NICE National Institute for Health and Care Excellence

External Assessment Centre correspondence log

MT477 Alpha-Stim AID for anxiety

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
1.	20/05/2020	**Company** Initial questions	Could the company provide some insight as to why the variation to the population? • Should Alpha-Stim not be used by patients with diagnosed anxiety disorders? • Is this variation to do with the available evidence or is the company suggesting that people with diagnosed anxiety disorders would limit the use of Alpha-Stim? Could the company clarify the age demographic that the device is suitable for i.e. children and adults?	Stated that mental health on spectrum and that patients do not need to meet full diagnostic criteria for GAD to benefit from Alpha-Stim. For instance, some people with confirmed primary diagnosis of other mental health conditions may not be diagnosed for anxiety disorders. Prof. Morris suggested broader scope to include patients with symptoms of anxiety but without a diagnosis of an anxiety disorder. Alpha-Stim can be used for children as well as adults.

2.	20/05/2020	**Company** Initial questions	What version of the device is currently available/would be provided to the NHS? It will be helpful to note what changes made to the device although mode of action has not changed.	AID version is currently available. Alpha-Stim M can also treat pain. Core device and mode of action unchanged between different versions of the device. The evidence from the older versions of the device is applicable to the current version. The latest model (AID) has been significantly modified, with new electronic features to help usability. The device has an option to lock the treatment cycle which can be very useful for clinicians and an alert feature to tell the patient when the device isn't connected. Over time the device has dramatically reduced in size and external appearance and functionality with no change in mode of action.
3.	20/05/2020	**Company** Initial questions	Additional question depending on response above: • Could the company comment on the fact that different versions are available to purchase online? • How does the company regulate the resale of older models?	No other versions available to buy but company aware that a small number of second-hand versions come up for sale on Ebay etc. The UK distributor does not have any control on resale. The UK Distributor offers no support for these devices.
4.	20/05/2020	**Company** Initial questions	The electrical pulse generator is operated by 2 1.5-volt batteries, How long would batteries last in typical use, FAQ suggest 20-30 hours. How long is typical use for anxiety? Web page suggests for depression 20mins -60mins every day to start any plans for rechargeable version	The device uses lithium batteries which last about 40 hours or 1 month use (£2.50 in battery costs). Company will supply batteries. Average use 20- 60mins/day. Increase intensity to start, reduce setting until no more dizziness (sub-perception). At a setting of <2 (level 1)= 1 hour use >2.5-3 = 20 mins. Can lock device at level 1

				Not demonstrated that patients develop tolerance to treatment. Rechargeable version not currently available but likely in future (both AID and M).
5.	20/05/2020	**Company** Initial questions	Point of clarification There is a suggestion that patients may need more than one device. “participants were able to utilize the same Alpha-Stim device repeatedly during each study.” • Could the company clarify this point? Is there an expectation that patients may need to replace devices? • Could the company comment on the patient specific, non-reusable parts of the device? • Could the company comment on whether the device is recyclable? • Does this depend on recycling facilities available? Does the user have to break up the device in any way to dispose of it sustainably?	No service requirement. Current model – if not working it switches of and will sound an alarm also if clips not applied properly. No experience for needing to recycle the device. If it is broken, send it back to the company to be fixed.
6.	20/05/2020	**Company** Initial questions	Could the company provide some insight as to why the meta-analysis is highlighted ‘Academic in Confidence’ Royal 2020? All studies included in the meta-analysis appear to be published and publically available therefore it is unlikely that all of this information could be classed as confidential. If any of the data in the individual studies is confidential (for example, updated results from trials that have not yet been published), this should be highlighted both in section 6 and in section 7. The company should be aware that the EAC may undertake their own meta-analysis of the published data and if the data are all publically	NICE: There is a plan to publish the results therefore company and NICE will look at AIC section again. Happy to work with company on this. EAC can do meta-analysis of their own with the published data.

			available, the results of the EAC analysis will not be considered to be confidential. Please could the company consider which specific aspects of the meta-analysis should be considered academic in confidence?	
7.	20/05/2020	**Company** Initial questions	Price 2013 listed in table 2 of submission, link doesn't work Please supply a copy	Document sent by company
8.	20/05/2020	**Company** Initial questions	Do patients use medication as well as Alpha-Stim?	Both can be used during therapy as is shown in the Paroxetine study. Initially it was an alternative to medication – there are lots of people who buy the device directly because they want to come off medication. We would like to see people using the device as a first line treatment before medication as a treatment for anxiety, along with drugs for depression.
9.	20/05/2020	**Company** Initial questions	How long does device last for?	If you're going to get an improvement you'll see it in the first 8 weeks. After that the device is returned to the NHS provider. Can treat 20-25 patients in a year with one device.
10.	22/06/2020	**Company** Follow-up questions	Part of the clinical pathways in Section 3 of the evidence submission describe "Telephone support within 72 hours". Can the company clarify who would provide this support?	This would be provided by a practice nurse.

11.	22/06/2020	**Company** Follow-up questions	The company's proposed pathway indicates, but doesn't explicitly state, that at the end of 6 weeks of Alpha-Stim treatment the following options are available: • Stop Alpha-Stim treatment and return device if GAD-7 score shows ?? remission • Re-enter pathway at the same point to consider drug treatment of high intensity psychological interventions if GAD-7 score ≥10 • 6 weeks more Alpha-Stim treatment if patient shows partial response, e.g. 25-50% reduction in GAD-7 score and ≥8 Please indicate if these options are correct. And what GAD-7 score would indicate the treatment can be stopped?	We would suggest a maximum of 8 weeks treatment initially rather than 6. Stop the Alpha-Stim treatment when the GAD-7 score reaches 7 or below - this is remission as measured by IAPT services. Remission may be achieved happen before the 8 weeks treatment is completed so the patient has the option of returning the device at this point. The second option applies after 8 weeks, if the third option of a 5 point GAD-7 reduction hasn't been achieved We would recommend a further course of Alpha-Stim treatment, up to 8 weeks, if the patient has achieved a clinically significant reduction of 5 points or more on the GAD-7 scale during the first 8 weeks. I have attached a document with a revised flow-chart for pages 12 and 13 that I hope clarifies the situation and answers your questions below. **Files included in Appendix 1.**
12.	29/06/20	**Company** Follow-up questions	In each of the 3 settings in your submission (page 12-13) can you check over the following information: • Criteria for starting Alpha-Stim (GAD-7 score) • Duration of initial Alpha-Stim treatment • Criteria for stopping Alpha-Stim treatment • Criteria for extending Alpha-Stim treatment • Duration of extended Alpha-Stim treatment	Please attached the revised flow-chart. GAD-7 of 8 or above is the criteria to start CES 6 weeks initial treatment GAD-7 7 or below patient stops the treatment. GAD-7 8 or above after 6 weeks patient is offered further 6 weeks Alpha-Stim treatment if deemed appropriate by clinician and patient.

