	Consultee 2 Neurotherap eutics Ltd (Neupulse)	3.3 3.3 Evidence collection plan	My understanding of this design would be a case-control study. Patients assigned to receive Neupulse or treatment as usual. Patients would be matched ideally for age, sex, tic severity, and maybe similar co-occurring condition profile. We might get several UK clinics to collaborate. Once we have regulatory approval, then no need for MHRA. would be suitable for NIHR funding.	Thank you for your comment. The longitudinal, parallel cohort methodology was proposed to minimise selection and confounding bias, which may be more difficult to control for a case-control study design. More information can be found in NICE's decision support unit technical support document 17.
26	Consultee 2 Neurotherap	3.4 Baseline information	The YGTSS measures tic severity of a period of 7 days. This measure is therefore not appropriate for measuring changes in tic severity/frequency during stimulation compared to immediately before stimulation or	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
	eutics Ltd (Neupulse)	and patient outcomes	immediately after stimulation. We would need to design a questionnaire measure that could be used to assess tic severity before, during and after Neupulse stimulation.	The committee noted that the Yale Global Tic Severity Scale total scores severity scale is not the best tool to capture long-term quality of life data. Information about the impact that the technology has on people's symptoms should be recorded using the Yale Global Tic Severity Scale total scores, the Clinical Global Impression Score – Improvement, and ideally the Goal Based Outcomes scale.
27	Consultee 2 Neurotherap eutics Ltd (Neupulse)	3.4 Baseline information and patient outcomes	The YGTSS measures tic severity of a period of 7 days. This measure is therefore not appropriate for measuring changes in tic severity / frequency during stimulation compared to immediately before stimulation or immediately after stimulation. We would need to design a questionnaire measure that could be used to assess tic severity before, during and after Neupulse stimulation.	Thank you for your comment. Please see response to comment 26 above.
28	Consultee 2 Neurotherap eutics Ltd (Neupulse)	5 5 Minimum evidence standards	The clinical evidence is based on a double blinded RCT as well as additional published experiment testing	Thank you for your comment. Section 5 of the evidence generation plan for Neupulse on the minimum evidence standards describes the criteria that any new technologies must meet to be eligible for inclusion in the new assessment following the evidence generation period.

Comment number	Name and organisation	Section number	Comment	NICE Response
				The EAG thinks "Experimental testing" needs to be further clarified and explained.
29	Consultee 2 Neurotherapeutics Ltd (Neupulse)	5 5 Minimum evidence standards	Suggest 'some' evidence is removed. The clinical evidence is based on a double blinded RCT as well as additional published experiment testing	Thank you for your comment. The EAG thinks "Experimental testing" needs to be further clarified and explained. Committee considered the evidence presented and decided that further evidence is still needed to support decision making, hence the plan states that “some clinical evidence” is available.
30	Consultee 2 Neurotherapeutics Ltd (Neupulse)	5 5 Minimum evidence standards	AEs determined during the clinical trial did not meet the criteria for being ‘reportable to the MHRA’ under the guidelines. There were no serious AEs. Electrodes in direct contact with skin was the only AE. These findings were submitted to MHRA and will be published at Clinical trial.gov	Thank you for your comment. Section 5 of the evidence generation plan for Neupulse on the minimum evidence standards describes the criteria that any new technologies must meet to be eligible for inclusion in the new assessment following the evidence generation period. It does not summarise the evidence on Neupulse.

Comment number	Name and organisation	Section number	Comment	NICE Response
31	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Not specified	NIHR or other funding would be required to be found in order to generate the evidence requested in the plan.	Thank you for your comment. See response to comment 9 above.
32	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.23 Evidence gap review	In our trial: 20% had ADHD, 27% had OCD, 14% had autism, 23% had anxiety disorder Our data show that Neupulse stimulation significantly reduces ADHD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and OCD symptoms (Cohen's D = -0.76, t = -2.73, p < 0.02) and generalised anxiety (Cohen's D = -0.52, t = -2.02, p < 0.05) 50% of Neupulse trial participants were adults.	Thank you for your comment. Please see response to comment 14 above.

