National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT330 Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery

Consultation comments table on second medical technologies consultation document

Final guidance MTAC date: 22 June 2018

There were 80 consultation comments from 60 consultees (1 carer, 4 NHS healthcare professionals [abroad], 5 healthcare other, 38 NHS professionals, 2 NHS professionals [expert adviser], 6 patients, 4 professional organisations). The comments are reproduced in full, arranged in the following groups according to the main issue raised in the relevant comment (**some comments contain multiple issues and have been split**):

- Clinical evidence (comments 1 to 40)
- Recommendations (comments 41 to 64)
- Benefits of the technology (comments 65 to 74)
- Costs (comments 75 to 80)
- Technical (comments 81 to 88)
- General (comments 89 to 104)

Clinical evidence:

Comment no.	Consultee ID	Role	Section	Comments	Response
1	38	Professional society	-	On behalf of the council of the Neuromodulation Society of the UK & Ireland (NSUKI) we are writing to express our views with the latest draft of the Senza consultation document. We did point out the De Andres et al, 2017 in your last consultation. Since the last consultation phase for this review of Senza, this study has been subject to an unusual inquiry by the invited editors of the initial article Prof Sam Eldabe and Dr Richard North. The letter to the editor recently published in Pain Medicine explains there are important questions associated with the conduct of this study (attached). This investigation confirms very limited compliance with accepted standards in clinical study execution. For example, the author admits that written informed consent was not obtained which is not compliant with EU and international norms. Further, the study was initially presented, not as interim results, but as a standalone “prospective observational study” in previous congresses and abstracts. The author when specifically asked (question 6 from the letter) declined to specifically state if the data were collected concurrently for both arms. After reading the letter to the editor on De Andreas et al, we feel this study has deficiencies: • Study not done in accordance with studies in the UK • Scrutiny of the methodology, reveals that the lead placement is not appropriate for the optimal delivery of HF10 therapy, which raises the question of outcome comparison to other published studies and case series • Both traditional low frequency SCS and Senza to achieve such a weak therapeutic effect, questions must be raised about whether suitable patients were selected through robust multidisciplinary team assessments as is standard practice in the UK	Thank you for your comment. The controversy associated with the RCT evidence for Senza SCS and the large number of comments received during consultation prompted the medical technologies evaluation programme (MTEP) to seek a second independent HTA viewpoint on the RCT evidence (Kapural et al. 2016 and De Andres et al. 2017) for the committee to take into account. Please see the EACs advisory documents for further details of the reviews. After careful consideration of the comments and the evidence the committee noted the weaknesses in both randomised controlled trials, including the potential for bias and concerns about the relevance of the results to the NHS, it agreed with the EAC’s conclusion that Senza is at least as effective as low-frequency SCS in terms of relieving pain and decided to make some minor amendments to section 1 and 4 of the final guidance.

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2	23	Professional organisation	-	Similarly, the results of the De Andres study are poor across the board for all therapies - much worse than most reported studies of any frequency. If such results were used to assess SCS as a whole, it is unlikely that it would be thought a viable therapy. Despite this, the committee gave considerable weight to it. It is therefore important to clarify a number of points of inaccuracy and misinterpretation in some detail: Ethical Conduct of DeAndres Study See also publication (23/4/2018 online, Pain Medicine 2018; 0: 1–2 doi: 10.1093/pm/pny064) 1. A highly unusual recently published Letter to the Editor (by the original invited editors North and Eldabe) regarding the DeAndres publication raised many concerns regarding the ethical and methodological conduct of this study. For example, contrary to prevailing Spanish and EU regulations the author admits to the editors that no written informed consent was obtained. The study was not registered or reviewed with any regulatory agency. 2. The study was initially presented in congresses as a "prospective observational trial" - not as interim results of an RCT - then later re-characterised as an RCT. When asked directly if the data for both arms of this RCT was collected concurrently the authors declined to answer (question 6). 3. The study does not comply with many CONSORT and other guidelines such as reporting of enrolment dates. 4. When asked if he had sought regulatory review, the author declined to directly answer stating only that he was told by the AEMPS: "You should contact the Subdirectorate General of Medical Devices, which will determine the requirements necessary to carry out this clinical investigation." No evidence or statements is provided that this guidance was followed.	Thank you for your comment. Please see the response to comment 1.

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3	23	Professional organisation	-	Methodology in DeAndres Study 1. The EAC wrongly states (section 5.3): Firstly, whilst it was impossible to blind participants, clinical assessors and investigators were blinded in the study, which should lead to a reduced risk in detection bias (biased measurement of outcomes). The authors state: The evaluators who collected pain ratings and other outcome measures were blinded to the subjects' group allocations throughout the process. Only the clinic personnel who collected patient self-reports are described as blinded. Thus, despite being described as a "blind" the study was fully open label: all the investigators, patients, clinicians, commercial programmers, data analysts were fully aware of the treatment they were receiving. 2. The primary outcome measure was "a reduction of at least 50% in pain intensity in the NRS score in the 12-month evaluation"; however, analysis of this primary outcome was not reported anywhere in the publication. No responder rates are reported. 3. A neuropathic pain component is required under TA 159. The authors state that Douleur Neuropathique 4 questionnaire (DN4) was used to validate this at all time points yet the results are not reported. 4. The Pain Detect Questionnaire (PD-Q) was also collected and was reported. However, at baseline the HF10 reported score was 16.23 and was 11.5 at the time of implant (Table 3). The authors indicate that these scores should be interpreted as (pg.5) "unlikely NeP (<13), unclear NeP (13–18)". Thus, the HF10 cohort were "unlikely" to have neuropathic pain at the time of implant and never had clear indications of neuropathic pain at any time point. 5. Pain medication usage and region of pain (eg. Back and or leg pain) was not reported. 6. Pain reduction of at least 50% during the trial is listed as required for moving to permanent implant. However, the actual	Thank you for your comment. Please see the response to comment 1.

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				pain reduction at trial is not reported. At the time of implant (t2, table 3) the amount of pain reduction was listed as only 34% for conventional and 40% for HF10. 7. There are many factual and technical errors and impossibilities when describing how the devices were programmed. (Stating for example (p4) that in HF10 “pulse widths were increased beyond 30 μs” which is to our knowledge not technically possible). 8. It appears from the illustrations and discussion that, contrary to appropriate published technique and manufacturer recommendations, the HF10 arm had leads positioned according to traditional low frequency practice (figure 1.) and that paraesthesia mapping was performed: “If the patient had good coverage except for a small percentage (toe, lower back), pulse width was increased.” Findings in DeAndres Study 1. The EAC states regarding this study: “The latter study did not report on the proportions of patients who elicited a 50% reduction in pain, nor was there the granularity of information to calculate this (although the longitudinal data reported suggest there were very few, if any, responders)” 2. This study does not compare to the many sponsored and non-sponsored large scale studies using the same and similar devices that on average provide long term VAS reduction of about 50% whereas in the DeAndres’ report the reduction was 15-20%. In summary, this controversial study with many caveats deviates from virtually all high level published literature for both standard and HF10 SCS and should be interpreted cautiously in that context.	

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4	20	NHS professional - expert adviser	-	HF10 is certainly superior to low frequency stimulation. The quality of De Andres paper is poor and hence should NOT be taken into consideration Van Buyten paper on explant data does NOT discuss the efficacy of HF10 or low frequency SCS. The patient population is completely different from UK population (SCS is NOT done for angina, cancer pain, peripheral vascular disease, abdominal pain etc in UK). The Senza RCT is a landmark study that was tightly regulated by FDA. Although It was NEVRO sponsored study, the conventional arm has Boston Scientific Representatives doing the programming meticulously resulting in overall improvement in outcomes in the conventional arm compared with the older RCTs and clinical experience. Despite this however the HF10 was far superior to the conventional low frequency arm. The 24 month data showed sustained pain relief. A lot of emphasis has been placed on the De Andres paper. This paper is of poor quality and has several flaws. The invited editors of the Pain Medicine have addressed concerns of other physicians on their editorial. The RCT is not registered Parts of the data presented at the INS meeting in May 2017 as a poster presentation. The study was characterised as on observational study Its a single centre study with a small number of cases The study reports poor result in both conventional and high frequency arm, which is contrary to most studies and clinical experience. The electrodes were not placed appropriately in this study	Thank you for your comment. Please see the response to comment 1. The EAC reviewed the evidence available for explantation data and considered the Van Buyten study published the most relevant information on unanticipated explantation rates. The study by Van Buyten had several strengths. Firstly, the methodology employed allowed for inclusion of a large number of subjects which might not have been feasible for an RCT. The sample size was sufficiently large to allow for appropriate time to event analysis and subgroup analysis so SCS technologies could be compared. In addition, as routine data were used, it should be generalisable to real world practice. To the EAC's knowledge, this study represented the most comprehensive review of this important outcome, device explantation, currently publically available. The data was not used for estimates of efficacy, rather unanticipated explantation. The committee considered the explant comment carefully and decided not change the guidance.

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				Responder rates and pain medication usage not mentioned In the high frequency arm (page 4) its mentioned that ' if the patient had good coverage except for a small percentage (toe , lower back) the pulse width was increased.'. This does not make sense as HF10 SCS does not rely on coverage of pain area and besides the pulse width is kept constant in HF10 therapy Complication shown in figure 2 page 7 does not tally with table 7 page 15 There is a difference in the assessment of patients at the five different time points. The authors mention this in their methodology where they recall patients to adjust stimulation in the CF group but not the HF group. Such a difference can influence outcomes. They quote the Perruchord study as evidence for bad patient selection for HF studies page 16 but this was 5K HF study. Finally they say that their outcomes differ from other studies because they used proper definition of FBSS compared to other studies. They also say that FBSS can be due to variable causes and I agree with them. However they do not mention the underlying pathologies on their groups. And yet the references they use for defining FBSS mentions no discrimination according to pathologies.	

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5	26	Professional organisation	-	This is a response to the NICE draft guidance (2) on Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery. The response was agreed through discussion at a meeting of the specialist interest group of Neuromodulation Nurses & Associated Practitioners (SNNAP) on 18th May 2018. The consensus amongst the group is that we have all seen the benefits of spinal cord stimulation in our clinical practice amongst appropriately selected patients. We believe that in our experience it can offer significant benefits not only in the reduction of pain and in the use of medication but also in the quality of life, improved function and reduction in the use of other healthcare services. Our group is aware of the lack of robust and unbiased research around Spinal Cord Stimulation and that further research is required in this area. It is within the scope of the group aims to encourage further research amongst our members. There were specific concerns amongst the group regarding the relevance of the DeAndres study to clinical practice. All members present agreed that patient selection in their centres is dependent upon at least a 50% reduction in VAS score during trial and that it would not be expected to attain such low overall pain scores post implant.	Thank you for your comment. Please see the response to comment 1.
6	27	NHS Professional	-	We will like to point out the flaws noted in De Andres' study as below: - Ethical conduct of De Andres Study Please see attached publication (23/4/18 online, Pain Medicine 2018; 0: 1-2 doi: 10.1093/pm/pny064) 1. A highly unusual recently published Letter to the Editor (by the originally invited editors North and Eldabe, Pain Medicine 2018 ; 0:1-2, doi: 10.1093/pm/pny064) regarding the De Andres publication raised many concerns regarding the ethical and methodological conduct of this study. For example, contrary to the prevailing Spanish and EU regulations the author admits to the editors that no written informed consent was obtained. The	Thank you for your comment. Please see the response to comment 1.

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				study was not registered or reviewed by any regulatory agency. 2. The study was initially presented in congresses as a "prospective observational trial" - not as interim results of an RCT – then later recharacterised as an RCT. When asked directly if the data for both arms of this RCT was collected concurrently; the authors declined to answer (question 6). 3. The study does not comply with many CONSORT and other guidelines such as reporting of environmental dates. 4. We are unsure of the process followed to lock the study data for independent analysis. This information is unavailable and not provided by the authors. Methodology in De Andres Study 1. The EAC wrongly states (section 5.3): Firstly, whilst it was impossible to blind participants, clinical assessors and investigators were blinded in the study, which should lead to a reduced risk in detection bias (biased measurement of outcomes). The authors state: The evaluators who collected pain ratings and other outcome measures were blinded to subjects' group allocations throughout the process. Only the clinic personnel who collected patient self-reports are described as blinded. Thus, despite being described as a "blind" indeed the study was an open label: all the investigators, patients, clinicians, commercial programmers, data analysts were fully aware of the treatment they were receiving. 2. The primary outcome measure was "a reduction of at least 50% in pain intensity in the NRS score in the 12 month evaluation"; however, analysis of this primary outcome was not reported anywhere in the publication. No responder rates are reported. 3. Pain medications usage and the region of pain treated (e.g. back and or leg pain) was not reported. 4. Pain reduction of at least 50% during the trial is listed as required for moving to the permanent implant. However, the actual pain reduction at trial is not reported. At the time of implant (t2, table 3) the amount of pain reduction was listed as	

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				only 34% for conventional and 40% for HF10; so if this is the case then why were these patients implanted (less than 50% pain relief at SCS trial). 5. There are many factual and technical errors and impossibilities when describing how the devices were programmed. (Stating for example that HF10 pulse widths were increased beyond 30 µs which is not technically possible, pg. 4). Findings in De Andres Study 1. The EAC states regarding this study: The latter study did not report on the proportions of patients who elicited a 50% reduction in pain, nor was there the granularity of information to calculate this (although the longitudinal data reported suggest there were very few, if any, responders) While the EAC points to this study to suggest similarity of conventional SCS to HF10; overall findings are inconsistent with extensive published evidence regarding SCS in general and must diminish the value placed on the findings of this study. 2. This anomalous study can be compared to the many sponsored and non-sponsored large scale studies using the same and similar devices that on average provide long-term VAS reduction of about 40%; whereas in the De Andres' report the reduction was only 20-25%. In summary, this controversial study with many caveats deviates from virtually all standards of high level published literature for both conventional SCS and HF10 SCS and should be considered only in that context.	

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7	8	NHS Professional	form 1 to 5	Please see comments that I've numbered below. 1. I am suprised that NICE has decided to use De Andres study. This was single centre study which published some poor SCS outcomes and shows poor research methodology. The results of this small study conflict the results of more robust studies e.g. North, Kumar, and Kapural studies. 60 patients were divided into two arms: Senza and Medtronic Average pain relief went from around 7.5 VAS to around 6 VAS, NRS in both arms, representing 15-20% relief The results of this study conflict with PROCESS and North, which underpin NICE TA159. De Andres is single centre whereas the others are multicentre Short term data of one year Patients did not receive HF10 therapy due to lead placement and programming parameters listed in the publication that are not possible with HF10 therapy 2. In total studies of over 450 HF10 patients were included in the NICE review '" all showed consistency in pain relief with HF10 therapy Tiede 2012 (n=24 implanted pts) Al-Kaisy 2014 (n=71 implanted pts) Senza-RCT (n= 101 implanted pts) Russo 2016 (n=189 implanted pts) Rapcan 2016 (n=21 implanted pts) Al-Kaisy 2016 (n = 20 implanted pts) Al-Kaisy 2018 (n=33 implanted patients)	Thank you for your comment. Please see the response to comment 1.

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8	15	Health professional (within NHS)	-	I will like to point out the flaws noted in De Andres' study as below: - Ethical Conduct of De Andres Study Please see attached publication (23/4/2018 online, Pain Medicine 2018; 0: 1'"2 doi: 10.1093/pm/pny064) 1. A highly unusual recently published Letter to the Editor (by the originally invited editors North and Eldabe, Pain Medicine 2018; 0:1-2, doi: 10.1093/pm/pny064) regarding the De Andres publication raised many concerns regarding the ethical and methodological conduct of this study. For example, contrary to the prevailing Spanish and EU regulations the author admits to the editors that no written informed consent was obtained. The study was not registered or reviewed by any regulatory agency. 2. The study was initially presented in congresses as a "prospective observational trial'' - not as interim results of an RCT - then later recharacterised as an RCT. When asked directly if the data for both arms of this RCT was collected concurrently; the authors declined to answer (question 6). 3. The study does not comply with many CONSORT and other guidelines such as reporting of enrolment dates. 4. I am unsure of the process followed to lock the study data for independent analysis. This information is unavailable and not provided by the authors. Methodology in De Andres Study 1. The EAC wrongly states (section 5.3): Firstly, whilst it was impossible to blind participants, clinical assessors and investigators were blinded in the study, which should lead to a reduced risk in detection bias (biased measurement of outcomes).	Thank you for your comment. Please see the response to comment 1.