			If you want to send a revised flow-chart to help explain then it might be easier.	
13.	29/06/20	**Company** Follow-up questions	Why is the GAD-7 score threshold for starting Alpha-Stim different when GAD is diagnosed by a GP compared to the IAPT pathway?	This has been amended so the threshold is the same for all pathways. Please see attached the revised flow-chart
14.	29/06/20	**Company** Follow-up questions	The company states that a "Practice nurse, health care assistant or company collects Alpha-Stim CES". In what circumstances would the company collect the device from a patient?	This has been removed (please see revised flow-chart) as it was only inserted to allow for Covid-19
15.	29/06/20	**Company** Follow-up questions	Can you confirm whether the economic model presented in your submission is the exact same one as that in the Morriss et al. (2019) paper?	Yes - the economic model is the same one used for the Morriss paper.
16.	09/07/20	**Company** Follow-up questions	RE: iCBT Response rates: 0.542 (0.49-0.59) The point estimate response rate can be found in Gyani et al (2013). Could the company shed some light on how the range for iCBT response was selected?	We used the mean value (0.542). A probabilistic sensitivity analysis using a beta distribution and a modelled 1000 patients were implemented to get a range of outcomes around the mean value
17.	09/07/20	**Company** Follow-up questions	RE: Probability of response to Alpha-Stim 0.47 (0.38-0.48) The point estimate response rate can be found in Morriss et al (2019). Could the company shed some light on how the range for Alpha-Stim response was selected?	We used the mean value (0.47). A probabilistic sensitivity analysis using a beta distribution and a modelled 1000 patients were implemented to get a range of outcomes around the mean value

18.	09/07/20	**Company** Follow-up questions	Table 3 of the company submission states standard practice includes only 8 low intensity (60 min) sessions and 8 high intensity (90 min) sessions. Can the company clarify that standard practice is 8 sessions (guessing this is just a typo in the table)	Yes it's a typo. Standard practice as it was advised by clinical experts was 8 low intensity sessions (60 min)
19.	09/07/20	**Company** Follow-up questions	Could the company provide some details around how the cost per patient of Alpha-Stim device has been calculated? The cost in the company submission is based on a device cost of £450 with 15 patients using it plus additional costs (£70) however in the model, the cost is calculated as £350 with 5 patients using it with no additional costs. While this is also £70 per patient, the EAC need to be clear on the cost of the device to the NHS as well as cost of any additional elements.	Alpha-Stim CES cost per treatment was a manufacturer estimate from the unit cost of the device of £450.00 (excluding valued added tax) with a utilisation of 15 patients over an average product lifetime of 3 years (based on average 10-week sole use per patient). It allowed for losses with respect to the quoted 5- year warranty that was estimated to reduce average product lifetime by 2 years. Additional therapist time, training and consumables was estimated at £40, yielding £70 per duration of the treatment per patient. The breakdown is below; Cost per treatment/patient over lifetime of device £30 per patient Consumables per year (if applicable) and over lifetime of device £10 per patient Maintenance cost per year and over lifetime of device Nil Training cost over lifetime of device £5 per patient Other costs per year and over lifetime of device £25 per patient Total cost per treatment/patient over lifetime of device £70 per patient

20.	24/11/20	**Company** Follow-up phone call after submission of primary care model. ***PLEASE NOTE:*** Responses have not been verified by the company due to time limitations.	1. We need some clarity on whether this is a primary care pathway or whether it is just a difference between nurse led clinic and GP led? Why would a GP led practice not introduce Alpha-Stim there? This would just be a cost difference at this point for staff? 2. Are the pathway stages defined anywhere? It is unclear what exactly is included in each of the treatment stages 3. How was the proportions of patients in nurse led branch defined? 4. AlphaStim response taken from patient level data for the primary care pathway (differs from A/S response in the IAPT pathway but response to CBT is the same - is there a justification for this)? 5. Why is it a 2 month time horizon? Does the response not last longer than this? If no treatment are they expected to get better within 2 months? Or is there just no treatment, and so there's no ongoing costs? 6. Do we know what the cohort data is – can we confirm that this is the unpublished Royal study and what are the current plans for published this?	1. The model used is based on how Alpha-Stim was introduced in the study led by Dr Royal where patients with anxiety symptoms were directed to a nurse led clinic. The company have added an assumption that a small proportion of patients will go via GP rather than nurse led clinic. 2. Treatment stages in the model correspond with stages of the IAPT pathway and will be added to a revised version of the model. (Cedar have now received this). 3. The proportions of patients going to the nurse led branch are an assumption, but based on observed behaviour during the Royal study. 4. The study collected response rates for patients treated in primary care, and therefore these are used for the Alpha-Stim response rate. Data for individual CBT response was not part of this study and the same response rate, taken from published literature for this model was used as in the IAPT model. 5. The two month time horizon is based on the availability of data. The effectiveness is not known over a longer period. 6. The cohort data is taken from the unpublished Royal study. The protocol can be shared with Cedar.
21.	26/11/20	**Company** Follow-up email sent via NICE.	In the sheet 'Cost calculation' Table: Hospital & Community Health Services where the inflation ratios are listed and the source is Curtis & Burns 2019. The Table says that is the Hospital & community health services however when I check the reference the numbers in Curtis & Burns,	Thank you for spotting this Apologies, that was a mistake that was not spotted earlier.

			• the numbers in the first column (under ratio) correspond with the values for the Building Cost Information Services (BCIS) – could the company clarify this please? • The ratios (second column) appear to be calculated using the BCIS values and do not correspond to any inflation indices in Curtis&Burns – could the company briefly explain what they have calculated here • In the table where the inflated cost of CBT is calculated, the calculation is using the value corresponding to 2009 of the inflation index table (1.33) – again, could the company just clarify exactly how they have worked out the inflated cost of iCBT?	• Indeed by mistake the BCIS was used. I have updated the file with the Hospital & Community Health Services (HCHS) Inflation Index. • The ratios column calculates the difference from the latest year as 1/ (HCHS Pay and Price index in year reported in literature / HCHS Pay and Price index) in the current or latest year) so to have a comparable measure for all the years to the latest year which is treated as year of basis and the ratio is equal to 1 • The reported results are not affected because they were based on a calculation provided by the study leads. The results are affected by the index if the  option is selected
22.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Does a proportion of patients on the waiting list drop out before iCBT in standard care (e.g. drugs from GP start to work, patient recovers)? If so, what proportion?	I am unable to ascertain what proportion of patients on the waiting list drop out before iCBT. It would be surprising if there were not some but it appears to be a low proportion. Patients who complete low intensity intervention and turn up for a further assessment are usually committed to treatment and unlikely to improve spontaneously or as a result of treatment from the GP. However,
23.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Are there any important features about the clinical pathway used to treat GAD in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE GAD pathway.	The pathway is largely followed in clinical practice when generalised anxiety disorder is recognised and diagnosed. The main issue is that many patients with GAD are not diagnosed with a mental health condition but as someone with headaches poor sleep etc or are diagnosed with depression when they have GAD.

24.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Does use of Alpha-Stim as an alternative to drug treatment and high intensity psychological interventions after steps 1 and 2 of NICE GAD pathway seem appropriate? These are patients with a diagnosis of GAD for whom step 1 treatment (education and monitoring) and step 2 treatments (low intensity psychological interventions) have not been effective.	Yes the use of alpha-stim after steps 1 and 2 seems appropriate. These are either patients where step1 or step 2 are ineffective or are refused. Many patients with GAD have recurring problems and have preferences based on past experience.
25.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Would a GP/nurse use the GAD-7 questionnaire to diagnose GAD? What are the approaches for diagnosis of GAD?	The GAD-7 questionnaire is used in some practices but its use in primary care is not common. Instead GAD is diagnosed clinically because of persistent and constant worry that is out of proportion to the stress with a range of other physical and mental symptoms. GPs report lots of patients with both GAD and depression or patients with out of proportion worry with physical symptoms present for much less time than 6 months.
26.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	How is the IAPT pathway for patients with symptoms of anxiety different to non-IAPT? Once referred, do both IAPT and non-IAPT follow the NICE guideline for GAD in the same way? Would IAPT impact the way Alpha-Stim is used?	In the IAPT pathway facilitated self-help low intensity programmes are easy to access and offered routinely. Outside IAPT, self-help programmes for anxiety are available but they are relatively ineffective because the facilitation is rarely available. Patients in IAPT will not be offered the option of antidepressant medication. Patients outside IAPT can rarely access high intensity psychological interventions unless they can pay for them so most are offered medication. Alpha-stim is likely to be offered through primary care rather than IAPT unless NICE approves the technology. The choice in primary care if no progress with education or pure self-help is a choice of IAPT, medication or alpha-stim, and if the person goes through IAPT first they are likely to get low intensity Psychological intervention, then stepped up high intensive CBT before medication or alpha-stim.