Comment number	Name and organisation	Section number	Comment	NICE Response
33	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.23 Evidence gap review	Does this mean when using the device? The rationale for using the Neupulse device is that it delivers a significant reduction in tics on demand, at the push of a button. It is designed to reduce tic during stimulation. It was not intended to produce a cure or to have long lasting effects. instead, it should be considered as a safe, non-invasive, analog of deep brain stimulation insofar as it reduces tics during stimulation.	Thank you for your comment. Committee noted that Neupulse device is designed to reduce tic during stimulation. It was not intended to produce a cure or to have long lasting effects.
34	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.23 Evidence gap review	There were no Adverse Events six months post stopping usage.	Thank you for your comment. NICE did not have the six-month data from the company. It would be valuable to see these data, including details on the types of outcomes that were collected.
35	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.23 Evidence gap review	The Neupulse device is designed to be intuitive and easy to use, with little need for intervention by the user. Simple instructions are provided with the device (within the Neutrack App) in the form of videos, / images, and text to set up the device to suit the needs of the individual. Parents / carers can set up a device for young people using the Neutrack App Once approved and launched outside of the UK, the instructions will be available in multiple languages Can be used 'on the go' – connection to app only required to adjust	Thank you for your comment. The committee considered the comment.

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			settings Technical support will be available via our website	
36	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.5 Clinical effectiveness	We had a 3 month and 6 month follow-up period during the clinical trial. We collected YGTSS and AE during the follow up period. Note - the participants only used the device for 1 month. Benefits are sustained during the month of use as demonstrated by reduced YGTSS scores taken at base line and end of week 4 when the device was off.	Thank you for your comment. Please see response to comment 34 above.
37	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.6 Managing risks	Clarification - these two sentences contradict each other. AEs did not meet the criteria for being 'reportable to the MHRA' under the guidelines. There were no serious AEs. Electrodes in direct contact with skin was the only AE. These findings were submitted to MHRA and will be published at Clinical trial.gov	Thank you for your comment. Thanks for the clarification. Section 3.6 in the final guidance has been amended to "The company for Neupulse said that it had monitored and recorded adverse events but had not published this information. It mentioned that the only adverse

Comment number	Name and organisation	Section number	Comment	NICE Response
				event to date is skin irritation, caused by electrodes in direct contact with the skin. The company for Neupulse stated that Neupulse device complies with current standards and regulations. The committee noted that patient support for Neupulse is important because it is a self-administered device."
38	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.6 Managing risks	The Neupulse device is safe to use, incorporating many standards and regulations including: ISO 13485 Medical Device European Medical Device Regulations (EU MDR 2017/745) BS EN 60601 Safety and essential performance of medical electrical equipment ISO 601-2-10 Particular requirements for the basic safety and essential performance of nerve and muscle stimulators	Thank you for your comment. The committee noted the comments on how the company manage risks of using Neupulse.
39	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.6 Managing risks	The Neupulse device is safe to use, incorporating many standards and regulations including: ISO 13485 Medical Device European Medical Device Regulations (EU MDR 2017/745) BS EN 60601 Safety and essential performance of medical electrical equipment ISO 601-2-10 Particular requirements for the basic safety and essential performance of nerve and muscle stimulators ISO 601-2-10 sets a maximum allowed current that can be delivered from a device to the human body at 50 mA is the maximum a device can emit,	Thank you for your comment. Please see response to comment 38 above.