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				1. The EAC states regarding this study: The latter study did not report on the proportions of patients who elicited a 50% reduction in pain, nor was there the granularity of information to calculate this (although the longitudinal data reported suggest there were very few, if any, responders) While the EAC points to this study to suggest similarity of conventional SCS to HF10; overall findings are inconsistent with extensive published evidence regarding SCS in general and must diminish the value placed on the findings of this study. 2. This anomalous study can be compared to the many sponsored and non-sponsored large-scale studies using the same and similar devices that on average provide long-term VAS reduction of about 40%; whereas in the De Andres' report the reduction was only 20-25%.	
10	28	NHS Professional	-	21 May 2018 Dear Colleagues We feel compelled to express our severe reservations regarding the apparent strength of evidence ascribed to the paper by De Andres et al. The paper raised significant concerns about the conduct of the trial and these concerns are highlighted in the letter to the journal editor by Eldabe and North. We are extremely concerned that this paper is being used by the committee as class I evidence to suggest that high-frequency stimulation is no better than conventional simulation. The most concerning aspect of the De Andres paper is that neither group reach their primary endpoint; that is 50% or greater reduction in the numerical rating scale. In fact in both groups the improvement in the numerical rating scale is in the order of 20 to 25%. This is obviously a significant variance to the published literature, and indeed to the assumptions which TA 159 were based upon. The most likely reason for this failure to achieve	Thank you for your comment. Please see the response to comment 1.

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				primary outcome in both groups is that the trial was underpowered. It is hard to see how this trial with so many concerning features could be used to add to the literature on either conventional or high-frequency spinal-cord simulation. These results published by De Andres do not represent our real-world experience of both conventional or HF 10 stimulation. We hope that you will look critically at the De Andres's paper before using it to make informed clinical decisions.	
11	31	NHS Professional	-	As a user of this technology and specialty lead for Chronic Pain Services at RCHT, I would like to make the following comments: 1. Are the summaries of clinical effectiveness and resource savings reasonable interpretations of the evidence? I don't recognise the results of the De Andres study as a true reflection of outcomes in clinic practice in Cornwall. We have 'real-world' outcome data for every implanted patient since 2013, including some patients with 2 year follow up. I don't believe it is reasonable to give the same weight of evidence to the De Andres study as the Senza-RCT.	Thank you for your comment. Please see the response to comment 1.
12	29	NHS Professional	-	Dear National Institute for Health and Care Excellence (NICE) Re: Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery'' (GID-MT515) (2018) I am a consultant in Pain Medicine and Neuromodulation at St Bartholomew's Hospital, Barts Health NHS Trust. I am the lead clinician for Neuromodulation. I have implanted in excess of 100 Spinal Cord Stimulators, of which more than 70 were HF10 systems. I would like to voice my major concerns about your latest draft of the MTEP on Senza/HF10. I would like to draw your attention to the following points: 1. Inclusion and equal weighing of De Andreas study (Pain Medicine 2017) in your evaluation process.	Thank you for your comment. Please see the response to comment 1.

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				This study has very poor methodology and has major validity flaws. These range from the consenting process of the subjects, inclusion/exclusion criteria and blinding to the published results, which entirely contradict not only all other studies but the results of my patients too. I do not understand how a study of such poor quality could have been included at all in your evaluation process, let alone given the same importance as other, properly rigorous, studies. In my clinical experience, more than 80% of patients proceeded to second stage (>50% improvement in pain from the baseline) and this response has been generally maintained to date.	
13	34	NHS Professional	-	The deAndreas paper, is in summary a significant negative outlier from previous studies and in fact reflects poorly on both conventional and HF10K systems. Additionally this is a single centre trial which has been questioned about the recruitment and the assessment of the patients enrolled and implanted.	Thank you for your comment. Please see the response to comment 1.
14	6	NHS Professional	-	The PROCO study has raised some interesting questions on the mechanisms of pain relief from non-paraesthesia based stimulation. However it is unfair to reference the DeAndres study in the same breath to support the claim that other therapies are equally effective. The DeAndres study has compared high frequency SCS with conventional therapy and has shown relatively poor outcomes from both therapies. This is completely at odds with the larger body of published literature and with real world experience. The evaluation of HF-10 should be a systematic review of the evidence base reflecting the significant congruence of many clinical studies and real world evidence from UK specialist centres which show the outcomes delivered by Senza. There is considerable consistency of outcomes across the studies of HF10 with the exception of De Andres which is an outlier in all respects and is not generalizable to our outcomes with this therapy.	Thank you for your comment. Please see the response to comment 1.
15	12	Health professional (abroad)	-	I have been in academic pain practice for nearly 20 years at Boston's Beth Israel Deaconess Medical Center (a teaching hospital of Harvard Medical School) and I am in chief of the Pain Management Center. My comment includes the documentation of De Andres Prospective Randomized Blind Effect on Outcome Study of Conventional vs High Frequency in Patients with the	Thank you for your comment. Please see the response to comment 1.

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				Failed Back Syndrome. This is a single center study of only 30 patients in each arm that failed to demonstrate any significant average improvement in pain and disability in patients treated with conventional or high frequency (HF-10) SCS. This small study is in conflict with two decades of work in the field of spinal cord stimulation, namely multi-centered trials published by Kumar, North, Deer, and Kapural. There are strong concerns for regulatory and protocol violations in this study brought up in an accompanying editorial. Despite the title of the paper implying blinding, there was none during the follow up visits by physicians or programmers. Selection criteria for the device was documented but clearly not followed because most of the implanted patients failed to achieve significant benefit in either arm of the study. With respect to the HF-10 programming in the methods section, it was very unclear if the study subjects were following the strict algorithm need to bring relief to theses patients. They describe varying the pulse width and frequency which does not keep the 10 kHz at a stable frequency. Therefore, I am left to wonder if they actually did HF-10 therapy. The Letter to the editor that accompanies this article brings up regulatory concerns for the De Andres study making it of question if it can be used in the evidenced based literature of spinal cord stimulation for failed back surgery syndrome. In my own experience, I have found HF-10 particularly effective against the back pain as well as the leg pain of this syndrome. I have also seen patients benefit who have chronic inoperable low back pain. Although a high proportion of patients treated with SCS today have had previous spine surgery, evidence from Al-Kaisy, the Senza-RCT, and in my own clinical practice demonstrate that these patients experience the same superior clinical outcomes as those patients that have had surgery previously. There are more published studies for non-surgical back pain for HF10 therapy than all other SCS devices and therefore HF10 should not be limited to FBSS. In summary, the De Andres study is inconsistent with the current literature as well as physician experience with spinal cord stimulation used to treat back and leg pain.	

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16	22	Healthcare Other	-	Section 5: De Andres (2017) 5.2 'The study by De Andres was a single-blind randomised controlled trial that compared the efficacy of Senza HF10 therapy with conventional low frequency SCS in patients with chronic, intractable pain of the trunk and/or limbs that was refractory to conservative therapy for at least 6 months following the development of FBSS. Since the publication of this study there has been a great deal of discussion regarding the methodology and outcomes of this study. As a result, the original commenting editors asked the author (De Andres) to publicly respond to a series of questions that was subsequently recently published (Pain Medicine 2018; 0: 1“2 doi: 10.1093/pm/pny064). A serious concern is whether the study was an RCT or was in fact a single arm, observational trial as was it was first described in medical congresses. While De Andres admits that the Senza HF10 data was previously presented as a single arm trial, when directly asked if the data in the two arms was collected concurrently the author declined to answer. In 5.6 the EAC speaks to the importance of compliance with Good Clinical Practice (GCP). Contrary to GCP, De Andres states that he 'relied on verbal consent’ in a study where randomization is said to be how selection of the surgical device was accomplished. There was also no registration of the study and the author declined to answer whether there was any regulatory oversight. 5.5.4 'Although this is a general issue, it is widely accepted that industry-sponsored studies, where principal investigators have financial ties to the technology, are associated with more positive results than independent studies [33]. The PI of the SENZA-RCT had absolutely no financial ties to Nevro, received no payments and the research support was paid	Thank you for your comment. Please see the response to comment 1.

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				to a third party facility unrelated to the PI. Multiple investigators including the PI did however have active consulting agreements with Boston Scientific, which was the control arm of the study.	
17	22	Healthcare Other	-	5.5.2 'However, the population characteristics in the De Andres study are otherwise relatively poorly described, so there is some uncertainty concerning generalisability of the two populations. TA159 specifically applies to patients with evidence of neuropathic pain. However, the De Andres study appears to have largely excluded such patients. Two tools were stated to be used at baseline and at each visit to assess likelihood of neuropathic pain: Douleur Neuropathique 4 questionnaire (DN4) and painDetect Questionnaire (PD-Q). DN4 results were not even reported and the PD-Q findings revealed that the subjects were 'unlikely' to have neuropathic pain at the time of implant. Leg pain, a strong indicator of neuropathic pain and required in the SENZA-RCT, was not required for the De Andres study. 5.5.3 'Additionally, the authors stated that the use of 'standardizing patient programming' reduced differences between programming personnel and their interactions with patients, potentially eliminating another source of bias. The SENZA-RCT did not provide sufficient granularity of information to ascertain if there was a risk of bias through programming. However, there were no apparent differences in the programming parameters described for either technology. Senza HF10, when delivered as studied in the SENZA-RCT and recommended by the manufacturer is entirely standardized and is published in detail in the SENZA-RCT publication. Additionally, the programming parameters for the conventional arm are reported in the SENZA-RCT but not the De Andres study. In the De Andres publication the HF10 therapy arm reports non-standard, non-recommended lead placement (figure 1) and	Thank you for your comment. Please see the response to comment 1.

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				statements of non-standard pulse widths and non-standard mapping to cover certain areas of the body. 5.6 'The study was methodologically superior in that it blinded the assessors and investigators.' None of the investigators were blinded. The only masking described by the authors were the clinic personnel 'who collected pain ratings and other outcome measures', i.e. patient reported outcomes on questionnaires were collected by 'disinterested clinic personnel.' The implanting physician, the treating clinic personnel, the patients, the industry supplied programmers and evaluators, the data analysts were all completely 'open-label. 7.2.1 'The latter study did not report on the proportions of patients who elicited a 50% reduction in pain, nor was there the granularity of information to calculate this (although the longitudinal data reported suggest there were very few, if any, responders)' This should be the most important aspect of the De Andres study to the EAC: Unlike all RCTs prior, performed with multiple technologies at multiple centers over decades, many thousands of case reports and extensive long term observational studies - this single center, small study failed to find a clinically significant benefit of SCS. The EAC, rather than discounting the value of such an anomalous, poorly executed and reported study chose to place this as superior to the highly rigorous SENZA-RCT even using these findings to call into question the whole of SCS stating (Section 8): 'It is possible that a substantial proportion of pain reduction observed in SCS is due to non-specific effects, such as the placebo effect.'	

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18	21	Healthcare Other	3.1	We appreciate NICE have included the randomized trial by De Andres et al. 2017 in the clinical evidence. We believe the inclusion of this trial enhances the robustness of the evaluation when comparing high frequency versus lower frequency SCS devices.	Thank you for your comment.
19	14	Health professional (abroad)	-	5/18/2018 Dear MTEP Committee, I am writing to you as the Principal Investigator (PI) of the SENZA-RCT1 to address statements made regarding the ethics, validity and conduct of this clinical trial as made by the External Assessment Centre (EAC, produced by Newcastle and York) as part of the 'Advice on Senza HF10 SCS consultation comments.' In section 5.5.4 the EAC report states: Although this is a general issue, it is widely accepted that industry-sponsored studies, where principal investigators have financial ties to the technology, are associated with more positive results than independent studies [33]. And in section 5.6 the EAC report states: The study was methodologically superior in that it blinded the assessors and investigators. In addition, the study was funded independently of industry. Starting with the first statement, during the course of this study, I was not a consultant for Nevro, did not receive any payments, equity interest or promises thereof from Nevro. Research support was paid to a facility in which I have no financial interest. I was, however, a paid consultant for the manufacturer of the control arm (Boston Scientific), as well as were most of co-investigators. The SENZA-RCT was a multicenter randomized controlled trial with extensive monitoring and outside oversight. Conformance with Good Clinical Practice (GCP), Food and Drug Administration (FDA) and Consolidated Standards of Reporting Trials (CONSORT) was assured. There were independent committees that approved patient selection through review of records (by 2 medical monitors) according to pre-specified protocol,reviewed and adjudicated adverse events (Data and	Thank you for your comment. Please see the response to comment 1.

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				Safety Monitoring Board [DSMB]). Independent data collectors (disinterested clinic personnel) entered the patient level data into a locked data base. FDA auditors verified data integrity by tracing source data at clinical sites to pre-approved case report forms and to the final study database, which was provided to FDA in its entirety. There were at least four detailed or confirmatory analyses performed by independent statisticians (two separate study biostatisticians working independently, FDA statisticians, and journal statisticians). Analyses were performed to ensure that each individual center results were in-line with all other centers. The EAC report states that there may have been bias towards HF10 arm since an internet search could have led to the understanding that it was a "novel therapy' (Table 5). Enrollment candidates were told that both therapies were thought to be equally effective. Regardless, if a randomized subject was of the belief that one therapy was better than the other, then one would expect that those receiving randomization to a therapy viewed as potentially less effective would more likely withdraw and obtain the other therapy. A statistical analysis of withdrawal rates for each arm of the study was performed which supports the conclusion that there was no bias in favor of the Nevro device. Further, the Boston Scientific website, their commercial representatives and marketing brochures were highly supportive of their device and that the MOA required paresthesias to be present for effective use. Nevro was not approved and did not utilize marketing materials such as brochures in the US. Further, given that Nevro patients did not "feel anything' it is quite possible, if not probable, that bias existed in favor of the proven Boston Scientific device with sensory enforcement that it was 'working'. The EAC report states (5.5.3): Additionally, the authors stated that the use of "standardizing patient programming' reduced differences between programming personnel and their interactions with patients, potentially eliminating another source of bias. The SENZA-RCT did not provide sufficient granularity of	

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				information to ascertain if there was a risk of bias through programming. In fact, with regard to HF10 therapy, the opposite is true. In SENZA-RCT, for HF10 therapy, a standardized program (10,000 Hz frequency, 30 µs PW, standardized electrode placement) was used in 100% of the HF10 arm. The De Andres paper describes and illustrates a non-recommended lead placement (figure 1), non-recommended and technically impossible pulse width adjustments and non-recommended non-standard paresthesia mapping (Pg. 4: Pulse width: The initial pulse width was 30 µs. If the patient had good coverage except for a small percentage (toe, lower back), pulse width was increased.). It is technically not possible to increase pulse width beyond 30 ï• s when delivering 10,000 Hz. Regarding the conventional arm, after reviewing with several experts we are not able to determine from the provided information how "standard programming' was applied. Regarding "granularity' in the above quote and in section 5.2, the EAC notes the extraordinary length of this publication at greater than "12,000 words'. Quality journals such as Anesthesiology and Neurosurgery have strict word limits and are very carefully reviewed. So, the great detail of patient level data in the SENZA-RCT could not be included in a single publication. However, full transparent public access to this large data base is available on the FDA supplied Summary of Safety and Effectiveness Data (SSED, https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130022b.pdf) . In 5.4.3 the EAC report states: The SENZA-RCT did not report QoL outcomes. While the EAC rightly notes that much of the critical data was not reported in the De Andres publication (see chart below) EAC is incorrect in that extensive measurements of quality of life (QoL), including the Short form (SF-12) quality of life, detailed pain and outcomes diaries and all the following were meticulously captured and reported for SENZA-RCT either in the publication or in the SSED:	

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				PEA, Primary Endpoint Assessment; SEA, Secondary Endpoint Assessment; VAS, visual analog scale; PPR, percent pain relief; ODI, Oswestry Disability Index; MPQ, McGill Pain Questionnaire; SF-12, Short Form “ 12; PCS, physical component summary; MCS, mental component summary; BDI, Beck Depression Inventory; PSQI, Pittsburgh Sleep Quality Index; GAF, Global Assessment of Functioning; GIC, global impression of change , MMED, Milligrams morphine equivalent dose Additionally, detailed programming parameters for both arms, detailed financial disclosures, safety data, pain regions, and pre-specified statistical plan are disclosed in the SSED. This should be compared to the very limited reporting of key data and methodological limitations of the De Andres publication:	

Comment no.	Consultee ID	Role	Section	Comments	Response
				<table><tr><th></th><th>SENZA -RCT</th><th>De Andres</th></tr><tr><td>Blinded</td><td>No</td><td>No</td></tr><tr><td>Disinterested Data Collectors</td><td>Yes</td><td>Yes</td></tr><tr><td>Enrollment dates, CONSORT</td><td>Yes</td><td>No</td></tr><tr><td>Multicenter</td><td>Yes</td><td>No</td></tr><tr><td>Regulatory oversight, Auditing</td><td>Yes</td><td>No</td></tr><tr><td>Locked database</td><td>Yes</td><td>No</td></tr><tr><td>Daily pain, QoL diaries</td><td>Yes</td><td>No</td></tr><tr><td>Independent Data and Safety Monitoring Board</td><td>Yes</td><td>No</td></tr><tr><td>PI financial conflicts</td><td>No</td><td>No</td></tr><tr><td>Independent Statisticians</td><td>Yes</td><td>No</td></tr><tr><td>Defined study protocol</td><td>Yes</td><td>No</td></tr><tr><td>Correction for multiple testing (Type 1 errors)</td><td>Yes</td><td>No</td></tr><tr><td>Detailed predefined statistical plan reported</td><td>Yes</td><td>No</td></tr><tr><td>Public access to patient level data</td><td>Yes</td><td>No</td></tr><tr><td>Trial results reported</td><td>Yes</td><td>No</td></tr><tr><td>Pre-specified and reported primary endpoint</td><td>Yes</td><td>No</td></tr><tr><td>Responder rates reported</td><td>Yes</td><td>No</td></tr><tr><td>Medication usage reported</td><td>Yes</td><td>No</td></tr><tr><td>Standardized programming</td><td>Yes</td><td>No*</td></tr><tr><td>Pain region reported</td><td>Yes</td><td>No</td></tr><tr><td>Neuropathic pain</td><td>Yes</td><td>No</td></tr><tr><td>Well described population</td><td>Yes</td><td>No</td></tr><tr><td>Baseline functional impairment</td><td>Yes</td><td>No</td></tr></table> *At least not with HF10 therapy arm To the extent that the MTEP committee has relied on the findings of 'methodological superiority' of the controversial De Andres publication as compared to the SENZA-RCT publications in providing guidance is a gross mischaracterization and the draft guidance should be reconsidered in this context.	
20	27	NHS Professional	-	Large cohort FDA regulated SENZA RCT Published by Kapural et at in Anesthesiology in 2015 supported superiority of high frequency 10k hertz stimulation in comparison to conventional frequency spinal cord stimulation. There is criticism that this study was industry sponsored however industry funding also underpins the landmark PROCESS trial published in 2007 as an RCT on SCS on its added value to conventional medical management (considered as key evidence for SCS TAG 159). Many other key studies are also industry sponsored (e.g. North et al – Medtronic sponsored, SUNBURST – Abbott sponsored	Thank you for your comment. Please see the response to comment 1.