27.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Are there any important features about the clinical pathway used to treat social anxiety disorder in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE clinical guideline on social anxiety disorder.	In reality it is very difficult to access psychological treatment for social anxiety disorder through IAPT or any other source. Patients tend to turn to self-help or medication if they consult the health service at all. Therefore the NICE clinical pathway is rarely followed.
28.	09/06/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Would Alpha-Stim be an initial treatment options for adults with social anxiety disorder (see page 19 or NICE clinical guideline on social anxiety disorder) ?	Alpha-stim should not be offered to people with social anxiety disorder unless they also have generalised anxiety disorder as well. There is no evidence based for alpha-stim ion social anxiety disorder.
29.	09/06/20	**EXPERT – Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)**	Other than GAD and SAD pathways are there any other key pathways where Alpha-Stim could be used for the treatment of anxiety disorders?	Many patients in reality have both depression and generalised anxiety disorder. There is evidence for improvement in moderate severity anxiety and depression symptoms but not for depression alone. There is insufficient evidence to support alpha-stim use in other anxiety disorders.
30.	09/06/20	**EXPERT – Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Would Alpha-Stim be a treatment option for people referred to secondary care for anxiety? What does this pathway look like?	GAD is a common comorbidity for many physical and other mental long-term conditions adversely affecting their functional recovery and quality of life. Many such patients might be functionally compromised by drug treatments e.g. loss of alertness so alpha-stim might be a useful adjunctive medication if psychological treatments are ineffective or partially effective. In secondary care mental health services it might be prescribed by community mental health teams and in out-patient settings by mental health professionals skilled in the assessment of GAD. In other long-term conditions there may be a need for an assessment of GAD before alpha-stim or any other treatment for GAD is offered. Most hospitals have such services.

31.	09/06/20	**EXPERT – Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Patient pathway questions	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	GAD may be a temporary condition but it is often oa long-term condition that is never fully in remission for many years. Courses of alpha-stim are likely in reality to be one of a number of treatment options employed when GAD is particularly severe. When it is used in my experience it is often in addition to skills learnt through cognitive behaviour therapy rather than instead of CBT. Once patients have had one or more courses of CBT they rarely gain anything from going through another course of CBT so they use alpha-stim to gain remission from symptoms rather than use drug treatments which might become addictive given the recurring nature of GAD. I doubt if there is any data on this but there may be lived experience. Testimonials. At the moment such ways of coping with GAD are only an option for those who can afford it. There is a potentially a major issue in relation to inequalities through lack of income. This disproportionately affects people with long-0term conditions who have limited options for work and therefore cannot afford alpha-stim. Ironically a proportion might be able to work if they could access a treatment that keeps GAD at bay, Data on intermittent but recurrent long-term use (e.g How frequently does it need to be used as a course of treatment? Does alpha-stim lose its effectiveness over time?) may be important because I suspect this is a reality for a substantial proportion of the population diagnosed with GAD, and as a mental health specialist this is what I tend to see in clinical practice
32.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Does a proportion of patients on the waiting list drop out before iCBT in standard care (e.g. drugs from GP start to work, patient recovers)? If so, what proportion?	I do not know the answer to this. IAPT national stats might provide this answer.

33.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Are there any important features about the clinical pathway used to treat GAD in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE GAD pathway.	I do not know the answer to this.
34.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Does use of Alpha-Stim as an alternative to drug treatment and high intensity psychological interventions after steps 1 and 2 of NICE GAD pathway seem appropriate? These are patients with a diagnosis of GAD for whom step 1 treatment (education and monitoring) and step 2 treatments (low intensity psychological interventions) have not been effective.	Could have after step 1 and after step 1 and 2. Enhancing patient choice is important.
35.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Would a GP/nurse use the GAD-7 questionnaire to diagnose GAD? What are the approaches for diagnosis of GAD?	GAD-7 is a good diagnosis measure for a nurse or other clinician to use. Gaining patient experience is also valuable: asking the degree anxiety is impacting on their lives, functioning and ability to do things they want/need to do.
36.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	How is the IAPT pathway for patients with symptoms of anxiety different to non-IAPT? Once referred, do both IAPT and non-IAPT follow the NICE guideline for GAD in the same way? Would IAPT impact the way Alpha-Stim is used?	IAPT is the pathway for access to psychotherapy, although they do also, bibliotherapy, EMDR, psychoeducation and referral to other/secondary services. As far as I am aware other pathways are GP (who can prescribe meds or refer to IAPT or secondary services) and directly into secondary services. Different services apply NICE guidelines as appropriate to how they are working with individual patient needs and health conditions. IAPT is a good service to adopt Alpha-Stim because it takes a stepped care approach and specifically works with people who present with anxiety.

37.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Are there any important features about the clinical pathway used to treat social anxiety disorder in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE clinical guideline on social anxiety disorder.	I do not know the answer to this.
38.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Would Alpha-Stim be an initial treatment options for adults with social anxiety disorder (see page 19 or NICE clinical guideline on social anxiety disorder) ?	Yes it could be.
39.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Other than GAD and SAD pathways are there any other key pathways where Alpha-Stim could be used for the treatment of anxiety disorders?	Yes, many people who have long term physical health conditions also experience anxiety. These people are often not offered treatment for anxiety. They might not able to attend sessions of psychotherapy (travel issues, cost, commitments [job, caring responsibilities, child care]), and are on many prescriptions meds and so adding more meds might not be best. Some long term conditions (COPD, asthma and diabetes) are interlinked with anxiety (one making other worse) and so treating anxiety may reduce psychical health symptoms. Alpha-Stim could be offered through community nursing services. Due to lack of side effects and good safety record Alpha-Stim could be valuable for anxiety treatment in people under 18.
40.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Would Alpha-Stim be a treatment option for people referred to secondary care for anxiety? What does this pathway look like?	Yes, people could be offered Alpha-Stim when patients are offered other treatments (e.g. psychotherapy, meds). It could be as an alternative to meds or as an addition. It could be as an alternative to psychotherapy, offered whilst on waitlist for psychotherapy, or as an addition (some psychotherapists in the IAPT service where Alpha-Stim was used, used Alpha-Stim together with a

				course of psychotherapy). Patients referred to secondary care for anxiety could be offered Alpha-Stim and also those referred for other mental illnesses, but who also display symptoms of anxiety.
41.	08/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	No answer provided
42.	25/06/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Patient pathway questions	Telephone call with EAC	Improving Access to Psychological Treatments teams (IAPTs) are the standard structure of service provision for people with anxiety and depression, with similarity in all regions of the UK. Patients are referred to IAPT by their GP or they can self-refer. The economic model's decision tree is broadly aligned to the pathway used in clinical practice. Alpha-Stim could be offered by GP practices as an alternative or in addition to existing treatments and referrals for GAD. Enabling patient choice is an important factor in selection / order of therapies. SSRIs are in very commonplace use. SSRIs are an inexpensive option but are associated with significant side effects for some people and many patients struggle to cease their use i.e. experience withdrawal issues. Based on decades of use, Alpha-Stim CES does not have the side effects associated with SSRIs. Mild tingling on the ears during use has been reported by some patients using Alpha-Stim. The US FDA has recorded no serious adverse events. The cost of Alpha-Stim should consider the purchase cost (c£450) and consumables (c£5 per patient).We will carefully check the sources of costs.