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			The Neupulse device has a 14 mA limit. Discomfort is the worse outcome, by adjusting the settings, the level of stimulation can be controlled to ensure both efficacy and comfort for the user The device is part of the TENS category of devices and this category has a good safety record. The regulatory processes ensure that good support is used for patients. Patients would in addition be advised to continue with their treatment as usual as was the case during the clinical trial.	
40	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.7 Managing risks	A Medical Director will be in place and a escalation process with support staff available to deal with problems as they arise including a complaint process. A key requirement of ISO 13485 is having a process for receiving feedback on the device and this includes Post Market Surveillance. Through the companies external audits to gain ISO 13485 certification we will need to show that the PMS processes are effective	Thank you for your comment. Please see response to comment 38. Section 3.7 in the final guidance has been amended to “The company for Nepulse stated that it has an escalation process with support staff available to deal with problems.”
41	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.8 Managing risks	The clinical trial showed that the device is effective without a formal diagnosis.	Thank you for your comment. Please see response to comment 6 above.
42	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.8 Managing risks	Stephen Jackson's research group at the University of Nottingham were funded by the MRC to directly investigate the effects of Neupulse stimulation on the most common conditions that co-occur with Tourette syndrome, i.e., OCD, ADHD and generalised anxiety disorder (GAD). These studies demonstrated that Neupulse stimulation significantly reduced the symptoms of OCD (Cohen's D = 0.76, t-value = 2.73, p-	Thank you for your comment. Please see response to comment 14 above.

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			value < 0.02) and GAD (Cohen's D = 0.52, t-value = 2.2, p-value < 0.05). Data available on request. With respect to individuals with functional tics, our clinical trial data indicated that Neupulse stimulation was effective for functional tics. With respect to the proposal that Neupulse stimulation could increase suicidal thoughts. This seems highly speculative and lacks credibility as we know of no evidence for this idea, and can conceive of absolutely no mechanism that would link median nerve electrical stimulation to increased suicidal thoughts. We would always recommend and encourage individuals with tics, functional or otherwise, to maintain a regular and close contact with their healthcare professional. However, we note that many individuals with tics report enormous difficulty and long waiting time to obtain a diagnosis and to receive healthcare for their tic disorder. We also acknowledge the report published by Tourettes Action indicating that many individuals on obtaining a diagnosis are then discharged from clinical care with no further treatment. In these circumstances it seems preferable to allow such individuals to the Neupulse device that is proven to substantially reduce their tics on demand.	Section 3.8 of the final guidance has added that "The company for Neupulse stated that they would always recommend and encourage individuals with any types of tics to maintain regular and close contact with their healthcare professionals."
43	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.8 Managing risks	A Medical Director will be in place and a escalation process with support staff available to deal with problems as they arise including a complaint process. A key requirement of ISO 13485 is having a process for receiving feedback on the device and this includes Post Market Surveillance. Through the companies external audits to gain ISO 13485 certification we will need to show that the PMS processes are effective	Thank you for your comment. Please see response to comment 38 above.

Comment number	Name and organisation	Section number	Comment	NICE Response
44	Consultee 3 Tourettes Action	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	The document also states that “Longer-term data on the clinical impact of Neupulse It is unclear if the technology leads to a clinical benefit beyond 4 weeks. Follow-ups should be a minimum of 3 months after the intervention, and ideally at 6 months. This would improve the data available to populate future health-economic models and reduce uncertainty.” Is this referring to patients still wearing the device, so the patient is wearing the device beyond 4 weeks and clinical impact is measured or is it asking if clinical impact is beneficial after the 4 week period when the device has stopped being used? It is not clear.	Thank you for your comment. The EAG agreed that clarification is needed regarding the recommended duration of device use and the specific time points at which outcomes should be assessed. The committee considered that it is unclear if the technology leads to a clinical benefit beyond 4 weeks. Follow ups should be recorded at 3 and 6 months after commencing or ongoing use of the intervention, and ideally at 12 and 18 months. This would improve the data available to populate future health-economic models and reduce uncertainty.

THEME: Care pathway and comparators

Comment number	Name and organisation	Section number	Comment	NICE Response
45	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Are the recommendations sound and a suitable basis for guidance to the NHS?	No. Unclear how our device will be made available and by whom (which Healthcare professional). The pathway for referral in unclear. The Neupulse device is still in development and manufacturing has not yet begun.	Thank you for your comment. The committee acknowledged that there is no standard care pathway for the diagnosis and management of tic disorders in the UK, which was addressed by both clinical experts and lay experts. Section 2.3 of the final guidance clarifies that "There is no standard care pathway or comprehensive clinical guideline for the diagnosis and management of tic disorders in children and young people or adults in the UK, but clinical experts mentioned that there are other available clinical guidelines from other countries. Section 3.1 of the final guidance also highlights the unmet need.
46	Consultee 2 Neurotherapeutics Ltd (Neupulse)	1 1 Purpose of this document	Neupulse would like clarification of where in the care pathway the device could be made available within the NHS setting. The NICE press release mentioned GPs but TS treatment and diagnosis is not currently from GPs.	Thank you for your comment. See response to comment 45 above. Section 2.4 of the final guidance has removed the unclear description of the