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				and WHISPER – Boston sponsored). In our view taking into account the cost of the implant, the support from industry has been key in developing the evidence base required for this very high end and advanced pain management technique.	
21	34	NHS Professional	-	studies which were not allowed as evidence by the committee are Tiede 2012 (n=24 implanted pts), Al-Kaisy 2014 (n=71 implanted pts), Senza-RCT (n= 101 implanted pts), Russo 2016 (n=189 implanted pts), Rapcan 2016 (n=21 implanted pts), Al-Kaisy 2016 (n = 20 implanted pts), Al-Kaisy 2018 (n=33 implanted patients) these have shown significant benefit for scs. and not all for FBSS. Reviewing the committee justifications we/I also note the following points for consideration: 1. It is assumed that evidence from the USA is less (or not at all) comparable to the NHS setting than evidence from Spain, yet there is the SENZA-EU study which confirms the outcomes seen in the largest RCT conducted in SCS history 2. The evidence review makes a bold statement that SENZA RCT was more biased than De Andres because it was company funded. This fails to appreciate this was a head-to-head study between two manufacturers and both had full access to ensure their device was working optimally. It also ignores the FDA oversight and reporting which SENZA RCT was bound by. Indeed the outcomes for low frequency devices were the best reported in SENZA RCT which is inconsistent with a heavy bias towards the sponsor manufacturer. 3. The committee insinuate that the Principal Investigator of SENZA RCT has financial ties to the sponsoring manufacturer but do not confirm if that is the case or not. Has this been confirmed? 4. I would personally point out that there was no consultation with myself nor is there agreement from myself with	Thank you for your comment. Please see the response to comment 1. Tiede et al. (2013), Al-Kaisy et al. (2014), Kapural et al. (2016), Russo et al. (2016), Rapcan et al. (2015), and Al-Kaisy et al. (2016) was all included in the evaluation. Al-Kaisy et al. (2018) was deemed out of scope as it did not use the Senza device.

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				the statements by the Pain Society. The view expressed seems too biased and a user of NEVRO, Boston and Abbot DRG systems feel that having a variety of options for the treatment of peripheral neuropathic pain with clinical outcomes through a central data base would be the natural progression rather than the restriction offered in the guidance. On a final note- there is emerging support that medication/Opioid reduction has been achievable through SCS and again reduces risk for suitable patients	

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22	39	Joint response from 33 clinicans	-	Dear Med Tech Group and Project Lead, Liesl Millar, On review of draft guidance 2 of the GID-MT515 with deadline 21st May, our team at Guy's & St Thomas' Hospital felt it necessary to respond in unity with neuromodulators in the UK. It appears organisations such as the BPS and NSUKI have released statements somewhat contradictory to what we felt was representative of the common thoughts and practices of UK consultants. We drafted and disseminated a letter Friday 18th May to consultants offering them the opportunity to sign via DocuSign if they were in agreement with our statement. Please find attached this letter with collected signatures. We'd appreciate if our collective voice is heard and evidence reviewed in light of the committee meeting 3 scheduled for 22nd June 2018. Dear National Institute for Health and Care Excellence (NICE), We are neuromodulators from around the United Kingdom, who have major concerns about the latest draft of the MTEP on Senza dated 20 April 2018 - 21 May 2018. The previous draft (06 November 2017 - 04 December 2017) recognised that weight that should be given to the multicentre, FDA overseen, randomized controlled SENZA trial carried out in the USA and published in Anesthesiology in 2015 (1). This was a rigorous trial of the highest standards with scrutiny at all stages from the FDA and other interested parties. It showed that spinal cord stimulation is a very effective treatment for refractory failed back surgery syndrome back and leg pain and that HF10 (Senza) stim is clearly superior (statistically and clinically) to traditional lower frequency stimulation. The current draft statement calls the result of this landmark Grade 1 evidence paper into doubt by attaching equal weight to the De Andres study (2) published in Pain Medicine in 2017. The	Thank you for your comment. Please see the response to comment 1.

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				De Andres study is a single-centre study that has major design validity flaws that has led to published questioning of the authors (3). The De Andres study did not show significant benefit for either HF10 Senza SCS or traditional SCS – these are results completely at odds with other reputable published data and completely at odds to our clinical experience. The SENZA trial data almost perfectly match the data published in the preceding European open – design trial of HF10 (4, 5) 6 month and 24 month papers. It appears that the BPS and NSUKI representations to the NICE panel have led to excessive weight being given to the De Andres study. This is deeply troubling and we will be raising our concerns with the BPS and NSUKI regarding this. The latest draft also says that HF10 Senza should "only" be considered for Failed Back Surgery Syndrome (FBSS). HF10 Senza SCS has clearly been shown to be effective in neuropathic pain beyond FBSS. Cohorts of patients in the European and USA Senza trials had not had back surgery but did equally well with regard to both back pain and neuropathic leg pain improvement – as well as quality of life measures. Published work has shown good outcomes with HF10 Senza for other neuropathic chronic pain conditions and this matches our clinical experience (6). HF10 Senza is an important advance and offers an important alternative to traditional SCS for neuropathic pain. We (signed below) urge revision of the latest draft to remove the weighting given to the questionable De Andres paper and recognise that HF10 SCS may be offered for the full range of indications approved in the NICE SCS guidelines (7).	
23	9	Health professional (abroad)	-	Dear MTEP Committee, I am writing to you as the lead investigator and author of the of the VanBuyten et al publication1 that was used by the External Assessment Centre (EAC) in economic modeling of the Senza HF10 spinal cord stimulator device. This letter seeks to clarify a number of important considerations relating to the use	Thank you for your comment. The EAC outlined in the EAC advice on the consultation comments for MTCD1 the strengths and weaknesses of using the Van Buyten et al. (2017) explant data. The EAC considered the Van Buyten et al. (2017) study to be appropriate to use in the cost model because it

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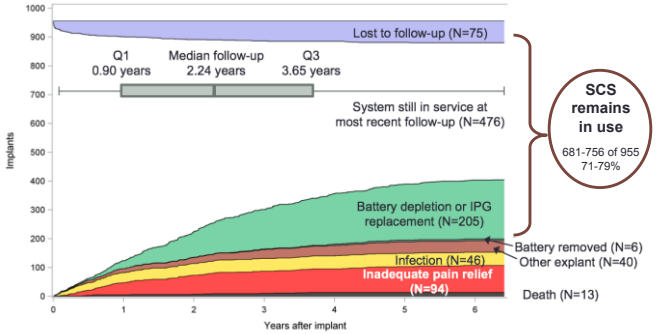
				and interpretation of that publication which the committee and NICE more broadly should consider carefully. 1. Overall Conclusion from the Study The primary goal of this long-term multicenter retrospective chart review was to provide insight into "real world' rates of SCS discontinuation due specifically to loss of efficacy. As is demonstrated in the Figure 1, the primary conclusion of the study is that, over 6 years between 71% - 79% of SCS device implants remained implanted and in use at 6 years follow up. Taking a view over 6 years the data generates an estimate of the annualised permanent explant rate for all devices between 3.4 %- 5.1% with the range depending on underlying assumptions of what happened to those patients lost to follow up (n=75). Figure 1: Timing of Outcomes for each SCS System Implanted  While a great deal of data are provided, the study was not structured as an economic analysis and the use of the extracted "overall explant rates' should be used with great caution in performing cost modeling.	provided the most comprehensive review of SCS unanticipated device explantation available. Further details of what the EAC changed can be found in appendix 1. The committee considered this comments carefully and decided not change the guidance. The committee considered this comment carefully and decided not change the guidance.

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24	9	Health professional (abroad)	-	2. Appropriateness of Comparison between Device Types The publication does not address these issues directly and anticipated service life of the various device categories was not reported. Therefore, the published overall explant rates should not be used in this fashion. As described in the article, for example, non-rechargeable devices that required replacement due to battery depletion as well as non-rechargeable devices that were replaced with rechargeable devices are not captured in these explant rates as these patients continued to benefit from SCS. Reported findings from the publication reveals: - 173/462 non-rechargeable devices (37.4%) were removed due to battery depletion (167 of which were then replaced) - 38/ 462 non-rechargeable devices (8.2%) were replaced with rechargeable systems for a variety of reasons. The mean observation period for this data set was 2.24 years. Thus, when calculating IPG replacement costs over 15 years an important consideration is the service life as well as the replacement costs of non-rechargeable vs rechargeable devices - which was not within the scope of this study. However, this data set supports a considerably shorter non-rechargeable service life than the 4-year duration utilized in the EAC economic model.	Thank you for your comment. The data from the Van Buyten et al. (2017) study was used as an alternative estimate of unanticipated explantation rate because the data in the company submission also had limitations. The assumptions and limitations in this approach were clearly stated in the EAC advice on the consultation comments for MTCD1. The Van Buyten et al. (2017) data did not inform the device replacement rate. The paper reported the explantation rate because of inadequate pain relief for each type (Table 3 in Van Buyten et al. 2017). It also reported the overall unanticipated explantation rate, but did not report this by device type (Table 2, Van Buyten et al. 2017). The EAC used this data to estimate the overall explantation rate by device type (re-chargeable and non-re-chargeable). This assumed the unanticipated explantation rate for reasons other than inadequate pain relief were proportional. These assumptions and limitations were fully described in the EAC's advice on the consultation comments for MTCD1 and erratum. The EAC did not use any battery depletion data. Device replacement was a separate input in the economic model, and the EAC did not use the Van Buyten et al. (2017) data to inform this. The EAC did not use the Van Buyten paper for device depletion as they considered it not to provide any usable comparative data on device longevity. The committee carefully considered this comment and decided not to change the guidance.

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25	9	Health professional (abroad)	-	3. Generalizability to UK Health System Generalizability of the data reported from this cohort to the UK patient population also has considerable limitations. The majority of this analysis was derived from Belgian implanting centers. In Belgium, rechargeable devices are not reimbursed except under certain specific circumstances where patients have higher more severe pain aetiologies and require much higher intensity of stimulation. There are therefore significant differences in patient characteristics and severity of patients receiving High Frequency rechargeable, conventional rechargeable and conventional non-rechargeable owing to inherent selection bias over which patient received which device. For this reason, there is a necessary selection bias: patient characteritics drive specific patient populations into specific device selections. In practice, the majority of initial IPGs during this study period were non-rechargeable and the more challenging patients were initially assigned to the newer rechargeable technologies such as Senza HF10. My understanding from colleagues in the UK is that the situation is quite different. There are therefore considerable challenges with generalising compaisons between groups with the standard clinical practices in the National Health Service. 4. Appropriateness of patient population to scope of NICE evaluation The patient population analysed in the publication to which your report refers deviates significantly from that envisaged in either the first or second draft of the Senza evaluation by NICE: 25% of all subjects had previous SCS implants, 9% had more than one previous implant and only 63% had predominant back and leg pain (Senza subjects were all back and leg pain). It should be noted that even with the patient selection differences, HF10 had the lowest annualized explant rate due to loss of efficacy among all rechargeable devices and '“ uniquely - was no different than non-rechargeable on conservative multivariable analysis.	Thank you for your comment. Please see the response to comments 4, 23 and 24.

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26	9	Health professional (abroad)	-	5. Correction in Evidence Report (**Check with Dr Van Buyten**) In section 3.2 of the evidence review it states: One hundred and seventy three implants (18.1%) were recorded separately as being due to battery depletion and were not counted as unanticipated events. The authors did not report what proportions of these were non-rechargeable or rechargeable, although it would be assumed most were of the former type. This equates to a rate of 7.7% per PY. The large majority of these implants (97%) were replaced. Additional, 38 implants (4.0%) were removed so they could be replaced with devices with additional features, including burst, high frequency, or high-density waveforms, MRI conditional systems, or additional leads. This should have been 173/462 ïƒ¨ 37.4% for replacement (6 permanently removed) and 38/462 (reimplanted at depletion time with rechargeable) ïƒ 8.2 % , therefore raw rate of IPG removal in non-rechargeable IPG"s due to battery depletion is 45.7% in 2.2 years. It could be because they did not know that all of these depletions were in the non-rechargeable group. As is common in retrospective chart reviews, there were considerable subjects lost to follow up (N =75) and 6-year reporting was not available on many subjects. However, under the criteria of the study 71% - 79% of SCS implants remained in use at 6 years resulting in an estimated annualised permanent explant rate for all devices of between 3.4% - 5.1% when averaged across the 6 years of the study. At the lower end this estimate is comparable with the 3.2% long term rate which the economic model base case previously used for all devices from year 3 onwards. I am pleased that NICE has taken notice of this important review of explant rates but it must be viewed within the context of the	Thank you for your comment. Thank you for your comment. Please see the response to comments 4 and 23. The EAC considered the numerical data provided in the comment. The EAC considered the 18.1% to be factually correct and reflected their analysis in the EAC's advice on the consultation comments for MTCD1. This data concerns anticipated explantation only, which was not used to inform the economic analysis. Only unanticipated explantation data from the Van Buyten study was used, which were taken directly from the published paper. Therefore the EAC concluded that the highlighted data did not offer any more relevant estimates for the modelling. The committee considered this comment carefully and decided not change the guidance.

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				data extraction goals and usual caveats associated with this type of heterogeneous cohort study which can be subject to significant confounding factors. Whilst it is a very large cohort, in this context the sample size does not increase certainty that this is more reliable or accurate than a data gathered from a Randomised Controlled Trial whose population much closer matches that being considered and has controlled for confounding and sources of bias. It is strongly recommended that the MTEP committee closely review the way in which these data points have been extrapolated from the publication to ensure the evaluation arrives at correct conclusions pertaining to UK health economic analyses. In summary the applicability and generalizability of the data from the study to the specific questions being examined by MTEP is highly uncertain and subject to considerable confounding factors. As it stands the committee interpretation, and emphasis placed on it, give cause for concern. Yours faithfully, Dr [redacted] MD PhD Van Buyten JP, Wille F, Smet I, Wensing C, Breel J, Karst E, et al. Therapy-Related Explants After Spinal Cord Stimulation: Results of an International Retrospective Chart Review Study. Neuromodulation. 2017 Oct;20(7):642-9.	