43.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Does a proportion of patients on the waiting list drop out before iCBT in standard care (e.g. drugs from GP start to work, patient recovers)? If so, what proportion?	30-40%
44.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Are there any important features about the clinical pathway used to treat GAD in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE GAD pathway.	No answer provided
45.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Does use of Alpha-Stim as an alternative to drug treatment and high intensity psychological interventions after steps 1 and 2 of NICE GAD pathway seem appropriate? These are patients with a diagnosis of GAD for whom step 1 treatment (education and monitoring) and step 2 treatments (low intensity psychological interventions) have not been effective.	The main evidence comes from Morriss et al. (2019). The sample size was small (n=169), there was a low uptake of the treatment (only 22% of potentially eligible participants took part), moderate retention rate (70%), and and remission was 45% while 'reliable recovery' (minimal 6 point improvement on PHQ9) was 63%. It's unclear what the rates of uptake, retention and recovery would be in a larger multisite sample.
46.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Would a GP/nurse use the GAD-7 questionnaire to diagnose GAD? What are the approaches for diagnosis of GAD?	Yes

47.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	How is the IAPT pathway for patients with symptoms of anxiety different to non-IAPT? Once referred, do both IAPT and non-IAPT follow the NICE guideline for GAD in the same way? Would IAPT impact the way Alpha-Stim is used?	Patients would be able to purchase the device themselves whether they are referred to IAPT or not, but the device is not currently in the NICE GAD pathway.
48.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Are there any important features about the clinical pathway used to treat social anxiety disorder in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE clinical guideline on social anxiety disorder.	No answer provided
49.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Would Alpha-Stim be an initial treatment options for adults with social anxiety disorder (see page 19 or NICE clinical guideline on social anxiety disorder) ?	Yes, it is a potential initial treatment. However, efficacy and rates of relapse are not known.
50.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Other than GAD and SAD pathways are there any other key pathways where Alpha-Stim could be used for the treatment of anxiety disorders?	No answer provided
51.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Would Alpha-Stim be a treatment option for people referred to secondary care for anxiety? What does this pathway look like?	If there is evidence that the treatment could be an augmentation strategy, then it could be a treatment option for secondary care.

52.	11/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	No answer provided
53.	26/06/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Patient pathway questions	Telephone call with EAC	In the Morriss study only 22% of eligible patients (awaiting iCBT) agreed to join the study and utilise Alpha-Stim, suggesting that patient preference is an important factor. The decision tree model broadly has a good fit with the pathway in clinical practice. It is conceivable that Alpha-Stim could be introduced at an earlier point in the pathway. The model does not include use of drugs. Commonly used drugs e.g. SSRIs could be used at any point in the clinical pathway. However we feel this would impact the model significantly only if there was differential use of SSRIs in patients using Alpha-Stim compared to patients using iCBT. For clinical evidence, randomised studies comparing Alpha-Stim versus sham comparators should provide the most robust evidence. Sham treatments have been given to mimic transcranial direct current stimulation (tDCS) which can provide a sensation to the patient but without delivering the therapy. We note that tDCS is not in the guidance scope for Alpha-Stim. We are advised to consider the duration of improvement of symptoms and also relapse rate following use of Alpha-Stim and iCBT. We are advised to make note of the drop out rate in clinical studies as an indicator of patient tolerance to the therapies.

				Thank you for referencing the Kennerly paper (2004). We will watch out for the double blind placebo controlled study that the authors planned.
54.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Does a proportion of patients on the waiting list drop out before iCBT in standard care (e.g. drugs from GP start to work, patient recovers)? If so, what proportion?	My impression is there is high dropout of patients in usual care which I would estimate is around a third for both offer of CBT referral or medication and even those initially taking medication I think figures are around a quarter dropout within the first month
55.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Are there any important features about the clinical pathway used to treat GAD in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE GAD pathway.	Reality is that there is very poor follow-up of people with generalised anxiety disorder it is not part of quality and outcome framework and not part of typical general practice therefore people followed up do not go through step to care pathway unless they are under IAPT, again the service has high dropout.
56.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Does use of Alpha-Stim as an alternative to drug treatment and high intensity psychological interventions after steps 1 and 2 of NICE GAD pathway seem appropriate? These are patients with a diagnosis of GAD for whom step 1 treatment (education and monitoring) and step 2 treatments (low intensity psychological interventions) have not been effective.	Personally I would've thought it could be offered at an earlier part of the pathway as I think it is likely to be more cost-effective than IAPT
57.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Would a GP/nurse use the GAD-7 questionnaire to diagnose GAD? What are the approaches for diagnosis of GAD?	Yes with training – It is not difficult to diagnose especially using questionnaires, primary care nurses have limited mental health experience. Brief half day/1 day training course this would be valuable.
58.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	How is the IAPT pathway for patients with symptoms of anxiety different to non-IAPT? Once referred, do both IAPT and non-IAPT follow the NICE guideline for GAD in the same way? Would IAPT impact the way Alpha-Stim is used?	Patient to do in gauge with IAPT to have some follow-up and could then be stepped up. IAPT Does offer some follow-up therefore likely to have slightly improved recovery rates and treatment

				as usual. I don't think it would matter if patients have psychological therapy at the same time as Alphastim. I think it will be working at different parts of the brain and most of the evidence suggests combination treatments are more effective.
59.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Are there any important features about the clinical pathway used to treat social anxiety disorder in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE clinical guideline on social anxiety disorder.	Social phobia is poorly diagnosed poorly followed up and rarely do we use specific questionnaires in General Practice People in IAPT services I would hope get NICE guidance approach – however I don't recall many patients giving positive recovery stories
60.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Would Alpha-Stim be an initial treatment options for adults with social anxiety disorder (see page 19 or NICE clinical guideline on social anxiety disorder) ?	Yes I think this would be a helpful opportunity and choice for patients
61.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Other than GAD and SAD pathways are there any other key pathways where Alpha-Stim could be used for the treatment of anxiety disorders?	I would be interested in the opportunity around PTSD which I think it's going to be especially relevant post COVID. Also opportunities around panic disorder and mixed anxiety and depression
62.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Would Alpha-Stim be a treatment option for people referred to secondary care for anxiety? What does this pathway look like?	I don't see why there would be a problem with it being used in voluntary sector, primary care or secondary care. In all cases I think it is as simple as explaining how the device is used, providing follow-up and enabling it to be integrated within other pathways.
63.	04/07/20	**EXPERT – Dr David Smart (GP)** Patient pathway questions	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	I have a long-standing interest in common mood disorder And remain surprised that it is not given more priority for intervention and implementation. This especially relates to the opportunity for education and training for frontline staff. Also for the opportunity of regular follow-up and attention step to care pathways