Comment number	Name and organisation	Section number	Comment	NICE Response
				current care pathway due to the variation in current practice.
47	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.3 3.3 Evidence collection plan	We would welcome discussion over when eligible for standard care would be defined for adults with TS who may have been in the system for many years.	Thank you for your comment. See response to comment 45 above.
48	Consultee 2 Neurotherapeutics Ltd (Neupulse)	3.3 3.3 Evidence collection plan	We would welcome discussion over when 'eligible for standard care' would be defined for adults with TS who may have been in the system for many years.	Thank you for your comment. See response to comment 45 above.
49	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.4 Care pathway	How does Neupulse device fit into the pathway? The press release from NICE (19th Nov 2024) suggests the device would be offered after clinical assessment by a GP. Please clarify where is the care pathway the device would be available. GPs do not diagnose or treat TS.	Thank you for your comment. See response to comment 45 above.
50	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.4 Care pathway	The availability of psychoeducation from local services for children and adults is unclear.	Thank you for your comment. The committee noted that the variations in expertise, access and availability of services across the UK, many people are not getting the diagnosis, treatment and support they need. Section 3.1 of the guidance also highlights the unmet need.
51	Consultee 2 Neurotherap	2.4 Care pathway	Correction - DBS is not available as a treatment for TS or CTDs.	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
	eutics Ltd (Neupulse)			Clinical experts confirmed that deep brain stimulation is not a treatment for people with chronic tic disorders. Section 2.4 of the final guidance has removed deep brain stimulation as a treatment option for chronic tic disorders.
52	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.5 Care pathway	It is not clear how available psychoeducation is.	Thank you for your comment. Please see response to comment 50 above.
53	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.5 Care pathway	Which HCP could refer people for these interventions? GP or other? If the NICE press release information is incorrect this needs correcting as it is confusing for the public. Could a GP prescribe the device if the patient already had a diagnosis and had psycho education?	Thank you for your comment. See response to comment 45 and 46 above.
54	Consultee 2 Neurotherapeutics Ltd (Neupulse)	2.7 The comparator	What is standard care for adults? This needs to be defined. A control group needs to be included in standard care.	Thank you for your comment. See response to comment 45 above.
55	Consultee 3 Tourettes Action	Has all of the relevant evidence been taken into account?	Section 3.1 'Unmet' need states "Provision of services for chronic tic disorders and Tourette syndrome varies across the NHS. Barriers to access include a shortage of trained therapists and limited access to behavioural therapy, which is only available at a small number of specialist treatment centres. As a result, experts estimate that less than 20% of children and young people with chronic tic disorders and Tourette syndrome currently have access to behavioural therapies (Marino et al. 2023). Clinical experts noted that there is often a long waiting list for	Thank you for your comment. Committee noted that there is inconsistent services availability which leads to shortage of trained therapists and limited access to behavioural therapy. Long waiting time for referrals to