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27	20	NHS professional - expert adviser	-	As far as Van Buyten study is concerned, the patient population in the study is different from that envisaged under TA159: 25% of all subjects had previous SCS implants, 9 % had more than one previous implant and only 63% had predominant back and leg pain. Many patients had indications well outside of TA 159 (table 1, angina, cancer pain, peripheral vascular disease, abdominal pain). Further, the study was not structured as an economic analysis; service life was not reported and replacements of non-rechargeable IPGs due to battery depletion, or when a non-rechargeable device was replaced with a rechargeable device was not counted as an explant in calculating the reported explant rates. There was extraordinary attrition of reported data over time. It should be noted that HF10 had the lowest annualized explant rate due strictly to loss of efficacy among all rechargeable devices and " uniquely - was no different than non-rechargeable on multivariable analysis. HF10 therapy had the lowest of all devices for explant due to infection HF10 therapy is now MRI Conditional.	Thank you for your comment. Please see the response to comments 4, 23 and 24.
28	22	Healthcare Other	-	7.2.2 'Whereas the SENZA-RCT reported (AiC) explantation rates for the Senza HF10 and Precision Plus Systems (Boston Scientific) only, the Van Buyten study also provided data on non-rechargeable device explantation rates, which were considerably lower in the 5 years of follow up.' The EAC fundamentally misunderstands the Van Buyten retrospective analysis. Non-rechargeable devices were explanted due to battery depletion at a very high rate (37.4% within 2.2 year median observation). Another 8% were replaced at the time of battery depletion with a rechargeable device such as Senza HF10. Long term cost modelling from the Van Buyten paper is not possible given the high attrition rate of data out to 5 or 6 years; 7% (32/462) reported with 5-year data for non-rechargeable.	Thank you for your comment. Please see the response to comments 4, 20, 23 And 24 which address issues raised about the Van Buyten study. Al-Kaisey et al. (2017) was identified during the first consultation and reviewed by the EAC and deemed in scope (section 4 from the EAC's advice on the consultation comments for MTCD1 for further details). The use of spinal cord stimulation for chronic neuropathic pain is recommended in NICE technology appraisal guidance on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. This guidance assesses the

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				HF10 had an explant rate of 2.6% due to infections whereas the other devices as a group had a 5.6% infection rate. Importantly, in the majority of patients studied (in Belgium) the choice of the device is guided by economic considerations. Rechargeable devices are authorized only in specific and limited circumstances so these results cannot be generalized to the UK where most SCS devices are rechargeable. Further 25% of the Van Buyten cohort had previously failed SCS and thus fall outside the TA159 guidance. The committee's proposal to restrict HF10 to FBSS only is neither evidence-based nor rational. TA159 has recommended SCS for chronic neuropathic pain since 2007. While the submission was not directed at this patient population, certainly among all SCS devices with long term randomized controlled trials, it is only the SENZA-RCT that included patients without previous back surgery (15%). It is the only SCS therapy with long term 3 year prospective published study data (Al-Kaisy et al, Long-Term Improvements in Chronic Axial Low Back Pain Patients Without Previous Spinal Surgery: A Cohort Analysis of 10-kHz High-Frequency Spinal Cord Stimulation over 36 Months, Pain Medicine 2017; 0: 1“8 doi: 0.1093/pm/pnx237) other ongoing UK, NHS prospective trials (https://clinicaltrials.gov/ct2/show/NCT02689375) and a current large-scale, long term, UK and European multi-centre RCT (http://www.isrctn.com/ISRCTN87648175).	evidence to support the additional benefits of HF10 therapy using Senza compared with low-frequency spinal cord stimulation in patients with chronic neuropathic pain. The committee concluded that most of the higher quality evidence for the clinical benefits of Senza is in people who have chronic back or leg pain despite previous back surgery. The committee also concluded that more evidence would be valuable about the potential role of Senza for neuropathic pain in patients who have not had previous back surgery would be valuable. The committee supported the undertaking of further research in these difficult circumstances and would encourage SCS users to include patient data following all implantations in the UK Neuromodulation Registry. The committee decided to amend section 1 and the title of the guidance.

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29	18	NHS professional - expert adviser	-	Following a review of new information after public consultation, NICE has produced a revised recommendation which differs radically from the previous one. Although fresh expert advice was sought, which was overwhelmingly positive, NICE seems to have ignored this - and the large amount of published evidence in favour of the Senza device - in favour of two recent papers involving small numbers of patients, in both of which the results are very poor. The paper by Thompson et al should not be used in this context as the Senza device was not employed. Instead, a device produced and paid for by a competing company was re-programmed to produce stimulation frequencies higher than the current standard. However, the guidance deals with a device, not a frequency: there are many other aspects of stimulation from the Senza device - principally anatomical placement and wave-form - which differ, and which have arisen as a result of considerable research. The trial was of too short a duration in each patient at each frequency to produce any meaningful results, as - unlike low-frequency stimulation - the clinical effect is not immediate. Results in the De Andres study are so poor for any frequency employed as to be meaningless. Response rates overall are less than a third of what would be expected, raising doubts regarding patient selection, electrode placement, etc. In addition, a number of issues have become apparent regarding ethics, blinding, etc, to the extent that the original editors - who had praised the study - have now publicly distanced themselves from it.	Thank you for your comment. Please see the response to comments 1 and 28. The External Assess Centre (EAC) reviewed the Thomson et al. (2017) study and considered it out of scope for this evaluation (see 2.1.2 of the EAC's advice on the consultation comments for MTCD1 for further details). The committee did not take this study into account when finalising the recommendations.

Comment no.	Consultee ID	Role	Section	Comments	Response
30	23	Professional organisation	-	The Thompson paper compared several different frequencies of stimulation in 20 patients over just 5 days, and concluded that no frequency was superior. This study used a Boston Scientific device, not Senza, and therefore cannot be considered relevant to this evaluation – which is of a device, NOT a frequency, as noted by your assessors. The implication was that the 10 000Hz stimulation (HF10) used was equivalent to Senza, but pulse width, wave-form etc are different, and the response rate was actually much poorer than in studies using the Senza device. Looking more carefully at the parameters used, it appears unlikely that the stimulation delivered would be sufficient to be therapeutic in any of the groups; it is also notable that 50% of patients preferred the last set of parameters tried! This suggests significant bias associated with the way patient preferences were reported.	Thank you for your comment. Please see the response to comment 29.
31	22	Healthcare Other	-	YHEC Report - Factual Inaccuracies We would like to draw the committee's attention to several factual inaccuracies in the YHEC report to the committee dated January 2018 and to newly available publications: 2.1.2.1 Thomson et al. 2017 We agree that this study is completely out of scope. We are surprised that this occupies such a prominent position in the EAC updated report. A great deal seems to have been made of the critique of this study which is entirely unnecessary and unusual for a study which has been ruled to be out of scope. The Thomson et al study (Neuromodulation 2018; 21: 67-76) did not evaluate the Senza device or utilise HF10 therapy. Although it is not stated in the published paper, the device studied was a modified Boston Scientific Precision SCS system (this is the same device as used in the SENZA-RCT comparator arm, see (https://clinicaltrials.gov/ct2/show/NCT02549183). The device, waveform, pulse width, 'sweet spot' selection, lead placement, and programming approach evaluated in the Thomson study are	Thank you for your comment. Please see the response to comment 29.

Comment no.	Consultee ID	Role	Section	Comments	Response
				not HF10 therapy but were selected by unblinded Boston Scientific personnel. 'Strengths of this study include that it was double blinded so that patients and investigators were unaware of the order of allocation of the frequency in the randomisation stage.' Perhaps the most important members of the investigative team were the fully unblinded Boston Scientific personnel who, through 'exhaustive' interactions with the subjects, performed all programming and evaluated the response of the patient to determine which programming parameters would be used at each frequency. It is important to note that preference for each frequency was evaluated for only 5 days, among 20 subjects and there was no preference for any particular frequency and the subjects most often just selected the last offered frequency.	
32	21	Healthcare Other	-	We appreciate the EAC highlighting the value of the PROCO study. We agree that the PROCO study illustrates the important relationship between SCS frequency and efficacy. However, we continue to believe the study is highly relevant for this assessment as it includes the device (Boston Scientific PRECISION) that was used as comparator in the Senza RCT. The study's relevancy and generalisability is further enhanced due to the location of the trial sites, which included three hospitals in England.	Thank you for your comment. Please see the response to comment 29.

Comment no.	Consultee ID	Role	Section	Comments	Response
33	23	Professional organisation	-	There is criticism of the original Senza trial for being funded by Nevro. With such expensive equipment on trial, industry funding is the only possible method: the Thompson paper was similarly company-funded. The Senza trial, however, had close oversight throughout by the FDA although was not completely blinded. NICE clearly feels that it was unwise to maintain that HF10 is superior to standard frequency in the first draft guidance. However the committee has seen published clinical studies reporting on over 450 HF10 patients, all of which demonstrate consistently an additional clinical benefit, yet seems to rely exclusively on the De Andres study of 26 HF10 patients to change their conclusions. It is even more difficult to understand the significant change in the recommendation on indications. Effectively Senza is approved in the revised guidance only for failed back surgery syndrome, while standard frequency stimulation - with no major added evidence - continues to be covered by the NICE technology appraisal guidance for SCS. Why the difference? There is considerable evidence from neurosurgeon implanters that HF10 is at least as effective as standard frequency in many other conditions, and we have had successes in patients who have failed standard frequency trials and implants. In 2008 the Technology Appraisal programme at NICE, acting entirely appropriately, concluded that patients should be given access to SCS irrespective of whether they failed prior surgery. It is irrational to discriminate against HF10 and restrict it to failed back syndrome, especially in light of the recent 3 year study of HF10 in those patients (Al-Kaisy et al. 2017). The committee should reinstate the guidance 1.2 of the first draft: 'Senza should therefore be considered for patients who are eligible for spinal cord stimulation as described in NICE technology appraisal guidance on spinal cord stimulation.' Thus, in both these areas the committee appears to be straying from the published evidence base to support a position advocated by the British Pain Society, an unofficial body which	Thank you for your comment. Please see the response to comments 1, 28 and 29. The EAC consider that commercial sponsorship of new medical technologies is common and is a recognised source of bias. However, it judged that that there was no evidence of undue influence in the conduct of the Kapural et al. (2016) study (for further details please the EAC's advice on the consultation comments for MTCD2). The committee considered this comment and decided to amend the title of the guidance.

Comment no.	Consultee ID	Role	Section	Comments	Response
				does not represent implanters, and a few other consultees. There is one final point – perhaps the most persuasive. The Senza system has the capability to deliver both high frequency AND standard stimulation. This does not apply to other devices. There is therefore no reason why this system should not be used according to the current guidelines for standard SCS – for all types of neuropathic pain. Both modalities can be tried: the Society knows of many instances where conversion from low- to high-frequency has been successful, and real world audit data from NHS centres are available which confirm this in clinical practice. While the initial draft guidance may have been interpreted by some - though not the majority of neurosurgeon implanters - as being overly optimistic, the revision has become stiflingly restrictive and does not in any way reflect the positive impact and advantages of this new therapy or the evidence base which supports it. We wish the revised guidance to allow the use of Senza on the same basis as standard SCS, and for the title to be changed accordingly. Reference: Adnan Al-Kaisy, Stefano Palmisani, Thomas E. Smith, Roy Carganillo, Russell Houghton, David Pang, William Burgoyne, Khai Lam, Jonathan Lucas; Long-Term Improvements in Chronic Axial Low Back Pain Patients Without Previous Spinal Surgery: A Cohort Analysis of 10-kHz High-Frequency Spinal Cord Stimulation over 36 Months, Pain Medicine, , pnx237, https://doi.org/10.1093/pm/pnx237	
34	33	Healthcare Other	2.5	Clinically superior pain relief for most people with back or leg pain. See comments on section 1.1. Other published and presented data from Russo, Kinfe, Muhammed, Thomson and Slotty also are non-corroborative of the SENZA RCT data.	Thank you for your comment. Please see the response to comment 29. Publications from Kinfe et al. (2016) and Mohammed et al. (2017) were excluded by the EAC as they were out of scope. Please see section 3.3 of the assessment report for further details. Slotty et al. (2014) was excluded by

Comment no.	Consultee ID	Role	Section	Comments	Response
					the EAC at the assessment report stage as Senza was not used
35	37	Health professional (abroad)	-	Dear Sir/Madam : In relation to the comments made by Newcastle and York External Assessment Center with regards to the HF10 Therapy provided by the Nevro-Senza, it is my intention as President of the Spanish Chapter of the International Neuromodulation Society to make the following comments: First of all I would like to transmit my concern and that of many of the Spanish colleagues regarding the general conclusions, extracted from some of the articles analyzed in this report, regarding the efficacy and efficiency of the use of neurostimulation in the treatment of Chronic pain. Keep in mind that the analysis of data from the series studied, especially those refereeing to complex pathologies such as Chronic Pain After Spine Surgery (FBSS) or the treatment of neuropathic pain that under normal conditions is difficult to homogenize in its stage or in its pathophysiological support, they prevent to assure reliable results in terms of comparison of effectiveness, especially in short series of patients (like the one of Dr De Andrés). Suffice is to observe in the last paper cited the poor results in terms of analgesia observable in both types of stimulation that are much worse than the unpublished data generally seen in Spain, and it is hard to understand why that is the case" As we are referring to a high-level therapy, which in most cases is the last resource that in the opinion of most specialists "helps" significantly to increase the quality of life of our patients, and at the same time we feel the need to obtain "evidence" in our clinical practice; that is reflected in a lack, of RCTs, known by everybody, in this complex field of multimodal patients, it would be an unfortunate decision to question the validity of a stimulation system that has shown evident examples to provide	Thank you for your comment. Please see the response to comment 1.

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				adequate therapy to our patients, and in a good number of cases managing to rescue the punctual inefficiency of which it seems, in a mistaken way, as its competitor, the tonic stimulation.	
36	11	NHS Professional	-	I am an experienced implanter of both low and high frequency SCS devices. I have implanted 89 HF-10 devices over the last 5 years. I have found the system to provide excellent pain relief for patients with both failed back and virgin back conditions. In my practice it provides superior pain relief for most patients over low frequency devices. I showcased our results nationally at the NSUKI conference in November 2017, and our results from Preston closely mirror those of the Senza RCT, the largest RCT in neuromodulation. I am concerned at the proposed restrictions around the Senza device as this does not fit with the clinical evidence base.	Thank you for your comment. Please see the response to comment 28.
37	17	NHS Professional	-	As a Pain consultant practising for the last 8 years who is trained and is performing spinal cord stimulator implantation, I would like to make the following comments regarding the latest NICE guideline draft. 1. The current document has not taken all evidence into account and it was clear that significant weightage was given to one particular study (The De Andres Study) which is not the true clinical reflection of the current evidence. 2. The summary is not a reasonable interpretation as the evidence considered was not based on best evidence available.	Thank you for your comment. Please see the response to comment 1.

Comment no.	Consultee ID	Role	Section	Comments	Response
38	32	Professional organisation	-	Thank you for giving us the opportunity to comment on the Medical Technology Consultation Document on ‘˜Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery’. The British Pain Society supports the draft document on broad terms, but would like to use this opportunity to comment on a few points that should be given due consideration. The document concludes that the evidence to support the claimed benefit of the superiority of Senza compared with low frequency spinal cord stimulation was uncertain due to the lack of long-term outcome studies and the absence of a sham control. However, the British Pain Society is of the opinion that at the very least, the results of Senza spinal cord stimulation is comparable with conventional low frequency spinal cord stimulation, but with the advantage of having no paraesthesia, which makes it popular among certain groups of patients. The British Pain Society support the comments from NICE acknowledging the advantages of easier and possibly faster implantation technique that avoids the use of paraesthesia mapping; there is also potential advantages of easier programming with the Senza HF10 system. Current clinical experience have not got anything to suggest that the therapeutic effect of Senza HF10 diminishes in ability over time. It is also very unlikely that the wider use of the Senza HF10 technology would incur additional costs over a long period of time. There have not been any major developments in the evidence-base for neuromodulation for pain management, though there have been technologies like DRG stimulation, Burst stimulation, Stimwave and also feedback via a closed loop; long-term data on efficacy are awaited. The British Pain Society recommends that NICE should not engage in technology appraisal until further evidence are available and suggests that the TA159 continue to be placed on the static list.	Thank you for your comment. Please see the response to comment 1.

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39	33	Healthcare Other	1.1 to 4.14	The draft guidance deserves further consideration with attention to whether the claimed benefits have been proven.	Thank you for your comment. Sections 1 and 4, respectively, summarise the committee's recommendations and considerations on the company's claimed benefits.
40	6	NHS Professional	-	Thank you for the opportunity to comment. The British Pain Society (BPS) has discussed the MTEP and provided a summary to NICE. We feel obliged to highlight some significant inaccuracies in this summary that are potentially misleading. The BPS statement has criticised the SENZA study on the basis that it was not blinded and was industry sponsored. This criticism is unfair as most studies in neuromodulation are industry sponsored. It was impossible to blind subjects as the therapies become immediately known due to the paraesthesia produced by low-frequency SCS. The study investigators could not be masked as there were differences in the placement, testing and programming between treatment groups. The SENZA-RCT is probably the highest quality evidence produced in the field of neuromodulation and has comprehensively demonstrated the superiority of high frequency, non-paraesthesia based stimulation over conventional therapy. We agree with the BPS statement that there are no high quality studies comparing it with other non-paraesthesia based modalities and with dorsal root ganglion stimulation.	Thank you for your comment. Please see the response to comments 1 and 33.