				and collaborative care pathways to be the norm rather than only in a few treatment centres. There is significant opportunity for a physical approach such alphastim to be utilised within medically unexplained symptoms and people with long-term conditions who have more of an attribution of the mental health towards a physical approach
64.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Does a proportion of patients on the waiting list drop out before iCBT in standard care (e.g. drugs from GP start to work, patient recovers)? If so, what proportion?	I am not sure what you are asking here when you say 'drop out before iCBT in standard care'. Do you mean stop attending appointments, or do you mean not respond to invitations to take up iCBT, or do you mean stop following a clinical pathway on their own initiative or on the advice of a clinician. I am assuming you mean stop attending standard care appointments and I would estimate 25-50%.
65.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Are there any important features about the clinical pathway used to treat GAD in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE GAD pathway.	The NICE pathway is a helpful guide but of course it doesn't necessarily reflect local service provision, particular patient and clinician factors and other constraints. Many patients have little enthusiasm with low level interventions and some have been struggling with their symptoms for some time. They have researched a lot of self-help and already accessed low intensity psychological interventions. Talking therapies do not suit everyone by any means and many are averse to using medication.
66.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Does use of Alpha-Stim as an alternative to drug treatment and high intensity psychological interventions after steps 1 and 2 of NICE GAD pathway seem appropriate? These are patients with a diagnosis of GAD for whom step 1 treatment (education and monitoring) and step 2 treatments (low intensity psychological interventions) have not been effective.	Yes it seems appropriate to me certainly.

67.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Would a GP/nurse use the GAD-7 questionnaire to diagnose GAD? What are the approaches for diagnosis of GAD?	GAD 7 is a very helpful diagnostic tool but it is best used by an experienced clinician with the confidence to pick up abnormal and severe presentations that may not be detected by questionnaires.
68.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	How is the IAPT pathway for patients with symptoms of anxiety different to non-IAPT? Once referred, do both IAPT and non-IAPT follow the NICE guideline for GAD in the same way? Would IAPT impact the way Alpha-Stim is used?	Alpha-Stim, like IAPT can be used alone and alongside other interventions on the pathway including medication. IAPT would not impact the way Alpha-Stim is used.
69.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Are there any important features about the clinical pathway used to treat social anxiety disorder in real-life practice compared to how it is described in NICE's clinical pathway? Please refer to NICE clinical guideline on social anxiety disorder.	It is rarely practical or necessary to try and distinguish between the anxiety disorders in primary care prior to an IAPT assessment.
70.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Would Alpha-Stim be an initial treatment options for adults with social anxiety disorder (see page 19 or NICE clinical guideline on social anxiety disorder) ?	After assessment, education and a period of reflection on self-help resources. I would not envisage giving anyone a unit on first presentation.
71.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Other than GAD and SAD pathways are there any other key pathways where Alpha-Stim could be used for the treatment of anxiety disorders?	See answer to Q.6

72.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Would Alpha-Stim be a treatment option for people referred to secondary care for anxiety? What does this pathway look like?	Its very difficult to get anybody seen by secondary care mental health services that does not present a degree of risk to themselves or others. I am sure if such a hypothetical situation existed and it had not been tried already alpha-stim would be an option.
73.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Patient pathway questions	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	No
74.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	The company model references 3 models of iCBT: • Standard Practice model that includes 8 low intensity iCBT sessions costing • 'Heimberg model' with one session of 90 min iCBT followed by 15 sessions of 60 min iCBT • Clark and Wells model' with 14 sessions of 90 min sessions of iCBT In your experience, which model is most common? Are they all used in the IAPT service? How do you decide which model of iCBT to use?	Only the standard practice model is used by IAPT.
75.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Would patients be offered a condensed model of iCBT (fewer/shorter) sessions?	In some IAPT services, IAPT may offer 6 or 7 sessions rather than 8 but this is likely to be less severe cases (e.g. GAD-7 score less than 12, no comorbidity or people who have not failed other treatment) than the ones presented in the evidence.

76.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	What proportion of patients who fail first line iCBT take up the second round of iCBT?	IAPT services are very unlikely to offer a second course of iCBT, only if there were administrative or other reasons for not having a full course of iCBT on the first occasion.
77.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Would patients ever be offered a 3rd round of iCBT?	None
78.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	The economic model uses a response rate of 54.2% (range 0.49 – 0.59) for patients treated with iCBT for GAD. Is this a reasonable figure and range?	Yes this is a reasonable range.
79.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Do patients have the same response rate of 54.2% to first and second rounds of iCBT? Please estimate values. Do patients who have iCBT after failing to respond to Alpha-Stim have the same response rate? Please estimate values.	Generally response rates to a second round of iCBT would be very low which is why I have never known IAPT to offer it. Patients who have not responded to Alpha-stim will have a slightly lower response rate to iCBT nearer to 0.50 rather than 0.59.
80.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Are patients who show recovery after the first line of iCBT offered a second round?	Patients are discharged and then usually have to wait 12 months before they are offered another course of IAPT treatment.

81.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Is a response rate to Alpha-Stim (for GAD) of 0.47 (range 0.38-0.48) reasonable?	Yes
82.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	How is recovery or remission from GAD defined? i.e. at which point would treatment for GAD be stopped?	A score of 7 or less on the GAD-7 score is considered remission.
83.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	The economic model uses a cost of £110.96 for a 60 min iCBT and £199.17 for 90 mins. Does this seem reasonable?	Yes
84.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	What proportion of patients with GAD will receive medication? Will this proportion be the same for patients treated with iCBT compared to Alpha-Stim?	Approximately 50% will receive medication, most often antidepressants. There are unlikely to be differences between iCBT and alpha-stim. Some prefer these treatments as an alternative to medication and others are seeking greater effectiveness than medication alone.
85.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	What are the most common drugs and dosages for treating GAD? Are these specific to GAD or are they used to treat depression also?	SSRI antidepressants are most commonly used, sometimes at lower doses than for depression e.g. 50mg sertraline per day and sometimes similar doses as for depression e.g. 100-200mg per day. Some patients take benzodiazepine drugs continuously or more often when needed, others take low dose or similar dose to depression tricyclic or SNRI

				antidepressants. Propranolol I and low dose antipsychotic drugs are still sometimes used and pregabalin or gabapentin increasingly.
86.	08/07/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	What proportion of patients with GAD (at Step 3 of pathway) refuse iCBT? What treatment is used at this point?	10-15% of patients refuse iCBT if they completed low intensity psychological treatment in IAPT and are still symptomatic. At this point patients are referred back to the GP and placed on medication.
87.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	The company model references 3 models of iCBT: • Standard Practice model that includes 8 low intensity iCBT sessions costing • 'Heimberg model' with one session of 90 min iCBT followed by 15 sessions of 60 min iCBT • Clark and Wells model' with 14 sessions of 90 min sessions of iCBT In your experience, which model is most common? Are they all used in the IAPT service? How do you decide which model of iCBT to use?	I do not know the answer to these questions. Please contact IAPT or look for published figures. I think each IAPT service differs in its approach.
88.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Would patients be offered a condensed model of iCBT (fewer/shorter) sessions?	I do not know the answer to this question. Please contact IAPT or look for published figures. I think each IAPT service differs in its approach.
89.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	What proportion of patients who fail first line iCBT take up the second round of iCBT?	I do not know the answer to this question. Please contact IAPT or look for published figures