Comment number	Name and organisation	Section number	Comment	NICE Response
			referral to specialist services." The unmet need is not solely to do with a lack of trained therapists, more often it is due to a lack of a commissioned service or specific ruling around who can access the service. Sometimes clinicians are trained in behavioural therapy for tics but patients cannot access them under commissioning rules. Some rules state that patients can only be accepted if they have cooccurring anxiety or cooccurring ADHD or OCD, having Tourette syndrome only would mean that the referral would be declined. Thus creating a barrier to accessing therapy. Patients who do not have a local Tourette's service in place are also unable to access specialist tertiary services. Tertiary services will not accept a referral from primary care, they will only accept a referral from secondary care, therefore if there is no secondary care service in place, patients are left with nothing. Section 3.15 talks about the Patient considerations, it is important to note here that the NICE survey highlighted that 60% of people completing the survey had never been offered treatment.	specialist services. Commissioning rules often restrict access, excluding patients with only Tourette syndrome. Section 3.1 of the final guidance highlights this unmet need. Section 3.17 of the final guidance has added that "Care pathways currently vary across the UK and some areas lack established and commissioned pathways. This makes it difficult for people living in areas without local services to access specialist tertiary services."
56	Consultee 3 Tourettes Action	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	Section: 2.6 'The comparator' states "The comparator is standard care for managing chronic tic disorders and Tourette syndrome, including psychoeducation and behavioural therapy. Standard care varies significantly across clinical practice. Digital therapy would be used in addition to standard care. 2.7 There was no evidence comparing any of the interventions with current standard care. The online psychoeducation may be a more active comparator than face-to-face psychoeducation in current UK clinical practice. In the economic modelling, the comparator for ORBIT is online psychoeducation in children and young people. The comparator for Neupulse is a waitlist control (that is, no stimulation) in	Thank you for your comment. The committee considered the comment. Clinical experts explained that it would be costly and infeasible to design a comparative trial comparing ORBIT and Neupulse with face-to-face therapy.

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			children and young people 12 years and over, and in adults." The comparator is listed to be standard care, stating that psychoeducation and behavioural therapy are what is routinely offered, these provisions are in fact rarely offered. Standard care for the majority of patients, as highlighted in the NICE survey is to be offered no support (60% of people stated they had been offered nothing). A better comparison may be: ORBIT compared to receiving no care ORBIT compared to receiving face to face therapy Neupulse compared to receiving no care Neupulse compared to receiving face to face therapy	
57	Consultee 3 Tourettes Action	Are the recommendations sound and a suitable basis for guidance to the NHS?	Section 2.3 'Care pathway' states "The scope for this early value assessment included a targeted population of people with a diagnosed primary tic disorder who have had psychoeducation, but their tics continue to be bothersome." Limiting the population to those who have had access to psychoeducation would prevent a huge amount of people from accessing the digital treatment. Many patients are diagnosed and discharged and offered nothing. No psychoeducation, no treatment, just discharged. Having a stipulation that states only those who have accessed psychoeducation can access the digital treatment options, creates further barriers for those who are already unable to access services. The document states that digital therapies should be offered after psychoeducation has been given but no details about what this psychoeducation should entail. Would it be a leaflet, a video, an online session, a face to face session, an eLearning module? The provision of	Thank you for your comment. The committee considered that many people are not getting the diagnosis, treatment and support they need due to the variations in expertise, access and availability of services across the UK. Section 3.1 of the final guidance highlights this unmet need. Clinical experts explained that psychoeducation is a first line option and behavioural therapies for people who still

Comment number	Name and organisation	Section number	Comment	NICE Response
			this varies dramatically throughout the country, with some individuals receiving nothing, if this is a recommendation prior to receiving the digital therapy, details of what it is to entail should be given. The document also states that current NICE's guidance says that children with significant impact should be referred to either specialist mental health services, neurodevelopmental teams or for neurological assessment, this however does not work in practice. If these local services are not commissioned to treat Tourette syndrome, they will decline these referrals and will not see the patients, meaning they are unable to access a diagnosis or any form of treatment, regardless of the impact the tics are having. The document also states in Section 2.4 "In the UK, people with chronic tic disorders and Tourette syndrome attend an initial appointment with a GP in primary care. When a tic disorder has a significant impact on a person's quality of life, they are usually referred to appropriate secondary or tertiary care services (depending on the presentation, comorbidities, and local specialist clinics). Children and young people may be referred to mental health services (including to the Children and Young People's Mental Health Services), neurodevelopmental teams, paediatric teams or paediatric neurology teams, depending on local services and pathways" The current process is that patients are referred to secondary care services if there is a commissioned service in their area. GPs cannot refer to tertiary services. Tertiary services will only accept referrals from a secondary care service such as CAMHS or Paediatrics. Therefore if a patient lives in an area where secondary services are not commissioned to see patients with Tourette's, these patients are not able to get care locally and they are also not able to be referred to the tertiary service.	have difficulties with their tics. Psychoeducation aims to empower individuals by enhancing their understanding of their conditions, which can lead to better treatment adherence and overall outcomes. Experts suggested psychoeducation is always useful even if people were diagnosed with Tourette syndrome many years ago, as it is continually updating the understanding of the condition. Please see the updated section 2.5 of the final guidance.