Recommendations:

Comment no.	Consultee ID	Role	Section	Comments	Response
41	18	NHS professional - expert adviser	-	The British Pain Society appears to be against the use of this device. Why would any body interested in pain relief choose to limit the application of a promising new technique, even if they felt that the evidence to date was insufficient? No study has shown that HF10 therapy as delivered by the Senza device is inferior. As this device can also deliver low-frequency stimulation, why should its use be limited to one small area of pain control? There seems to be no rationale for changing the title of the guidance, or for limiting the use of the device, on the basis of the new evidence. It does not reflect well on the workings of NICE. I hope the committee will be persuaded to reconsider, and to allow practitioners to access this device on the same basis as other SCS devices.	Thank you for your comment. Please see the response to comments 1, 28 and 33.
42	20	NHS professional - expert adviser	-	HF10 should NOT be restricted to FBSS patients alone. Clinical experience suggests that it is useful in other neuropathic pains as well	Thank you for your comments. Please see the response to comment 28.
43	32	Society	-	There are two areas in the document that raises some concerns. Point 1.2 of the draft document reads Senza should only be considered for patients. The British Pain Society finds that this is too restrictive and recommends the removal of the word only so that the statement read as Senza should be considered for patients. Point 4.4 summarises that due to lack of strong evidence comparable with that of failed back surgery and mainly has chronic back and leg pain, it is not recommending the use of Senza HF10 in other neuropathic pain states and conditions like CRPS. The British Pain Society welcomes the view that further evidence is warranted, however support the views of the clinical advisors that until that is available, we should be able to offer Senza HF10 to these patients and once spinal cord stimulation is considered as an option, the decision to use appropriate technology including Senza HF10 should be left with the treating	Thank you for your comments. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				clinician and dictated by patient choice. Patients who cannot tolerate the paraesthesia from conventional spinal cord stimulation or those who prefer paraesthesia-free stimulation during a trial period stimulation, should not be denied the Senza technology.	
44	31	NHS Professional	-	2. Changing the title from 'treatment of neuropathic pain' to 'treatment of chronic back and leg pain after failed back surgery' needs to be substantiated. We follow TA159 which reads: Spinal cord stimulation is recommended as a treatment option for adults with chronic pain of neuropathic . We have seen good outcomes in patients that are not suffering from failed back surgery syndrome (FBBS). It is true that FBBS represents the biggest group but are by no means the only indication. It would be detrimental to restrict this therapy without due consideration.	Thank you for your comments. Please see the response to comment 28 and 33.
45	41	NHS Professional	-	Dear Sir/Madam, As a neurosurgeon and implanter of the SCS devices, I am concerned with the discrimination given to the Senza device with regards its use in neuropathic pain, as outlined in previous guidance for all SCS versus failed back surgery syndrome alone. In my experience as implanter I have found that the device has the capability to be used in both low frequency and high frequency stimulation and offers a range of therapies to the patients once implanted. In a sense offering the best of both worlds, being effective in managing a variety of pain syndromes as well as FBSS. My worry is that if you are to confine the use of one system then this will lead to a slippery slope where a final change will be made to the original guidance and therefore use of any SCS system being prohibited in any pain other than FBSS. I myself have experience of SCS systems including Senza helping Complex regional pain syndrome (CRPS), phantom pain, neuropathic pain in the limbs and axial neuropathic pain.	Thank you for your comments. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				The unit in which I work in at the moment has a vast experience of use of Senza in all the patient groups above with outcomes far superior to the cited De Andres paper. Before making such dramatic changes to guidance I believe appropriate review of everyday real world practice and the concerns of the SCS implanters should be considered	
46	11	NHS Professional	-	We also do not feel that HF10 should be limited to FBSS: Although a high proportion of patients treated with SCS today have had previous spine surgery, evidence from Al-Kaisy, the Senza-RCT, and in my own clinical practice demonstrate that patients without prior surgery experience the same superior clinical outcomes as FBSS patients. There are more published studies for non-surgical back pain for HF10 therapy than all other SCS devices and therefore HF10 should not be limited to FBSS in our opinion. I hope that this draft recommendation will be reconsidered taking into context our experience as a group of experienced implanters of both low and high frequency SCS devices. We also do not feel that HF10 should be limited to FBSS: Although a high proportion of patients treated with SCS today have had previous spine surgery, evidence from Al-Kaisy, the Senza-RCT, and in my own clinical practice demonstrate that patients without prior surgery experience the same superior clinical outcomes as FBSS patients. There are more published studies for non-surgical back pain for HF10 therapy than all other SCS devices and therefore HF10 should not be limited to FBSS in our opinion. I hope that this draft recommendation will be reconsidered taking into context our experience as a group of experienced implanters of both low and high frequency SCS devices.	Thank you for your comments. Please see the response to comments 1 and 28.

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47	17	NHS Professional	-	3. Spinal cord stimulation using HF10 along with the multidisciplinary input and self management strategies has proven to be beneficial beyond the mentioned indication like failed back surgery. The paragraph 1:2 clearly restricts the use of a clinically proven therapy to a limited clinical use and this will be detrimental for many chronic pain patients who would benefit from this therapy. 4. The HF 10 therapy is a proven therapy for persistent pain due to many other clinical reasons along with failed back surgery. paragraph 1:4 will cause a lot of confusion and unnecessary stress to many patients who are treated successfully by this therapy. SCS is a clinically proven therapy for a selected group of patients with complex persistent pain. Persistent pain poses a huge socioeconomic burden on the current healthcare set up. Restricting the use of this superior therapy without the full consideration of current evidence will be detrimental to many patients who could be potentially benefitted by this treatment modality.	Thank you for your comments. Please see the response to comment 28.
48	22	Healthcare Other	-	The committee's proposal to restrict HF10 to FBSS only is neither evidence-based nor rational. TA159 has recommended SCS for chronic neuropathic pain since 2007. While the submission was not directed at this patient population, certainly among all SCS devices with long term randomized controlled trials, it is only the SENZA-RCT that included patients without previous back surgery (15%). It is the only SCS therapy with long term 3 year prospective published study data (Al-Kaisy et al, Long-Term Improvements in Chronic Axial Low Back Pain Patients Without Previous Spinal Surgery: A Cohort Analysis of 10-kHz High-Frequency Spinal Cord Stimulation over 36 Months, Pain Medicine 2017; 0: 1“8 doi: 0.1093/pm/pnx237) other ongoing UK, NHS prospective trials (https://clinicaltrials.gov/ct2/show/NCT02689375) and a current large-scale, long term, UK and European multi-centre RCT (http://www.isrctn.com/ISRCTN87648175).	Thank you for your comments. Please see the response to comments 1 and 28.

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49	27	NHS Professional	-	We have significant concerns regarding the latest proposed changes to the SENZA MTCD and I believe that the reversal from the initial recommendation is founded largely on flawed analysis based on inappropriate weighting of a single centre, very controversial recent publication (De Andres J et al. Pain Med 2017;18 912): 2401-21). Our clinical experience with HF 10 SCS in real life has helped many patients who would have otherwise been considered unsuitable for conventional SCS. Further, the latest draft includes a restriction to the use of HF10 SCS in patients who have not had any previous spinal surgery. This is directly contradictory to the extensive recent evidence review and recommendations supplied by NICE regarding TA 159 (see SA268 12, August 2016) without any intervening evidence to support such a change. In our clinic, practice of implanting SCS (using all makes of SCS devices), we have not noted any significant expansion in implantation rates of spinal cord stimulator because of updated evidence in favour of HF-10 as well as conventional SCS. In our view, this is due to the rigorous application of patient selection and assessment within MDT set up as recommended by NICE. It is recommended by NICE and the British Pain Society that spinal cord stimulation is offered in the NHS to appropriate and only well selected patient population with neuropathic pain with realistic expectation. In our experience of using HF10 and conventional spinal cord stimulation, patients report significant improvement in pain scores (more than 2-point reduction in pain on numeric pain rating scale -10), reduction in Oswestry Disability index scale (average 10 points reduction) as well as improvement in anxiety and depression scores after implantation of SCS. These are the outcomes reported from our prospective audit of 96 patients with mean duration of treatment follow up over 12 months. Our clinical outcome data shows a high level of patient's satisfaction with care and patient's global impression of change following spinal cord stimulation. This data also includes patients implanted with HF10 SCS who have not had spinal surgery but had neuropathic pain. This data in our centre is collected and	Thank you for your comments. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				analysed by the disinterested third party not treating the patients (unbiased and independent). We have treated very complex patient population with HF 10 SCS who would otherwise not be considered for conventional SCS (cf. patient population as in PROCESS RCT trial i.e. mainly radicular pain rather than back pain). In our implanted cohort of patients the ODI score (disability scores 65/100 Vs De Andres study score 27/100) are much higher. This means that we have treated much more complex and disabled patient population with a much better outcome (assessed/analysed in the similar fashion to De Andres study). We find it very difficult to understand (only 20-25% reduction in pain in De Andres' single centre study). The committee's proposal to restrict SENZA to FBSS only is neither evidence-based nor rational. Technology Appraisal 159 has recommended SCS for chronic neuropathic pain since 2007. While the submission was not directed at this patient population certainly among all SCS devices with long term randomised controlled trials it is only the SENZA RCT that included NSRBP (15%), the only SCS therapy with long term 3 year prospective published study data (Al-Kaisy) et al, long-term Improvements in Chronic Axial Low Back Pain Patients Without Pervious Spinal Surgery: A Cohort Analysis of 10-kHz High-Frequency Spinal Cord Stimulation over 36 months, Pain Medicine 2017; 0:1 1-8 doi:0.1093/pm/pnx237). There are other on-going UK, NHS prospective trials (https://clinicaltrials.gov/ct2/show/NCT02689357) and a large scale long term, UK and European multi-centre RCT (http://www.isrctn.com/ISRCTN87648175). As the technology appraisal programme at NICE rightly concluded, the benefits of SCS should not be denied to patients without previous spinal surgery. This MTEP guidance is in direct conflict with the NICE Technology Appraisal. The proposal to single out the only SCS device with significant supporting evidence for this specific patient population is arbitrary and not evidence based.	

Comment no.	Consultee ID	Role	Section	Comments	Response
				Our concern with the latest SENZA MTCD draft (Medical Technology Consultation Draft) is placing an undue and unfair restriction on the offer of spinal cord stimulation for patients with neuropathic pain; especially as the guidance states spinal cord stimulation to be inappropriate for patients who have not had previous surgery. We would also like to urge that multi-disciplinary assessment and the management of chronic pain (supporting self-management i.e. learning to live well with chronic disabling pain by adjusting lifestyle, activities of daily) not to be compared with spinal cord stimulation delivered with multi-disciplinary set up for the reduction in the level of pain and disability. These two-treatment approaches often need to be applied in conjunction for an optimal outcome to help patients with chronic pain. One approach cannot replace another. In our view, patients should have access to these options as preferred by them to improve their function, quality of life and rely less on painkillers avoiding detrimental long term side effects. So further restriction in access to pain relief techniques (options) for chronic pain for the patients having quality of life as low as those patients with neurological conditions (Multiple Sclerosis) is inappropriate. The current suggested approach is likely to increase the level of suffering further for those (patients and carer/families) who would otherwise access pain relief intervention as per the last NICE TAG 159. We would like the committee to reconsider in particular the two paragraphs as below from the draft for consultation: 1.2 SENZA SCS should only be considered for patients: With residual back and leg pain (at least 50mm on a 0 mm to 100 mm visual analogue scale) at least 6 months after back surgery despite conventional medical management. We urge you to remove the word “only” from the first line of section 1.2 above.	

Comment no.	Consultee ID	Role	Section	Comments	Response
				1.4 People using SENZA SCS for chronic back and leg pain without previous back surgery should have the option to continue treatment until they and their clinicians consider it appropriate to stop. We urge to reconsider SENZA SCS for chronic back and leg pain without previous surgery with in research setting. We appeal in the strongest terms that NICE and the committee follow the lengthy, earnest and transparent evidence synthesis and review process, and not restrict access to this therapy for patients with neuropathic pain with or without surgery.	
50	34	NHS Professional	-	We/I have been utilising scs for the past 15 yrs and have experience of both high frequency and conventional. the experience we have suggests that high frequency is just as useful for peripheral neuropathic pain as it is for failed back syndrome patients the senza data we have suggest that regardless of the underlying conditions patients respond if they have appropriate peripheral neuropathic pain regardless of surgery If we have restriction of options we may be leaving patients with little option for the treatment of their neuropathic pain other than surgery or nothing. Most of our patients have been through extensive rehabilitation and medications rationalised/optimsed and are well screened by an MDT for suitability. This is a robust process and results in a 95% implant rate with approaching an 80% satisfaction rate. This is in keeping with the published data but not with the De Andreas Paper - which is interesting.	Thank you for your comments. Please see the response to comment 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
51	15	Health professional (within NHS)	-	In my experience of using HF10 and conventional spinal cord stimulation, patients report significant improvement in pain scores (more than 2-point reduction in pain on numeric pain rating scale 0-10), reduction in Oswestry Disability Index scale (average 10 points reduction) as well as improvement in anxiety and depression scores after implantation of SCS. These are the outcomes reported from our prospective audit of 96 patients with mean duration of treatment follow up over 12 months. Our clinical outcome data shows a high level of patient's satisfaction with care and patient's global impression of change following spinal cord stimulation. This data also includes patients implanted with HF10 SCS who have not had spinal surgery but had neuropathic pain. This data in my centre is collected and analysed by the disinterested third party not treating the patients (unbiased and independent). I have treated very complex patient population with HF 10 SCS who would otherwise not be considered for conventional SCS (cf. patient population as in PROCESS RCT trial i.e. mainly radicular pain rather than back pain). In my implanted cohort of patients the ODI score (disability scores 65/100 Vs De Andres study score 27/100) are much higher. This means that we have treated much more complex and disabled patient population with a much better outcome (assessed/analysed in the similar fashion to De Andres study). We find it very difficult to understand (only 20-25% reduction in pain in De Andres' single centre study). I would like the committee to reconsider in particular the two paragraphs as below from the draft for consultation: 1.2 SENZA SCS should only be considered for patients: with residual back and leg pain (at least 50 mm on a 0 mm to 100 mm visual analogue scale) at least 6 months after back surgery despite conventional medical management I urge to remove the word 'only' from the first line of section 1.2 above.	Thank you for your comments. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				1.4 People using SENZA SCS for chronic back and leg pain without previous back surgery should have the option to continue treatment until they and their clinicians consider it appropriate to stop. I urge to consider SENZA SCS for chronic back and leg pain without previous surgery with in research setting.	
52	22	Healthcare Other	-	NICE have previously made it clear to Nevro that this process was within the jurisdiction of TA159 (NICE Scientific Advice SA 268 12, August 2016) and that a review by MTEP would be complimentary to that previous evidence review and would respect previous guidance issued. Without any intervening evidence this new and unexpected guidance has been incorporated into MTCD 2. We currently find ourselves in a situation where two NICE committees are proposing conflicting recommendations within the field of SCS, a situation which is both perverse and unjust. This position is indefensible and section 1.3 and 1.4 must be amended or removed. Changes to Guidance We are very concerned that both the Title and consequently the Scope of the entire evaluation has changed significantly between MTCD 1 and MTCD 2. MTCD 1: Senza for delivering high frequency spinal cord stimulation to treat chronic neuropathic pain MTCD 2: Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery The EAC must provide clarity as to how this change fits with the published processes and methods of the Medical Technology Evaluation Programme.	Thank you for your comment. Please see the response to comment 28 and 33. The NICE Scientific Advice and Medical Technologies Evaluation Programmes operate independently.