90.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Would patients ever be offered a 3rd round of iCBT?	I do not know the answer to this question. Please contact IAPT or look for published figures. I think each IAPT service differs in its approach.
91.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	The economic model uses a response rate of 54.2% (range 0.49 – 0.59) for patients treated with iCBT for GAD. Is this a reasonable figure and range?	I do not know the answer to this question. Please look at the reference used to calculate this figure
92.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Do patients have the same response rate of 54.2% to first and second rounds of iCBT? Please estimate values. Do patients who have iCBT after failing to respond to Alpha-Stim have the same response rate? Please estimate values.	I do not know the answer to these questions. Please contact IAPT or look for published figures
93.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Are patients who show recovery after the first line of iCBT offered a second round?	I do not know the answer to this question. Please contact IAPT or look for published figures. I think each IAPT service differs in its approach.
94.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Is a response rate to Alpha-Stim (for GAD) of 0.47 (range 0.38-0.48) reasonable?	Please look at the reference used to calculate this figure

95.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	How is recovery or remission from GAD defined? i.e. at which point would treatment for GAD be stopped?	There are cut off points for the GAD-7 measure used which define recovery or remission
96.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	The economic model uses a cost of £110.96 for a 60 min iCBT and £199.17 for 90 mins. Does this seem reasonable?	I do not know the answer to this question. Please contact IAPT or look for published figures
97.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	What proportion of patients with GAD will receive medication? Will this proportion be the same for patients treated with iCBT compared to Alpha-Stim?	I do not know the answer to these questions. There are probably published statistics available for the first question.
98.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	What are the most common drugs and dosages for treating GAD? Are these specific to GAD or are they used to treat depression also?	I do not know the answer to this question. There are probably statistics available for NHS specific drug prescription for specific disorders.
99.	07/07/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	What proportion of patients with GAD (at Step 3 of pathway) refuse iCBT? What treatment is used at this point?	I do not know the answer to this question. Please contact IAPT or look for published figures

100.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	The company model references 3 models of iCBT: • Standard Practice model that includes 8 low intensity iCBT sessions costing • 'Heimberg model' with one session of 90 min iCBT followed by 15 sessions of 60 min iCBT • Clark and Wells model' with 14 sessions of 90 min sessions of iCBT In your experience, which model is most common? Are they all used in the IAPT service? How do you decide which model of iCBT to use?	No response given
101.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Would patients be offered a condensed model of iCBT (fewer/shorter) sessions?	No response given
102.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	What proportion of patients who fail first line iCBT take up the second round of iCBT?	No response given
103.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Would patients ever be offered a 3rd round of iCBT?	No response given

104.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	The economic model uses a response rate of 54.2% (range 0.49 – 0.59) for patients treated with iCBT for GAD. Is this a reasonable figure and range?	This seems to be a reasonable figure and range
105.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Do patients have the same response rate of 54.2% to first and second rounds of iCBT? Please estimate values. Do patients who have iCBT after failing to respond to Alpha-Stim have the same response rate? Please estimate values.	If the clinical response after the first round of iCBT is limited, then the response after the second round of iCBT is often also limited, but it would be necessary to take into account any factors that might have contributed to the response in the first round. I don't know if there is literature on the response rate to iCBT after failing to respond to Alpha-Stim.
106.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Are patients who show recovery after the first line of iCBT offered a second round?	No response given
107.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Is a response rate to Alpha-Stim (for GAD) of 0.47 (range 0.38-0.48) reasonable?	This seems reasonable based on the literature to date.
108.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)**	How is recovery or remission from GAD defined? i.e. at which point would treatment for GAD be stopped?	Remission can be defined as no longer meeting diagnostic criteria for the disorder or can be defined as having symptoms which are less than a particular score on a specific rating scale, for example having a score < 7 on the Hamilton Anxiety Rating Scale (HAM-A) or a score of < 5 on Generalized anxiety disorder

		Questions relating to economic model		scale (GAD-7). For remission to be considered to be clinically meaningful, it should also be sustained for a period of time, usually over several consecutive weeks.
109.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	The economic model uses a cost of £110.96 for a 60 min iCBT and £199.17 for 90 mins. Does this seem reasonable?	No response given
110.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	What proportion of patients with GAD will receive medication? Will this proportion be the same for patients treated with iCBT compared to Alpha-Stim?	This depends on what a patient would prefer, if they might prefer iCBT or medication.
111.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	What are the most common drugs and dosages for treating GAD? Are these specific to GAD or are they used to treat depression also?	The most common medication is a selective serotonin reuptake inhibitor (SSRI), which is also used to treat depression. If this isn't effective, then another SSRI can be tried or a serotonin noradrenaline reuptake inhibitor (SNRI) can be tried, which are also used to treat depression. If these are not effective, then pregabalin can be considered, which is not generally used to treat depression.
112.	10/07/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	What proportion of patients with GAD (at Step 3 of pathway) refuse iCBT? What treatment is used at this point?	Patients would be offered a referral to a community mental health team or to specialist services and the treatments could include a combination of medication and psychological therapy or augmentation with medication, assessment of supports and relationships, withing a comprehensive care plan.

113.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	The company model references 3 models of iCBT: • Standard Practice model that includes 8 low intensity iCBT sessions costing • 'Heimberg model' with one session of 90 min iCBT followed by 15 sessions of 60 min iCBT • Clark and Wells model' with 14 sessions of 90 min sessions of iCBT In your experience, which model is most common? Are they all used in the IAPT service? How do you decide which model of iCBT to use?	As a full-time GP working in Nottingham I have little knowledge of the different types of CBT offered by IAPT services. I would have no means of influencing the type of CBT offered to patients as I almost exclusively encourage self-referral in my patients.
114.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	Would patients be offered a condensed model of iCBT (fewer/shorter) sessions?	Don't know
115.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	What proportion of patients who fail first line iCBT take up the second round of iCBT?	Approx. 50% will have another go at CBT
116.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	Would patients ever be offered a 3rd round of iCBT?	Very unusually in my experience and always from an alternative provider.

117.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	The economic model uses a response rate of 54.2% (range 0.49 – 0.59) for patients treated with iCBT for GAD. Is this a reasonable figure and range?	Yes
118.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	Do patients have the same response rate of 54.2% to first and second rounds of iCBT? Please estimate values. Do patients who have iCBT after failing to respond to Alpha-Stim have the same response rate? Please estimate values.	I am not able to answer this question with any high degree of confidence but my feeling based on experience is that about half of pateints who dont respond to a first course will respond to a second and I think this will be about the same as pateints who have not responded to Alpha-Stim.
119.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	Are patients who show recovery after the first line of iCBT offered a second round?	Not immediately in Nottingham – usually asked to consolidate for three months.
120.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	Is a response rate to Alpha-Stim (for GAD) of 0.47 (range 0.38-0.48) reasonable?	Yes, in my experience with 50 users
121.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	How is recovery or remission from GAD defined? i.e. at which point would treatment for GAD be stopped?	This would not be as simple as attaining a threshold score on GAD-7 for instance. There would need to be a degree of concordance between patient and clinician.