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			The documents state that there should be comparable standard care in the device and control groups with data collected from the point at which a person becomes eligible for standard NHS care. This is not however clearly defined. If a patient was diagnosed 20 years ago, they would have been eligible for standard NHS care some 20 years prior but potentially given no treatment up until this point as there is no service local to them. Would the digital therapy only be available to new people just gaining a diagnosis or should it be available to all with a diagnosis? The document also mentions that psychoeducation is a requirement to receiving treatment but some patients may have never been given this, so would they also not be able to access treatment, it would also not be relevant to give patients diagnosed 20 years previously psychoeducation on a condition they have lived with for many years, so does this mean this cohort of patients cannot access the digital options?	
58	Consultee 3 Tourettes Action	Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?	Section 2.5 states “Accepted evidence-based treatment options for diagnosed tic disorders are psychoeducation as a first line option and behavioural therapies for people who still have difficulties with their tics. For some people, behavioural approaches may not be as effective, feasible or accessible and other possible treatments (with or without behavioural therapies) will be discussed. Digital therapy for chronic tic disorders and Tourette syndrome would be offered after clinical assessment and diagnosis. These interventions should only be considered if the person (and parent or carer where appropriate) has had access to a form of psychoeducation. If the tic disorder continues to cause difficulties, a healthcare professional may consider referring people for these interventions.” Although it is true that psychoeducation should be the first line option for patients, it is rarely offered if there is not a locally commissioned service, so limiting treatment to only those who have already had psychoeducation would prevent many patients from accessing the	Thank you for your comment. Please see response to comment 57 above.

Comment number	Name and organisation	Section number	Comment	NICE Response
			service. How would these patients who have not had psychoeducation access the treatment? The document does not make it clear where in the care pathway the digital treatments would be offered, would it be at the point of diagnosis or would it be at a treatment clinic. There is no standardised pathway for the diagnosis and treatment of Tourette syndrome, meaning that every area will, and does, do things differently. Some areas: - have one service who will diagnose and also treat the condition - have one service to diagnose and a different service to treat - have one service to diagnose but will not treat, will just discharge - some areas will neither diagnose nor treat in their services This needs to be carefully considered as to not limit the availability of these options. Adults in the community may have been diagnosed many years ago and never offered any form of treatment. Many are not under any specific service, so if access to these treatments can only be obtained through a specific clinic, this would create a further barrier and also add further to the waiting lists. Another point to mention is that the NICE press release stated that GPs would prescribe these digital therapies but the digital options would only be available post diagnosis and after psychoeducation but GPs do not currently diagnose or treat Tourette syndrome, so it is unclear how they would then prescribe the digital therapy. The consultation document does not mention GPs as a prescriber but as this was mentioned in the press release, I think it is important to raise this, as we have already had service users asking us if these options will be available to them from their GP. Clear guidance needs to be given to patients on who will be prescriber and how and under what circumstances.	Please see response to comment 45 above.

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			Currently, GP aren't equipped to do this, many do not understand the complexities of Tourette syndrome and if they are to be the prescriber of these digital therapies they would need to have adequate training on Tourette syndrome (Tourettes Action have recently launched an eLearning module specifically for GPs) and they would also need to ensure that the patient had a diagnosis of Tourette syndrome. The document also states that "the studies should be run across multiple centres, aiming to recruit centres that represent the variety of care pathways in the NHS." What about situations where no pathway is in place? These patients are currently the most disadvantaged, as they cannot access treatment either locally or further afield at the specialist tertiary clinics. Limiting the access of digital therapy at a centre with a pathway in place would also mean that these patients would be unable to access digital therapy, causing further disadvantage to them.	
59	Consultee 8	2.4	Para 2.4 needs to differentiate between treatments recommended for adults and children as we do not offer botox and TBS for children.	Thank you for your comment. Clinical experts confirmed that deep brain stimulation is not a treatment for people with chronic tic disorders. Section 2.4 of the final guidance has removed deep brain stimulation as a treatment option for chronic tic disorders. Botox is for adults only has been added in section 2.4 of the final guidance.