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53	25	NHS Professional	-	The Specialised Pain Clinical Reference Group read the second draft of the consultation document with interest. We applaud the rebalancing of the document but fear the pendulum may have swung slightly too far in the opposite direction. We appreciate that the evidence for effectiveness of Senza in low back and leg pain prior to surgery is limited to a prospective case series and a small number of participants in the Kapural et al study, we however feel that the guidance as it stands creates a perverse clinical incentive for people with low back pain to undergo surgery in order to access the therapy. The CRG recommends that further research should be encouraged to answer some of the unanswered questions that the MTEP has raised. As such we believe the SENZA should continue to be available within a robust independent research project specifically to provide evidence on the benefits or otherwise of SENZA in back and leg pain without previous surgery. We recommend further independent UK based research comparing this technology to traditional SCS or otherwise given the conflicting RCT evidence to date. Consider paragraph 4.4 - ˜It noted that more evidence about the potential role of Senza in these difficult clinical circumstances would be beneficial' Recommendation for research into the effectiveness of Senza vs traditional SCS would be in line with NHSE recommended research priorities.	Thank you for your comment. Please see the response to comments 1 and 28.
54	35	NHS Professional	1.2	Senza SCS should only be considered for patients: There are case reports as well as experience world wide that Senza SCS is useful for other neuropathic pain conditions. In the published clinical trials there are groups of patients that did not belong to FBSS. In my experience there are distinct advantages of using this sytem for upper extremity neuropathic pain. Patients are able to drive with the system switched on as there is no variation in paraesthesia. Limiting it to only residual back / leg pain	Thank you for your comment. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				following surgery is going to deprive other patients of distinct benefit this therapy offers.	
55	29	NHS Professional	-	2. The response of the British Pain Society. The British Pain Society suggests in its response that Spinal Cord Stimulation therapy and HF10 should be limited to Failed Back Surgery Syndrome patient population, having stated that this response was submitted after it had consulted its members. I personally have not been consulted by the BPS on the subject. I find this surprising, as I have been directly involved for many years in using this treatment modality. I entirely disagree with the BPS statement that endorsing this treatment (HF10) beyond FBSS would potentially increase the referral base quite dramaticall thus increasing the overall cost compared to current practice. The above response is not based on any known economic evaluation. In fact, Spinal Cord Stimulation and HF10 has been appropriately used for selected patients in accordance with NICE guidelines (TA 159) for many years and the use of this treatment has resulted in enormous benefit to chronic pain patients. Finally, I disagree with the proposed document. I base this statement both on my own experience in using HF10 and on the available evidence. I believe that limiting HF10 to Failed Back Surgery Syndrome patients will deprive chronic pain sufferers of a treatment that is of enormous benefit. I have also signed the document produced by Dr A Al-Kaisy of the Guys and St Thomas NHS Foundation Trust.	Thank you for your comment. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
56	10	NHS Professional	-	I would request an extension for comments for a further 2 weeks to gain a broader range of opinions from SPIN. (SPIN is a national nurse and AHP educational group for staff involved in the care of SCS patients and its members have a vast amount of experience in dealing with many SCS systems) On behalf of SPIN planning team we are concerned that the use of Senza for failed back surgery patients only will restrict our use of HF 10 therapy therefore some patients may be denied this effective treatment. We are following the NICE guidance TA159 2008 that would then require revision if version 2 of the Senza guidance was published. As practitioners who manage the SCS patients on a daily basis with a vast amount of real world experience with SCS we may find ourselves having to explain to existing HF 10 patients why they were implanted if they have not had failed back surgery. We have no evidence to suggest that those patients we have previously treated with HF 10 therapy without prior back surgery have come to any harm as a result of this. As all patients have a trial of HF 10 therapy before being considered for a permanent implant there is no evidence to suggest that this group of patients do not have successful trial, our clinical audit suggests that we have at least an 80% conversion rate from trial SCS to permanent SCS. SPIN members assess, manage and measure outcomes and the consensus from the planning team is that HF 10 should not be restricted to failed back surgery patients.	
57	30	NHS Professional	-	As a clinician I am able to judge the quality of studies undertaken within my area of expertise. I am also guided by my clinical experience. Both have led me to utilise HF10 systems for the management of post spinal surgical pain and other conditions characterised by neuropathic pain with very positive outcomes. Until I am provided with sufficient evidence of sufficient quality I will continue to practice as I have done, with excellent outcomes that match the study data that has been produced in clinical trials. I am very happy to alter my clinical decision making given sufficient evidence. As yet I have not seen sufficient evidence. I am not happy that I might potentially have to have to alter what has until now been a transformative	Thank you for your comment. Please see the response to comment 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
				therapy for my patients in the light of what seem to be dubious outcomes from a modest evidence base; I can think of no other aspect of practice that would be challenged on the basis of the evidence that I have seen and I expect more from those that are in a position to dictate our clinical activity.	
58	22	Healthcare Other	-	Summary: It is impossible to understand the justification for the move to equivalence in the recommendation given the large evidence base demonstrating consistent additional benefit with Senza HF10 over low frequency SCS. Outside of the De Andres paper, which has proved to be a controversial outlier, there is reproducibility and consistency in the superior clinical performance of Senza HF10 versus low frequency SCS. The limitation of Senza HF10 to FBSS patients is out of step with both the evidence base and TA159, which we were assured would remain in force. This change is at odds with the published processes and methods of the Medical Technology Evaluation Programme and renders the initial scoping consultation redundant. NICE sought advice from consultees, experts, and HF10 users in defining the Scope and Title initially and confirmed through the diligence leading up to the first consultation. It is apparent that this change has been made in response to consultee feedback, largely provided to NICE without any declaration of conflicts of interest. A deviation of this type at such a late stage in the evaluation draws into question the validity of the committee recommendations. It is paramount that any committee of NICE does not stray from the evidence and existing guidance to pacify a small number of conflicted respondents, particularly those operating under the relative anonymity of a ˜group or society'.	Thank you for your comment. Please see the response to comments 1 and 28.

Comment no.	Consultee ID	Role	Section	Comments	Response
59	33	Healthcare Other	1.1	The draft recommendation in section 1.1 is inconsistent with the claim in section 2.5. The draft states in section 1.1 that Senza SCS is 'as effective as low-frequency SCS in reducing pain and functional disability'' whereas the claim in section 2.5 is that Senza is associated with 'clinically superior pain relief, as well as better clinical and functional outcomes, for most people with back or leg pain''. The superiority claim has not been proven and it cannot be substantiated. The recommendation should therefore state that the case for Senza is partially supported, because the '˜case for adoption' is based on the claimed advantages.	Thank you for your comment. Please see the response to comments 1, 28 and 39.
60	38	Professional society	-	The NSUKI council feel that NICE should not engage in technology appraisal on slight variation to current available SCS systems in market. We have had an increase in modifying the way electricity could be delivered to achieve better pain relief and quality of life. We also have systems that not only deliver, but able to get feedback via closed loop coming into the market.	Thank you for your comment. Please see the response to comments 1 and 28. NICE medical technologies guidance evaluates a single medical technology based on the claimed advantages of introducing the specific technology compared with current management of the condition. It is not a multiple technology assessment and does not compare evidence for all similar technologies in a broader class and will not supersede NICE technology appraisal guidance on spinal cord stimulation. These principles are described in further detail in the Medical Technologies Evaluation Programme methods guide, and in the block of text at the beginning of the medical technology guidance. This text states that the case for adoption is based on claimed advantages of introducing the specific technology compared with current management of the condition. It also states that the specific recommendations in the medical technologies guidance on individual technologies are not intended to limit use of other relevant technologies which may offer similar advantages.

Comment no.	Consultee ID	Role	Section	Comments	Response
61	19	NHS Professional	-	In addition we have 2 further comments: 1, The new NICE draft appears to limit the use of HF10 Senza to the patients with failed back surgery syndrome. There is ample evidence on the efficacy of the spinal cord stimulation, including the HF10 Senza, in the effective management of a whole range of neuropathic pain conditions. We strongly recommend that spinal cord stimulation (including HF10 Senza) continue to retain the full range of indications as in the NICE Spinal Cord Stimulation (2008) guidelines. 2, As per our comment on the previous MTCD (Dec 2017) draft, given that HF10 therapy is not paresthesia producing and therefore not conducive to paresthesia mapping, we believe trial stimulation is of no added value in patients undergoing this therapy which essentially relies on an anatomically based implantation technique. Pain relief itself may take days, weeks or longer to be obtained, often well beyond the timeframe of trial stimulation. Removing the requirement for trial stimulation will of course eliminate the risks/ complications associated with performing the trial procedure as well as the associated costs. We like to thank the committee again for their hard work and attention.	Thank you for your comment. The committee considered this comment and other similar comments and additional information on the evidence for Senza SCS received during the second consultation. It concluded there is still uncertainty of the benefits for the broader patient population and so decided to keep the recommendation in section 1.2 for the patients with failed back surgery syndrome. However it understood that the technology appraisal recommendations are still valid for the all patients with chronic neuropathic pain. The committee considered the possibility of not using a trial and decided not to change the guidance.
62	35	NHS Professional	1.4	I do not understand at all what this section means.	Thank you for your comment. The committee considered this comment alongside other comments. It decided to remove this section for clarity.
63	35	NHS Professional	-	In my personal opinion there has been a huge swing in the assessment of this technology from the first draft to the second one. None of these documents reflect true nature of the therapy and true clinical experience. The studies on which these appraisals are based have their own significant biases. I am of the opinion that the whole medical technology appraisal for Senza should be scrapped. There are many systems on the market and each system offers distinct advantage over the other for very select group of patients. The literature does not provide	Thank you for your comment. This guidance is being developed under the NICE medical technologies guidance programme. This programme evaluates a single medical technology based on the claimed advantages of introducing the specific technology compared with current management of the condition. It is not a multiple technology assessment and does not

Comment no.	Consultee ID	Role	Section	Comments	Response
				enough evidence to justify superiority of one device over the other. NICE should abandon reviewing each individual spinal cord stimulator systems. In few years there may be enough evidence to review Technology appraisal guidance [TA159]. Till that time let the clinicians decide which system works best in their hands for their patient population.	compare evidence for all similar technologies in a broader class and will not supersede NICE technology appraisal guidance on spinal cord stimulation. These principles are described in further detail in the Medical Technologies Evaluation Programme methods guide.
64	11	NHS Professional	-	We write to you collaboratively from Lancashire Teaching (Royal Preston) Hospital's Neuromodulation Team which includes the following; • Mr [redacted], Consultant Neurosurgeon • Dr [redacted], Pain Consultant • Dr [redacted], Pain Consultant • Dr [redacted], Pain Consultant • Dr [redacted], Pain Consultant • Sister [redacted], Specialist Spinal Nurse • Sister [redacted], Specialist Spinal Nurse As a trust, we have been providing spinal cord stimulation therapy since the early 90's, started here by Professor Charles Davis. Over time this service has evolved into a multidisciplinary team offering a variety of neuromodulation options to patients. Our initial cohort over many years was based upon a low frequency SCS system supplied by Medtronic. This practice was supported by the PROCESS study and the NICE guidance TA159. We felt we could sufficiently treat neuropathic leg pain with this therapy and the evidence supported this. Later in 2013 we introduced two further therapies; DRG stimulation for focal neuropathic pain and Nevro Senza for Back or Mixed neuropathic pain based on further introduction of evidence (Senza-RCT) We started with our first Nevro Senza patient in 2013 using the early Senza-RCT evidence as support. We have now implanted 89 Senza patients (as of May 2018) across 5 years and we have our outcomes collated from the very beginning. We collect robust data at our trust and validate it between the pain and neurosurgical team. We collect VAS, ODI, BPI and patient reported outcome measures.	Thank you for your comment. The committee is grateful for information about your practice and your experience of using Senza SCS. The EAC excluded all conference abstracts because they did not provide sufficient detail to assess the study.

Comment no.	Consultee ID	Role	Section	Comments	Response
				We feel that in our practice, HF10 is a major advancement in SCS and has had a significant impact in treating patients refractory to other forms of neuromodulation therapy. We have been able to treat patients with both back and leg pain (FBSS and some without prior surgery), painful diabetic neuropathy, CRPS & upper limb pain. We have pleasure in enclosing our validated results (presented at NSUKI 2017) for your perusal. These are soon to be submitted, scrutinized for peer review and published. With the above clinical experience in mind, we are deeply concerned at the alterations to the draft and the evidence that has supported the changes. Starting with 1.1 of the revised draft, it is stated that Senza SCS is 'as effective' as low frequency SCS in reducing pain. Certainly we have found in our cohort that our HF-10 patients have superior pain relief over low frequency SCS. This is supported by the Senza RCT, which remains the largest RCT in neuromodulation. We do not feel the Committee should put the same weight on De Andres as the SENZA-RCT given a. It is a single site study an despite the title of the paper, patients, physicians and programmers were not blinded b. VAS reductions from ~7.5cm at baseline to ~6cm at 12 months are among the worst ever seen, and do not match the other RCTs over the last 20 years (Kumar, North, or Kapural) for low frequency or HF10. In addition, there are 7 other studies (totalling ~450 HF10 patients) which consistently showed high responder rates and low VAS scores to 24 months It appears to us the the DeAndres study has been given equivalence to the Senza RCT which would seem wholly inappropriate.	

Benefits of the technology:

Comment no.	Consultee ID	Role	Section	Comments	Response
65	1	Patient	-	I was implanted, after a successful trial, nearly a year ago. This device has changed my life. I can now carry out the simple things in life pain free. In the past this caused me so much pain. I'm now able to walk further and can stand, pain free, for a lot longer. I've had 2 Spinal Fusions so I'm not very flexible but this device enables me to carry out simple tasks free from pain. I look forward to seeing how the technology is improved over the years and hopefully having a smaller battery available. I'm delighted with the results so far.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.
66	2	Patient	-	I had failed back surgery in 2008 and, after MANY years of multiple treatments, finally was eligible for a Spinal Cord Stimulator. Whilst I still take a lot of meds, it has quite simply transformed my entire life. Whilst the original operation killed off nerves in my leg and foot, and I do walk with a stick, I can actually work full time and enjoy life again. Please, please continue with this procedure to help many more people. Yes, it was arduous and pretty scary, but I have NO regrets whatsoever. The ongoing support from James at Nevro has been exemplary, even when I had a problem "charging" and James called me late on Sunday evening to quell my fears. All in all, a major triumph for the NHS. I do not know what the procedure cost, but believe me, it was well worth it. I implore you to carry on. It was hoped that I would gain about 85% relief, but, whilst this was not to be, the level of relief I get is more than I thought it would be.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
67	3	Patient	-	Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery: In development [GID-MT515] I would like to share my experience having had a senza HF10 spinal cord stimulator implanted to help both my severe chronic back pain and leg pain after failed back surgery of 7 years. I also am currently completing my final module of an MSc in Clinical Management of Pain as I am also a registered General Nurse - hence have detailed insight to chronic pain from both a patient and a clinical perspective. Prior to having a senza HF10 stimulator fitted 4 years ago, I had had 6 spinal operations and was on huge amounts of opioids and gabapentinoids, struggling to work full-time and having given up any hobbies being in tears most days. My mixed and neuropathic pain never scored less than a 9 on any day and could not sleep longer than 2-4 hours. I had previously always struggled with the feelings of paraesthesia from a TENS machine so would not consider a low frequency spinal cord stimulator and I had also hoped one day to return to scuba diving and most stimulators only state that you can only dive to 10m ATM. Nor did I want any more major spinal surgery of paddles placed into my spine. On discussing options left with my consultant, it was explained that the senza HF10 had no paraesthesia induction, could be inserted quickly and the procedure carried out as a day case. Because there was no paraesthesia, I would be able to drive as well as also have it on during my sleep. The senza also states that one can scuba dive to 35 ATM which would mean that I may be able to eventually return to the one sport that I had carried out. I also wanted to reduce my opioid intake which at the time was the daily equivalent of 800mg of Morphine per day. Following excellent results during a trial period, a permanent implant was fitted. Positive results were immediate. My pain scores in my back and my legs went from 9-10 to 1-2 within 5	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
				days of the procedure and have never gone higher than 4 since the implant was fitted 4 years ago. My quality of life has improved beyond recognition. My opioid intake has reduced to a daily morphine equivalent of less than 100mg/day and I have been discharged from the chronic pain clinic. Personally for me, I am delighted that I have also been able to now return to scuba diving - in fact I have managed to complete further training to become a professional level scuba diver (dive master). I am now also able to drive for long periods, which I couldn't manage before as well as maintain full-time employment. The senza stimulator implant has given me back my independence and life that I had prior to the years of severe chronic pain and disability from my failed back surgery. I am also the Facebook Administrator of Nevro Senza Spinal Cord Stimulator UK Patient Group, which was set up in July 2014 to help fellow patients either considering a senza stimulator or already have one fitted. This patient group currently has 544 members and frequently it is reported how the senza stimulator has given people with severe chronic pain back their independence, allowing them to live life again. The only niggle ever commented on is the fact that the Senza has to be charged either daily or every other day which is significantly more frequent that low frequency traditional SCS but most members agree that this is a small price to pay for the improvement in quality of life and the re-charging just becomes part of your daily routine. Therefore I write this comment as a very strong advocate and expert patient for the" Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery." I am happy to be contacted, should further information or opinion be required.	