122.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	The economic model uses a cost of £110.96 for a 60 min iCBT and £199.17 for 90 mins. Does this seem reasonable?	I am not able to comment on this.
123.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	What proportion of patients with GAD will receive medication? Will this proportion be the same for patients treated with iCBT compared to Alpha-Stim?	I think an Alpha-Stim option would reduce the proportion of patients prescribed medication and/or using IAPT but I cannot put a figure on it.
124.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	What are the most common drugs and dosages for treating GAD? Are these specific to GAD or are they used to treat depression also?	SRRI antidepressants are the commonest in my experience, predominantly sertraline in a dose range 25-200mg and escitalopram in a dose range 5-20mg. SNRIs such as venlafaxine (37.5mg-300mg) maybe used as second-line or as an alternative an atypical such as mirtazapine (15-45mg)
125.	07/07/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to economic model	What proportion of patients with GAD (at Step 3 of pathway) refuse iCBT? What treatment is used at this point?	Few will refuse iCBT if they have not tried it before. Medication would be offered.
126.	02/09/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	If a patient does not respond to Alpha-Stim, what is the possibility/likelihood they will respond to iCBT (and vice versa)	This is unknown from current data. There is no scientific reason to suggest that treatment with alpha-stim would make someone more or less responsive to iCBT if they were given sequentially or vice versa. However, if patients have not responded to many treatments before, then they are less likely to respond to any further intervention (the concept is known as

				treatment resistance although there is no widely accepted definition for anxiety disorders). It is also possible that those who adhere badly to treatments, whether alpha stim or iCBT, might also find them ineffective. There is a possibility from the data in Morriss et al (2019) that those patients who did badly with alpha –stim in the first 12 weeks and then sequentially had iCBT might do badly. This could be because 6-12 weeks of alpha-stim with minimal benefit makes them unresponsive to iCBT (however 6 weeks of alpha-stim followed by or at the same time iCBT is given within the same 12 weeks was similar in response rate to no CBT), treatment resistance to any treatment or these are patients who do not adhere well to treatment. The design of the study does not allow an assessment of these possibilities. A further analysis of the data in Morriss 2019 just accepted for publication in the Journal of Affective disorders intriguingly suggests that continued improvements in anxiety and depression symptoms at 24 weeks are mediated by alpha stim effects on depression at 12 weeks but at earlier time points they are mediated by improvements with alpha stim on anxiety symptoms in the first four weeks. It is possible that sustained improvements in anxiety with alpha stim might require short-term effects in anxiety and more sustained benefits on depression (with alpha-stim or iCBT). However this is a tentative hypothesis.
127.	02/09/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Current published response rates for Alpha-Stim are around 47% and for iCBT are around 54%. From some published evidence, there is a suggestion that the response rate for patients who have both Alpha-Stim and iCBT may be much lower. Based on your clinical judgement and	From my clinical experience with severe and long-standing anxiety, iCBT and alpha-stim are complimentary in terms of keeping anxiety symptoms to a manageable level. Alpha-stim calms the mentation (worrying) and physiological arousal while iCBT gives the person cognitive and behavioural

			experience, if a patients does not respond to Alpha-Stim is there any reason to suggest that their response to subsequent iCBT would be much lower than 54%?	strategies to utilise, particularly when there are exacerbations of anxiety.
128.	02/09/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Could you provide some indication of what response rate might be realistic for patients who have not responded to an initial non-pharmacological treatment such as Alpha-Stim and gone on to receive a second type of treatment such as iCBT?	The response rates would be expected to be similar to iCBT whether or not they responded to alpha-stim. They have different sites of action – CBT on the content and form of negative thinking and behaviour that maintains the anxiety, while alpha-stim has a calming effect on mentation and physiology of the body. However, there is the possibility that those who do not obtain a clinically important change with alpha stim in the first 6 weeks might become unresponsive to iCBT unless it is given immediately. This is not compatible with my clinical experience though.
129.	02/09/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Could you comment on whether there is anything about non-responders which confound or impact the response rates? For example • Are these patients likely to have more severe symptoms or had symptoms for longer? • Are these patients likely to begin a course of treatment and not complete it for some reason? • Do some patients deteriorate during non-pharmacological treatments?	Non-responders are more likely to be treatment resistant to multiple types of treatment, and unwilling or unable to use every day for one hour for at least six weeks. Severity of symptoms, failure to improve with one form of psychological treatment, and the severity of initial depression, sleep problems or pain do not make alpha-stim less effective. The effects of illicit drugs and alcohol on response of alpha-stim in anxiety disorders is unknown. In previous research, patients did not deteriorate during alpha-stim but this has happened in clinically in the face of a new overwhelming life situation.
130.	02/09/20	**EXPERT - Prof Richard Morriss (Professor of Psychiatry & Community Mental Health)** Questions relating to economic model	Specifically in relation to data reported in the publication Clinical effectiveness and cost minimisation model of Alpha-Stim cranial electrotherapy stimulation in treatment seeking patients with moderate to severe generalised	In Morriss et al (2019), recovery rates at 24 weeks: All patients (n=161), 77 recovered (47.8%) No CBT (n=81), 53 recovered (65.4%) Any CBT (n=80), 24 recovered (30.0%) Alpha stim and iCBT completed together in first 12 weeks, 17 recovered (68.0%)

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<td>anxiety disorder Morriss et al (2019) we have some queries around the data reported

• Could you please clarify what the recovery rates at week 24 were for:
  ○ All patients
  ○ Patients treated with only Alpha-Stim
  ○ Patients treated with Alpha-Stim +iCBT
1.
Based on the numbers reported in table 3: we calculate the following

<table>
<tr><th>Treatment</th><th>Total N</th><th>Responders</th><th>Response rate</th></tr>
<tr><td>All patients (Alpha-Stim alone or with any other treatments)</td><td>161</td><td>77</td><td>47.8%</td></tr>
<tr><td>Alpha-Stim Only (no iCBT)</td><td>81</td><td>53</td><td>65.4%</td></tr>
<tr><td>Alpha-Stim + iCBT (not reported in the paper, calculated from the information provided)</td><td>80</td><td>24</td><td>30%</td></tr>
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<td>Stopped or completed alpha stim and then had iCBT, 7 recovered (12.7%). Note number of sessions of iCBT not recorded.</td>
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<td>However we note that in the text of the publication the following results are reported
<table>
<tr><th>Treatment</th><th>Total N</th><th>Responders</th><th>Response rate</th></tr>
<tr><td>Alpha-Stim Only (no iCBT)</td><td>81</td><td>53</td><td>65.4%</td></tr>
<tr><td>Alpha-Stim + iCBT (not reported in the paper, calculated from the information provided)</td><td>25</td><td>17</td><td>68%</td></tr>
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<td>131.</td>
<td>28/08/20</td>
<td>EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)

Questions relating to economic model</td>
<td>If a patient does not respond to Alpha-Stim, what is the possibility/likelihood they will respond to iCBT (and vice versa)?</td>
<td>There are research papers which describe iCBT response rates. There are different iCBT programs and so response rates differ. NICE and Cochrane reviews of evidence can inform answer to this. Morriss’s alpha-stim paper mentions iCBT</td>
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<tr>
<td>132.</td>
<td>28/08/20</td>
<td>EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)