THEME: General comments and requests for clarification

Comment number	Name and organisation	Section number	Comment	NICE Response
60	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?	No	Thank you for your comment.
61	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Not specified	Neupulse are delighted that NICE recognise the unmet needs of people with Tourette Syndrome and Chronic Tic Disorders. We welcome the opportunity to get involved at this level to improve the outcomes for those affected by this debilitating condition, who are typically under-represented and under treated. NIHR or other funding would be required to be found in order to generate the evidence requested in the plan.	Thank you for your comment.
62	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Not specified	Neupulse are delighted that NICE recognise the unmet needs of people with Tourette Syndrome and Chronic Tic Disorders. We welcome the opportunity to get involved at this level to improve the outcomes for those affected by this debilitating condition, who are typically under-represented and under treated.	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
63	Consultee 2 Neurotherapeutics Ltd (Neupulse)	Not specified	Neupulse are delighted that NICE recognise the unmet needs of people with Tourette Syndrome and Chronic Tic Disorders. We welcome the opportunity to get involved at this level to improve the outcomes for those affected by this debilitating condition, who are typically under-represented and under treated.	Thank you for your comment.
64	Consultee 4	Has all of the relevant evidence been taken into account?	I believe so.	Thank you for your comment.
65	Consultee 4	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	I think so.	Thank you for your comment.
66	Consultee 4	Are the recommendations sound and a suitable basis for guidance to the NHS?	Yes.	Thank you for your comment.

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67	Consultee 4	Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?	Not that I can see.	Thank you for your comment.
68	Consultee 4	Are there any other relevant ongoing studies that address the evidence gaps?	None that I am aware of but I also don't see any evidence gaps.	Thank you for your comment.
69	Consultee 4	Are there any other relevant ongoing studies that address the evidence gaps?	See above.	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
70	Consultee 5	Not specified	It is vital having the possibility to access remotely to this service. This not only will help people affected by Tourettes on a higher scale but will also give some kind of independence in the way we can manage our journey towards a better life	Thank you for your comment.
71	Consultee 6	Has all of the relevant evidence been taken into account?	Yes we understand	Thank you for your comment.
72	Consultee 6	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	Yes	Thank you for your comment.
73	Consultee 6	Are the recommendations sound and a suitable basis for guidance to the NHS?	Yes	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
74	Consultee 7	Has all of the relevant evidence been taken into account?	Yes	Thank you for your comment.
75	Consultee 7	Are the summaries of clinical and and cost effectiveness reasonable interpretations of the evidence?	Yes	Thank you for your comment.
76	Consultee 7	Are the recommendations sound and a suitable basis for guidance to the NHS?	Yes	Thank you for your comment.
77	Consultee 7	Are there any equality issues that need special consideration and are not covered in the medical technology	No	Thank you for your comment.

Comment number	Name and organisation	Section number	Comment	NICE Response
		consultation document?		
78	Consultee 7	Are there any other relevant ongoing studies that address the evidence gaps?	No	Thank you for your comment.
79	Consultee 8	3.5	Para 3.5. The use of treatments in children with comorbidities eg autism and ADHD, should include intellectual disability. It would also be useful to mention this more specifically in the list of why people might not be able to access digital or online treatments.	Thank you for your comment. Section 3.20 of the final guidance included intellectual disability in children with comorbidities and acknowledged it will be a barrier to accessing digital or online treatments.
80	Consultee 8	Not Specified	It would be very helpful to define the difference between mild, moderate and severe tics, so that doctors etc know whom to refer for the various treatments and what the advice might be for children with mild tics.	Thank you for your comment. Section 2.4 of the final guidance has added “Treatment options may vary based on the severity of the tics. Decisions regarding the choice of treatment should be made jointly by the

Comment number	Name and organisation	Section number	Comment	NICE Response
				healthcare professional and the person with a tic disorder.”