Comment no.	Consultee ID	Role	Section	Comments	Response
68	4	Patient	-	I had a Nevro Hf10 Spinal cord stimulator fitted March 2017. Since then I have gone from 8x10/500 codydramol to none a day and reduced my dose of pregabalin from 175mg to 150mg a day. I no longer feel pain down my left leg walking short distances so can now walk at a normal speed. I have managed to increase my activity and can swim/do aqua aerobics which were impossible before-this is helping me build core strength which should then also reduce my pain. I used to struggle to get through my days at work as the pain was getting unbearable 2 hours before home time but now after the implant I easily get to home time and frequently stay an hour extra. My quality of sleep has also improved.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.
69	5	Public	-	I have had this for only a short time but Senza H10 has changed my life. I am now able to do most of the activities that I was forced to stop due to lack of pain control after failed back surgery. I can now focus not only on living but on getting fit again as muscle has been lost due to inactivity. I cannot describe the difference this has made to my mental health as well as all other improvements. An amazing intervention	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
70	7	Patient		I injured my back in 1994, and had stabilisation and decompression surgery in 2004. In 2007 this hardware failed and I had to have a revision surgery with fusion at L4/L5. However, I was still left with severe pain and poor mobility. Following my diagnosis of fail back surgery syndrome, in 2010 I was given surgery to implant a Medtronic low frequency spinal cord stimulator. This system did nothing to help my pain and more often than not, the intense paraesthesia caused an increase in neuropathic pain in my legs. The positional changes were also very problematic for me because I fall or faint a lot and the increased paraesthesia when lying on a hard surface after a fall could leave my legs paralysed and I would be unable to get up. In 2008 I was also diagnosed with fibromyalgia.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.
71	7	Patient	-	In 2016 I was offered a trial of the Nevro Senza HF10 high frequency stimulator. Prior to the test my leg pain level was constantly at 7 or 9 out of 10 and my back pain was often 8 out of 10. My mobility was extremely poor and couldn''t walk more than 30 metres, even with walking aids. During the 8 day trial I tested the various programmes on the HF10 system and there was a noticeable improvement in pain within 2 days. Within 4 days I was able to walk around the ward without any walking aids. By the end of the trial I was walking even further around the hospital without walking aids.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
72	7	Patient	-	The HF10 system was implanted on 16th February 2016, piggy-backing the wiring from my old Medtronic system. Once I got home, I spent several weeks rigorously testing different programmes and optimising the system (my spreadsheet of my testing results is available upon request). The difference it has made to my life is beyond words. My leg pain is now down to 3 out of 10. Although electro stimulation is more efficient at dealing with neuropathic pain, I have still had some improvement in pain around my fusion hardware, with my pain score down to 4 or 5 out of 10, which was unexpected. Even more unexpected was the improvement in my mobility. I still have good and bad days, but on a good day I can walk half a mile with no walking aids, I can manage most days with just one walking stick and am no longer as reliant on my wheelchair and mobility scooter. Prior to having HF10 implanted, I would wake up 5 or 6 times a night in pain and often would go for weeks on end without sleeping more than 2 or 3 hours a night. Now I often sleep for 7 hours (assuming no pain from my fibromyalgia and carpal tunnel issues). Because there is no paraesthesia with HF10, I can leave the stimulator switched on 24 hours a day. There is no need to turn it off while driving, and there is no issue with shocks caused by changing body position so if I fall I am able to get back up again without help. If I turn off the stimulator, my pain and mobility both rapidly decline and within 90 minutes I am back to pre-HF10 levels.	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.
73	7	Patient	-	The improvement in pain and function has meant that I am now able to enjoy life again. I"m no longer restricted to one room of the house, I can enjoy hobbies and have been able to get out and give astronomy talks to astronomy societies and camera clubs. I am a musician and am now able to play regularly with 2 bands. This year I am hoping to look for some other part-time work as well. I cannot recommend Senza HF10 strongly enough. With almost half a million people in the UK alone suffering from persistent neuropathic pain	Thank you for your comment. The committee welcomes feedback from patients who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
				(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590098/), I feel that thousands of those people with similar issues to my own may benefit from this system.	
74	16	Carer	-	My wife recieved a Senza SCS unit in February 2016. It has been LIFE CHANGING for her. My wife has chronic back pain and weakness/pain in the legs following multiple back surgeries, the failure of a Dynesys unit followed by a fusion. As a result of these issues she was confined to a wheelchair when out of the house, often required a zimmer frame to move around our home and required help with showering and toilet. In 2010 she was fitted with a low frequency Medtronic unit, but this was not as useful as hoped. While it did alleviate some pain (notably period pain) the side effects were both paraesthesia and leg paralysis in certain positions. For example she was unable to use the unit while on her back as it caused complete paralysis in the legs. On more than one occasion she fell while the unit was active and was unable to get up, and we felt it too dangerous to use the Medtronic unit when alone due to the risk of becoming trapped. In 2015 she was offered a trial of the high frequency Senza NF10. She was in hospital for a week in Feb 2016, testing the system, and the benefit was immediate. Even before leaving hospital, my wife was able to walk unaided to the bathroom and could shower herself. When a cable was knocked loose from the external trial unit, the return of pain and weakness was almost immediate, and when the fault was fixed the pain receded again. Since receiving the unit my wife has been able to regain her independence. She can look after herself when I am at work, we no longer routinely need the wheelchair when we go out, and she has been able to resume playing guitar. She can walk to the village shop (albeit often with sticks), and can lie on her back without fear of paralysis. And to her - and my - deep joy, she was able to walk down the aisle unaided at our wedding in	Thank you for your comment. The committee welcomes feedback from patients and carers who have experience of using the technology.

Comment no.	Consultee ID	Role	Section	Comments	Response
				October 2016. We were even able to have a First Dance. It is no exaggeration to say that the Senza device has transformed both our lives beyond any expectation and I very much hope that others will be able to benefit from the same therapy.	

Costs:

Comment no.	Consultee ID	Role	Section	Comments	Response
75	6	NHS Professional	-	The British Pain Society statement explicitly warns that implementing the NICE guidance would '˜potentially increase the referral base quite dramatically" thus '˜increasing the overall costs as compared to current practice". This presumption has been based on the studies showing positive effects on patients with back pain who have not had previous surgery. This statement, we believe is naÃ¯ve at best and misleading at worst. The NICE committee itself acknowledges that this scenario is unlikely and that Senza would be considered for the same patients for whom SCS is recommended in NICE technology appraisal guidance.	Thank you for your comment.
76	33	Healthcare Other	2.4	Has there been a differentiation in the cost of rechargers for conventional and Senza devices? Rechargers have a finite lifespan that is determined by their usage, and as Senza requires more frequent recharging than conventional devices (as noted in section 4.9 of the draft guidance), is there a difference in length of service and therefore replacement frequency of rechargers? If there is a difference in replacement frequency and this is an additional cost to the NHS, has this been included in the cost model	Thank you for your response. The EAC concluded that it is not common practice to incorporate failure of device accessories into the economic models unless this would directly affect the patient (e.g. complications of implanted device). It would be possible to do this by changing the value of the base case; however, this should be done on the basis of evidence rather than anecdote, and evidence would also be required for the comparator, which the EAC has not been able to identify. Issues concerning battery charging and battery life are discussed in the EAC's advice on the

Comment no.	Consultee ID	Role	Section	Comments	Response
					consultation comments for MTCD1 in Section 6.1. The committee considered this comment carefully and decided not change the guidance.
77	33	Healthcare Other	2.5	No need for paraesthesia mapping during implantation, which allows shorter and more predictable procedure times. Whilst the point about paraesthesia mapping may be correct, conventional spinal cord stimulation generally requires one electrode to be implanted whereas Senza requires two electrodes, although this is not referred to in the guidance. Procedure time may be shortened by the avoidance of paraesthesia mapping, but more time is required to implant the additional electrode.	Thank you for your comment. Section 4.6 has been amended to reflect the number of electrodes used.
78	33	Healthcare Other	3.7	The assertion that non-rechargeable low-frequency SCS devices need to be replaced every 4 years is not correct and not reflective of real-world experience. Van Buyten et al (2017) showed that the majority of implants had not been replaced at up to 6 years follow up, with approximately 49% being non-rechargeable systems.	Thank you for your comment. The EAC concluded that no usable evidence was identified concerning the battery life of Senza HF10 and its comparators. Threshold sensitivity analysis provided by the company (please see the company submission for further details) reported that if device life of non-rechargeable SCS was extended to 7.5 years or above, Senza delivering HF10 therapy would cease to be the most cost saving option (please see section 7.2.4 of the EAC's advice on the consultation comments for MTCD1 for further details). The committee considered this comment carefully and decided not change the guidance.
79	35	NHS Professional	1.3	Cost modelling indicates that, over 15 years, Senza SCS has similar costs to low-frequency SCS using either a rechargeable or non-rechargeable device: None of the rechargeable devices have been around for 15 years. Most of the times you would require early replacement around 7-8 years as the battery stops retaining the charge. In the cost effectiveness analysis this needs to be taken account of.	Thank you for your comment. The company carried out a threshold analysis which indicated Senza delivering HF10 would cease to be cost saving if it needed replaced after 6.75 years compared with rechargeable low frequency SCS (fixed at 10 years). The

Comment no.	Consultee ID	Role	Section	Comments	Response
					committee considered this comments carefully and decided not change the guidance.
80	35	NHS Professional	4.11	I do not agree with this section at all. Many clinicians around the world in real life experience have seen the effectiveness of Senza diminishing over time. Outside the remits of clinical trials published, one needs to take into consideration number of Senza devices replaced as they have stopped working altogether due to device related problems. Perhaps the company could share this data.	Thank you for your comment. The EAC does not have data to substantiate these claims. A full discussion on battery life and charging is reported in section 6.1 of the EAC's advice on the consultation comments for MTCD1. The committee considered this comments carefully and decided not change the guidance.

Technical:

Comment no.	Consultee ID	Role	Section	Comments	Response
81	17	NHS Professional	-	6. The HF 10 is MRI conditional and out of all the SCS systems which are currently available, my understanding is HF 10 has got the MRI conditionality of various body parts which can provide clinically meaningful images and information.	Thank you for your comment.
82	20	NHS professional - expert adviser	-	HF10 therapy is now MRI Conditional.	Thank you for your comment.
83	27	NHS Professional	-	SENZA spinal cord stimulator system is MRI compatible with 1.5 Telsa setting in MRI scanner. This needs to be considered with the new guidance.	Thank you for your comment.
84	6	NHS Professional	-	There are further warnings on the issue of MRI compatibility that are no longer relevant as the Senza device is now full body MRI conditional.	Thank you for your comment.

Comment no.	Consultee ID	Role	Section	Comments	Response
85	17	NHS Professional	-	5. Regarding the paraesthesia- my clinical experience is that many patients prefer paraesthesia free pain relief option especially in certain parts of the body. As a female clinician I can relate to this patient preference and I strongly feel it should be a patient choice rather than a clinician's choice. 7. Another advantage of the HF 10 is that this device can be used while driving. This is an important aspect from a patient perspective. The biggest advantage of SCS is that this can help patients to return to work. This has got a bigger socioeconomic impact for patients who are from the working class population. 8. The HF 10 is quicker to insert with less theatre time needed as there is no paraesthesia mapping needed. This also improves the theatre efficiency.	Thank you for your comment.
86	33	Healthcare Other	2.5	No paresthesia, so treatment can be continued during sleep and while driving or operating machinery. This claim suggests that Senza is uniquely able to deliver paraesthesia-free neurostimulation at the spinal cord. This is not true. BurstDR stimulation, like Senza, does not create sensation of paraesthesia in most patients as shown in Deer et al (Neuromodulation 2017). Additionally, dorsal root ganglion stimulation generates a lower level of paraesthesia, and may not be perceptible in many patients. In the absence of DVLA confirmation that patients receiving Senza can drive and patients receiving conventional spinal cord stimulation cannot drive, this claim cannot be upheld. It should also be clarified whether patients receiving Senza are granted motor vehicle insurance where patients receiving conventional spinal cord stimulation are not. If the DVLA and insurance requirements do not differentiate between the different types of technology, then guidance should not uphold these claims. Has the MAUDE database been checked for any reports of paraesthesia and unwanted stimulation/shocks with Senza? If	Thank you for your comment. The scope of this evaluation is HF10 therapy using Senza, versus comparator(s) of low frequency spinal cord stimulation (up to 1200 Hz). Any other spinal cord stimulation frequencies / modes / systems were out of scope of this single MTG evaluation. Nevro provided a *"10186-Rev.-J-Physician-Manual-(International)"* as part of their evidence submission to NICE. This qualifies the Claim queried by this consultee: "**Operation of Vehicles (e.g., driving) or Machinery** - Patients using therapy that generates paresthesia (tingling sensations caused by stimulation) should not operate motorized vehicles such as automobiles or potentially dangerous machinery and equipment with the stimulation on when using paresthesia-causing programs. Stimulation

Comment no.	Consultee ID	Role	Section	Comments	Response
				such paraesthesia reports are found, the claim of no paraesthesia cannot be substantiated.	must be turned off first in such cases. For these patients, any sudden stimulation changes may distract patients from proper operation of the vehicle, machinery, or equipment. Nevro™ SCS system's high frequency settings are designed not to generate paresthesia and its use does not restrict operation of moving vehicles." The DVLA website lists notifiable health and medical conditions which should be reported to them: https://www.gov.uk/government/publications/g1-online-confidential-medical-information. This includes a category of "Spinal conditions, injuries or spinal surgery and driving". The DVLA website is clear that decisions are made regarding any future driving restrictions on the basis of the individual patient report, in consultation with their medical consultant, if necessary. The above Nevro Physician Manual should inform the advice from medical consultant to DVLA, according to the individual patient's condition. The EAC found no evidence that the DVLA generalises its decisions on any driving license restrictions in the manner suggested by this consultee. Four MAUDE reports were cited by a consultee at the first round of public consultation on the Senza initial draft guidance (November 2017). These were reviewed then by EAC. None of the 4 MAUDE reports relate to paraesthesias experienced by patients during driving.

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					One report relates to a patient undergoing trial of the Senza system, who did not proceed to permanent implant. Two reports relate to patients experiencing shocks at the IPG site during charging. The fourth report relates to a malfunction report for shocks at the IPG site and explant. The committee considered these comments carefully and decided not change the guidance.
87	21	Healthcare Other	-	In order to ensure that the final guidance accurately reflects the SCS technologies available today, and does not produce any confusion between device 'settings' and device 'capabilities', we respectfully ask that the committee consider further clarifying the definitions of 'high' and 'low' frequency stimulation/device, 'paraesthesia' and 'non-paraesthesia' stimulation/device. The recommendations, as currently drafted, could lead readers to incorrectly conclude that 'high frequency and non-paraesthesia stimulation' is an exclusive capability of Senza device. They may also assume that 'low frequency and paraesthesia stimulation' is the only possible stimulation that all other devices are capable of. However: ¢ 'High' or 'low' frequency stimulation is a device setting, not a device: o As we outlined in our initial comments, a vast body of literature recognizes 'high frequency' between a range of 500 and 10,000 Hertz and not specifically and only 10,000 Hertz. Likewise, there is consensus that the definition of 'low frequency' ranges from 30 to 300 Hz. o Senza device (referred to as 'high stimulation' device in current recommendations) is capable of low frequency stimulation: in a recent study published by De Carolis (2017), all study participants with the Senza device were programmed at low	Thank you for your comment.

Comment no.	Consultee ID	Role	Section	Comments	Response
				frequency stimulation (60 Hz). o Since all devices on the market have the ability to be programmed across a range of frequencies and capable of delivering both paraesthesia and sub-paraesthesia, we suggest it is inaccurate to define the Senza device as high frequency and all others as low frequency. At multiple occasions in the guidance, the expression 'low-frequency SCS device' is used, which may incorrectly suggest that these devices are 'restricted' to low-frequency stimulation capability, they are 'defined' by 'low-frequency' stimulation. Although these devices are 'capable' of low-frequency stimulation, they are not 'restricted' to low-frequency stimulation, and can be used with a large variety of stimulation settings, including high frequency and non-paresthesia. ¢ Paraesthesia or non-paraesthesia stimulation is the consequence of the device settings, not a device: o Non-Senza devices (referred to as 'low stimulation' and 'generating paraesthesia' in current recommendations) are capable of 'non- paresthesia' stimulation: PROCO study; SUNBURST study, PERRUCHOUD study. o Senza device (referred to as 'non-paresthesia' device/stimulation in current recommendations) is capable of generating paraesthesia, as shown in the De Carolis study, when programmed at low frequency settings. For these reasons, we respectfully suggest that each time Senza is mentioned that the guidance specifies 'when programmed at 10,000 Hertz' and that the guidance replaces 'low-frequency SCS devices' with 'SCS devices programmed at low-frequency settings.'	

Comment no.	Consultee ID	Role	Section	Comments	Response
88	27	NHS Professional	-	SENZA spinal cord stimulator system though is established as HF10 KHz frequency treatment, but, also has the ability to function at conventional frequency settings as other makes of SCS systems. This offers the option for patient to switch to lower frequency at the same time.	Thank you for your comment.