Questions relating to economic model</td>
<td>Current published response rates for Alpha-Stim are around 47% and for iCBT are around 54%. From some published evidence, there is a suggestion that the response rate for patients who have both Alpha-Stim and iCBT may be much lower. For patients receiving iCBT as a second therapy after trying Alpha-Stim but gaining no response, Would you expect a lower response rate from iCBT than the published value 54%?</td>
<td>I suppose it depends on individual reasons for trying Alpha-Stim instead of iCBT if a person had this option. If people chose Alpha-Stim because they did not think iCBT would work or if they did not like the idea of it then this group would be different to those who chose iCBT first and so their response rates could be lower.</td>
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133.	28/08/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Could you provide some indication of what response rate might be realistic for patients who have not responded to an initial non-pharmacological treatment such as Alpha-Stim and gone on to receive a second type of treatment such as iCBT?	No
134.	28/08/20	**EXPERT – Dr Chris Griffiths (Senior Research and Evaluation Fellow)** Questions relating to economic model	Could you comment on whether there is anything about non-responders which confound or impact the response rates. For example • Are these patients likely to have more severe symptoms or had symptoms for longer? • Are these patients likely to begin a course of treatment and not complete it for some reason? • Do some patients deteriorate during non-pharmacological treatments?	Re: '• Are these patients likely to have more severe symptoms or had symptoms for longer?' I do not know the answer to this Re: '• Are these patients likely to begin a course of treatment and not complete it for some reason?' yes Re: '• Do some patients deteriorate during non-pharmacological treatments?' this is true for all treatments
135.	09/09/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	If a patient does not respond to Alpha-Stim, what is the possibility/likelihood they will respond to iCBT (and vice versa)?	I would expect that the response rate to iCBT would be around 50%.
136.	09/09/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)**	Current published response rates for Alpha-Stim are around 47% and for iCBT are around 54%. From some published evidence, there is a suggestion that the response rate for patients who have both Alpha-Stim and iCBT may be much	If the form of the disorder is more of a treatment resistant form, this might be seen clinically as a lower response rate with consecutive treatment trials because it isn't possible to predict clinical outcome

		Questions relating to economic model	lower. For patients receiving iCBT as a second therapy after trying Alpha-Stim but gaining no response, Would you expect a lower response rate from iCBT than the published value 54%?	before the start of treatment for an individual patient at the present time. If there are distinct mechanisms for Alpha-Stim and iCBT, then I would expect that the response rate for iCBT following Alpha-Stim should be comparable. As there are likely some common mechanisms, such as the therapeutic relationship, as well as distinct mechanisms for Alpha-Stim and iCBT, it isn't clear whether the response rate for iCBT would be much lower.
137.	09/09/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Could you provide some indication of what response rate might be realistic for patients who have not responded to an initial non-pharmacological treatment such as Alpha-Stim and gone on to receive a second type of treatment such as iCBT?	The literature is quite limited for this question. I would expect a comparable response rate.
138.	09/09/20	**EXPERT – Prof Cynthia Fu (Professor of Affective Neuroscience/ Honorary Consultant Psychiatrist)** Questions relating to economic model	Could you comment on whether there is anything about non-responders which confound or impact the response rates. For example • Are these patients likely to have more severe symptoms or had symptoms for longer? • Are these patients likely to begin a course of treatment and not complete it for some reason? • Do some patients deteriorate during non-pharmacological treatments?	Having more severe symptoms is strongly associated with a reduced response rate. Having a longer duration of untreated symptoms is also associated with a reduced response rate. Comorbid disorders and some personality features can also impact on response rates. However, we do not have any clinical predictors at the level of the individual patient at the present time. These are clinical factors that are associated with clinical response. Starting a course of treatment and discontinuing it early could reflect a number of reasons, such as

				adverse events or personal characteristics, which would affect response rates. Being on a wait list control treatment arm has been associated with a deterioration in symptoms. Some patients do deteriorate during non-pharmacological treatments, and they tend to discontinue the treatment.
139.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	The protocol gives a number of treatment options available at the nurse clinic. Is there any additional information available concerning a. How many patients opted for these, and did not also receive Alpha-Stim? How many patients opted for these in conjunction with Alpha-Stim?	No additional information. Alpha-Stim was available to all participants who consented to the study as were all the other elements of the pathway. [redacted]
140.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	Were the same options (other than Alpha-Stim) available to patients in the comparator group who were seen by the GP?	Yes.
141.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	What types of treatments were received by patients in the comparator group?	Self-help, talking therapies, medication.

142.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	If additional modelling required information on medication use for each group, could this be made available?	If one takes prescriptions issued to participants during the study period as a proxy for medication use then the answer is a qualified 'yes' (it would take some time to review the records and extract the data). However, I am not convinced this would be a valid assumption since prescriptions may be lost, not used, issued early or late. Medication may be collected but not taken, not taken as intended or lost.
143.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	Do you consider ispero to be an essential part of running the nurse-led clinic, and what is its primary role?	None of the components were essential. Ispero was of particular vale in monitoring mental wellbeing while participants attended the clinic.
144.	02/12/20	**EXPERT – Dr Simon Royal (Honorary Assistant Professor Primary Care / GP)** Questions relating to unpublished study in primary care	What is the cost of providing Ispero (if available)?	Ispero, like Alpha-Stim, was provided free of charge to the study. [redacted]

Insert more rows as necessary

Appendix 1.

During correspondence with the company and experts, additional information is sometimes included as file attachments, graphics and tables. Any questions that included additional information of this kind is added below in relation to the relevant question/answer:

File attachments/additional information from question 11:

Primary care GP Services

Patient consults GP (or prescribing nurse) face to face or remotely who assesses the patient for anxiety.

↓

GP or prescribing nurse diagnoses Generalised Anxiety Disorder with GAD-7 score ≥8 has functional impairment at step 3 of NICE GAD pathway, offers Alpha-Stim CES as alternative to drug treatment and high intensity psychological treatment after steps 1 and 2 of NICE GAD pathway (step 1, education and watchful waiting 2 weeks, step 2 low intensity psychological intervention offered and not effective or refused by patient).

↓

2.

Practice nurse or health care assistant supplies Alpha-Stim CES and shows how to use (could be via telephone call and video presentation)

↓

Daily use by patient at home for 60 minutes for 6 weeks

↓

Telephone support within 72 hours

↓

3.

Practice nurse or health care assistant collects Alpha-Stim CES. Completes GAD-7. Patient is discharged if GAD-7 score is 7 or below. Patient is signposted to GP if GAD-7 ≥ 8 and in consultation with GP is offered further 6 weeks Alpha-Stim CES if appropriate. If functional impairment then patient may be referred for drug or high intensity psychological treatment.

4.

Primary Care Improving Access to Psychological Treatment (IAPT)

Self-referral or primary care referral.

↓

Generalised Anxiety Disorder diagnosed. Low intensity psychological intervention given. GAD-7≥8 because this is the current IAPT threshold to be offered high intensity psychological treatment. Eligible for high intensity psychological intervention, either on waiting list for high intensity psychological treatment or prefers to have Alpha-Stim CES.

↓

IAPT Psychological Wellbeing Practitioner (PWP) shows how to use Alpha-Stim CES and supplies for 6 weeks

↓

Telephone support within 72 hours

↓

IAPT PWP collects Alpha-Stim CES. Completes GAD-7. Patient is discharged if GAD-7 score is 7 or below. If GAD-7 ≥8 patient is offered further 6 weeks Alpha-Stim CES if appropriate and offered high intensity treatment if on waiting list for it already or offered high intensity if not or discharge to GP.

Secondary care mental health or long-term conditions pathway

Existing patient with serious mental illness or long-term physical condition diagnosed with comorbid Generalised Anxiety Disorder that is impairing function and GAD-7 ≥10 that has not improved with education and simple psychological intervention. Additional medication undesirable e.g. sedation, addiction potential or contraindicated.

↓

Mental health professional or support worker shows how to use Alpha-Stim CES and supplies for 6 weeks

↓

Telephone support within 72 hours

↓

Mental health professional or support worker collects Alpha-Stim CES. Completes GAD-7. Patient stops using Alpha-Stim CES if GAD-7 is 7 or below. If GAD-7 ≥8 patient is offered further 6 weeks Alpha-Stim CES if appropriate, in consultation with mental health professional.

Consider high intensity psychological treatment if GAD-7 score ≥8 and functional impairment.