General:

Comment no.	Consultee ID	Role	Section	Comments	Response
89	32	Society	-	The British Pain Society supports the initiative started in February 2018 by the Neuromodulation Society of UK & Ireland to have a National Neuromodulation Registry to monitor all the implanted neuromodulation devices and this is in partnership with Northgate, who currently run the National Joint Registry. This is would enable us to evaluate real world data regarding efficacy and cost-effectiveness over longer periods. The British Pain Society recommends that neuromodulation including Senza HF10 be considered as part of a multimodal strategy in pain management.	Thank you for your comment. The committee concluded that it would be beneficial for clinicians to routinely collect clinical and procedural outcome data on the use of SCS including Senza. It was encouraged to hear that the UK Neuromodulation Registry has well-established data collection arrangements to support the gathering of useful data and have recommended data collection using this registry (please see section 1.4 of the guidance).
90	38	Professional society	-	The way to keep the expanding modification assessed is to make data entry to a National Neuromodulation Registry as mandatory. We have launched this on February 2018 in partnership with Northgate, who currently run the National Joint Registry. This will be a valuable resource to prospectively assess the cost effectiveness in real world utilisation of high cost devices.	Thank you for your comment. Please see the response to comment 89.
91	21	Healthcare Other	4.3	We appreciate NICE highlighting the importance of patient choice regarding paraesthesia. We believe it is crucial that the patient clearly understands the role of paraesthesia and that she/he is involved in the decision process.	Thank you for your comment.
92	21	Healthcare Other	4.9	We are pleased to see that NICE considers the charging burden as an important factor that should be discussed with patients before choosing the device.	Thank you for your comment.

Comment no.	Consultee ID	Role	Section	Comments	Response
93	26	NHS Professional	-	All our patients are individuals with different clinical indications for spinal cord stimulation. We believe individual patients respond to different forms of stimulation and no single system works for every patient. There are a wide range of assessments undertaken that contribute towards the decision as to which system may be the most suitable for a patient. Factors including patient choice and their ability to use the system are also taken into account together with what is available within the trust and any potential need for MRI compatibility. Our group are most insistent that spinal cord stimulation provides a highly effective, drug free therapy for chronic neuropathic pain and we for many years have seen highly significant results using the various available devices and programming platforms in our patients. We do not wish to see any reduction in the variety of systems and stimulation therapies that are available for our patient group.	Thank you for your comment. Please see the response to comment 28.
94	35	NHS Professional	2.3 to 3.7	Senza II is a lot more expensive and does not have full body MRI labelling. This has not been considered into cost effectiveness calculations against other rechargeable or primary cell devices. By the time this appraisal is published majority of the patients would be using Senza II system. Senza II though indicated for patients with low BMI, it is not the smallest device on the market. In fact Senza II is much larger in size as compared to many rechargeable devices on the market.	Thank you for your comment. Has not been considered as part of this evaluation and is reflected in section 2.3 of the guidance.
95	33	Healthcare Other	2.3	The guidance should be more explicit and state that 'Senza II has not been considered as part of this evaluation therefore this guidance does not apply to Senza II''.	Thank you for your comment. Please see the response to comment 94.
96	33	Healthcare Other	1.1 to 4.14	The guidance should explicitly state that it does not apply to Senza II.	Thank you for your comment. Please see the response to comment 94.
97	23	Professions organisation	-	The Council of the SBNS has considered the two drafts of the recommendations, and we are worried to see such a massive change. This appears to be consequent on the volume of response to the first guidance draft. We are also concerned to see that the title of the topic has been changed: was this done	Thank you for your comment. Please see the response to comments 1 and 28. The Royal College of Surgeons is a registered stakeholder for this evaluation.

Comment no.	Consultee ID	Role	Section	Comments	Response
				after consultation with all stakeholders, and with members of all relevant professional societies and committees? There is no representation of the views of the Adult Neurosciences Commissioning Group, nor the Pain Commissioning Group; this guidance affects both groups. The British Pain Society (BPS) appears to be recognized as a stakeholder in the list of professional bodies whilst the Society of British Neurological Surgeons – a subgroup of the joint Royal Colleges' of Surgeons - is not. The Royal College of Physicians, whose members treat headache and facial pain, is the only professional royal college represented in the consultation document. To clarify the situation: The Faculty of Pain Medicine of the Royal College of Anaesthetists has produced guidance for the management of chronic pain in which it claims to be the only official body regulating this area. This is incorrect – the SBNS, on behalf of the joint Royal Colleges of Surgery, is another body, and indeed covers areas the Faculty of Pain Medicine cannot, for example deep brain stimulation. One further group – the UK Chapter of the International Neuromodulation Society – does represent all specialties, but does not have Royal College recognition. The BPS does not have any official standing, or links to any statutory Royal College. It does NOT represent the views of the majority of SCS implanters in Britain (there is only one (retired) neurosurgeon member, who was not consulted regarding this advice). Their comment contains inaccuracies: the Senza equipment IS in fact MRI-compatible, and there is nothing in the draft guidance to suggest limiting practitioners to one therapy. This situation leads to a lack of clarity regarding which professional body is responsible for SCS. The implanters fall	

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				into two groups – neurosurgeons and anaesthetists. The latter only carry out percutaneous approaches; the former can do open procedures, and will implant any type of system according to the patient's needs - or consider any other procedures that might be necessary. We are frankly astonished that a committee of NICE can change a recommendation so comprehensively on the basis of two very flawed studies and a partisan comment by the British Pain Society. A moment's perusal of the responses to the first consultation would make it obvious that many are solicited - not only are the same two references used, but the form of words is similar. The BPS also makes the specious comment that success of the therapy would lead to increased referrals and greater cost. Do they not want their patients to have good outcomes and access to effective treatments? There is in any case no cost effectiveness analysis, nor does it compare costs of conservative therapy and stimulation. The two studies which appear to have been most influential in changing the guidance are the Thompson and De Andres papers. Members of the SBNS have been circulated with these, and have considered them in some detail. Below is a synthesis of the responses received:	
98	33	Healthcare Other	2.5	Sustained and long-term improvement in pain relief and function, which may reduce the need for pain medication and follow-up attendance at pain clinics. If reductions in pain medication use and follow up attendance at pain clinics have not been proven within the published literature, this claim cannot be substantiated and this point should be explicitly noted in the guidance. Other experience is that use of Senza increases the number of follow up visits relative to conventional spinal cord stimulation because patients have to make more visits to clinics to assess whether the device is delivering pain control.	Thank you for your comment. Please see the response to comment 39.

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99	21	Healthcare Other	-	We are pleased to see the committee's consideration and inclusion of stakeholder comments and additional evidence in the second draft document. We believe the updated consultation document more appropriately reflects the evidence available for current SCS devices in the NHS and support the changes made in sections 1.1 " 1.4.	Thank you for your comment.
100	31	NHS Professional	-	3. Section 2.1 reads: The Senza spinal cord stimulation (SCS) system (Nevro) is a neuromodulation device that delivers electrical impulses to the spinal nerve root. This is not correct, it delivers electrical impulses in the epidural space near the dorsal columns. As far as I'm aware, only dorsal root ganglion stimulators deliver impulses to the nerve roots.	Thank you for your comment. The guidance has been amended.
101	31	NHS Professional	-	4. In the same paragraph (2.1) it goes on to say: The impulses are delivered by small electrodes, which are surgically placed in the spinal epidural space. This is not correct. Only a small proportion of leads are implanted surgically. All the leads in our centre are implanted percutaneously. It is important to be precise with the terminology.	Thank you for your comment. The guidance has been amended.
102	13	Healthcare Other	-	Thank you for your consideration of our comments in response to the Draft Guidance:1. To our current knowledge we are content that the relevant evidence has been taken into account in Draft Guidance:2 and have no further comments to add.	Thank you for your comment.
103	40	Department of Health	-	Dear NICE Thank you for the opportunity to comment on the consultation for the above medical technology I wish to confirm that the Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you for your comment.
104	22	Healthcare Other		We are writing to draw your urgent attention to concerns Nevro have about the process of evaluation conducted by NICE on Senza SCS system (MT330). We are very concerned that both the *Title* and consequently the *Scope* of the entire evaluation has changed significantly between MTCD 1 and MTCD 2.	Thank you for your comment. Please see the response to comments 28 and 33.

Comment no.	Consultee ID	Role	Section	Comments	Response
				MTCD 1: **Senza for delivering high frequency spinal cord stimulation to treat chronic neuropathic pain** MTCD 2: **Senza spinal cord stimulation to treat chronic back and leg pain after failed back surgery** Can you please detail what specifically has lead to this unexpected change of Scope at this late stage in the evaluation and why further consultation on the new *Title* and *Scope* have not been undertaken? Can you also please confirm how this change fits with the published processes and methods of the Medical Technology Evaluation Programme?	

Northern Medical Physics and Clinical Engineering
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Appendix 1

Sensitivity analysis on explantation rates for SCS technologies

Produced by Newcastle and York External Assessment Centre

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Project Name: MT330 Senza SCS
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Background

This is the third advisory document from Newcastle and York External Assessment Centre (NY EAC); supplementary to:

i) the original Assessment Report of Senza HF10 therapy (November 2017) [1],

ii) the first advisory document from NY EAC, (Jan 2018) [2], post-public consultation on the original Draft NICE Medical Technologies Guidance,

iii) the second advisory document from NY EAC (June 2018) [3], post-public consultation on the second Draft NICE Medical Technologies Guidance.

Section 7.2.2 of the first advisory document from NY EAC [2] fully described the background and reasons for undertaking an additional sensitivity analysis of device explant rates in the *de novo* economic model provided by the company in their economic submission to NICE [4], using newly published data from Van Buyten et al. (2017) [5]. The purpose was to provide an alternative estimate to the unpublished company explant rates in their model, in order to explore the potential impact of device explantations on the cost case for adoption of Senza HF10 therapy.
This third advisory document aims to clarify exactly how the EAC calculated the alternative estimates for the explant rates of non-rechargeable spinal cord stimulation (SCS), rechargeable SCS, and Senza HF10 therapy in Table 8 of the first advisory document [2], and provide further detail on the caveats and context around this.

'Device longevity' versus 'Explant rate' in the company economic model

'Device longevity' is an entirely separate input parameter from 'Explant rate' in the company economic model and the two should not be confused.
Issues with expected battery life of the technologies (defined as 'Device longevity' in the company economic model) were discussed in Section 4.2.7 of the original External Assessment Report (page 65) [1]. The EAC had asked the clinical experts whether the device longevity estimates in the company model were reasonable and they responded in the affirmative (question 10, page 29 of 48 in the EAC external communication log which is page 181 of 234 in the supporting documentation for the committee) [6]. In addition, the company had performed deterministic sensitivity analysis on these device longevity parameters, which encompassed the plausible range of values for battery life.
At first consultation, NICE asked the EAC to further investigate the claimed 10 year longevity of the battery life of Senza HF10 therapy specifically. After further communication with Nevro (documented in the updated EAC external communication log) [6] (June 2018, unpublished version), the EAC reviewed the engineering test report supplied by the company (commercial in confidence) and were satisfied that the 10 year device longevity was the correct input for Senza HF10 therapy in the model. This is discussed in Section 6.1 of the first EAC advisory document (page 33) [2].
Thus, there was no cause for disagreement with the quoted battery life for any of the SCS technologies and input parameters for 'Device longevity' in the company economic model were not altered in the EAC's additional sensitivity analysis.

Additional sensitivity analysis on 'Explant rate' for SCS technologies

The EAC's calculations for alternative explant rates as inputs to the company economic model were based on the following data published in the study by Van Buyten et al. (2017) [5]:

- From Table 2, there were 180 *unanticipated* explants. This represented 19% of the total number of implants (n = 955). This **did not** include planned explants resulting from battery depletion (see Device longevity).
- From Table 2, there were 94 *unanticipated explants due to inadequate pain relief*. This represented 10% of the total implant population. Therefore 52% of unanticipated explants were due to inadequate pain relief.
- Raw longitudinal time to event (Kaplan Meier) data for unanticipated explantation due to inadequate pain relief, covering 5 years follow up, was provided in Figure 5. This data was stratified by device type (non-rechargeable SCS, rechargeable SCS, and Senza HF10 therapy).
- Raw data on the event rate for unanticipated explantation rate for any reason was reported, but was not stratified by device type.

The focus of the Van Buyten paper was on unanticipated explantation rates, not scheduled replacements for battery life, as described in this verbatim quote from the paper:

> "The focus of this analysis is unanticipated explants related to SCS therapy. Unanticipated explants are defined as any removal of an IPG with the subject still alive, **except cases of battery depletion** or a decision to change to a different IPG with additional waveforms, MRI compatibility, or other lead configurations".

The Van Buyten paper did not provide any usable comparative data on device longevity, nor was it the intention of the EAC to adjust this input parameter in the additional sensitivity analysis.

'Explant rate' in the executable model from the company was defined as the rate of unanticipated device explantation for any reason. There were separate inputs in the economic model for this rate at 1 year, 2 years, and 3 years onwards, consistent with the model used in NICE Technology Appraisal TA159 [7].

As the Van Buyten study had published data on unanticipated explants for inadequate pain relief, but not on unanticipated explantation for any reason, by device type, a multiplier of 1.92 (derived from the inverse of 52%) was applied by the EAC to these data, to provide a crude estimate of overall unanticipated rates for any reason, by device type. For the alternative estimate model inputs of explant rates at 1 and 2 years, published data from Figure 5 in the Van Buyten study was used. For 3 years onwards, annualised incidence data (reported in Table 3 of the Van Buyten study) was used as the alternative estimate. The results and calculations are presented below.

Table showing EAC calculations and results for unanticipated explantation rate for any reason for 1 year, 2 years, and 3 years onwards. All data taken from Figure 5 of Van Buyten study unless otherwise stated.

Device type	Time point	Number at risk	Number of events*	Proportion**	Adjusted proportion†
Non-rechargeable SCS	1 year	366	13	3.5%	6.8%
	2 years	258	10	3.9%	7.5%
	3 years	2.8% ‡			5.4%
Rechargeable SCS	1 year	204	19	9.3%	17.8%
	2 years	156	7	4.5%	13.4%
	3 years	5.5% ‡			10.6%
Senza HF10 therapy	1 year	125	9	7.2%	13.8%
	2 years	107	6	5.6%	10.7%
	3 years	5.0% ‡			9.6%

* The number of events at 2 years calculated as cumulative number of events at year 2 minus events at end of year 1.
** Proportion is number of events divided by number of people at risk of the event.
† Adjusted proportion is to estimate the overall unanticipated rate of explanation, rather than the unanticipated rate for inadequate pain relief only. To do this, a multiplier of 1.92 (inverse of 52%) was applied.
‡ Annualised incidence data taken from Table 3 of Van Buyten (annualised incidence rate of unanticipated explantation for inadequate pain relief).

These revised data were then entered as alternative estimates of explantations by device type into the company economic model, to provide an additional sensitivity analysis of 'Explant rate'.

The reason the EAC provided an additional analysis for this parameter was two-fold: because the Van Buyten study provided real world data that had not been previously published, and because the company's own data, which had been withheld as academic in confidence, was not considered to be robust, largely due to the low number of events and the extrapolation of the RCT data to non-rechargeable SCS (which did not feature in the SENZA RCT [8]). Additionally, the company had made suggestions in their submission to NICE that the explantation rate might be higher with conventional SCS technologies due to removal for "intolerable paraesthesia". The study by Van Buyten found no evidence of this phenomenon, with reasons for explantation being for inadequate pain relief (10%) and infection (5%), followed by problems with the implanted pulse generator (2%), lead problems, pain at pocket,

freedom from pain (without the need for SCS), removal for Magnetic resonance imaging (MRI), and no specific reason identified (all < 1%). Additionally, the Van Buyten study did indicate that the unanticipated explantation rate was significantly lower for non-rechargeable compared with rechargeable technologies; speculated reasons for this are discussed in the paper. Thus, the assumption the company made that non-rechargeable and rechargeable SCS unanticipated explantation rates would be equivalent was not observed empirically.

The EAC was aware that the data extrapolated from the Van Buyten analysis was subject to considerable uncertainty, stating "This approach is not entirely satisfactory, because it does not account for any important technical differences that may have been unreported". Specific limitations included [2]:

- "Data for conventional low frequency SCS reported in the Van Buyten study were from various devices, in contrast to Senza HF10 which is a single technology. It is possible that some individual conventional technologies may perform worse than others.
- The data from Van Buyten were derived from a heterogeneous sample of patients with multiple pain aetiologies. This causes uncertainty as to the generalisability to the narrower group of patients described in the Scope.
- The EAC has extrapolated data from the Van Buyten paper because of incomplete reporting. This may not accurately reflect the real data. In addition, rates for 3 years onwards were estimated from annual rates using time to event analysis. This may not reflect the reality of higher explantation rates nearer the implantation date.
- Conventional low frequency SCS was not considered to be an appropriate comparator by some consultees".

The EAC would add that, as with all time-to-event analysis, there is also considerable uncertainty due to the nature of the heavy censoring of the Kaplan Meier data in the Van Buyten study.

All of these limitations need to be considered when interpreting the results of the economic model.

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