

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Final appraisal determination

Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin

1 Guidance

- 1.1 Spinal cord stimulation is recommended as a treatment option for adults with chronic pain of neuropathic origin who:
- continue to experience chronic pain (measuring at least 50 mm on a 0–100 mm visual analogue scale) for at least 6 months despite appropriate conventional medical management, and
 - who have had a successful trial of stimulation as part of the assessment specified in recommendation 1.3.
- 1.2 Spinal cord stimulation is not recommended as a treatment option for adults with chronic pain of ischaemic origin except in the context of research as part of a clinical trial. Such research should be designed to generate robust evidence about the benefits of spinal cord stimulation (including pain relief, functional outcomes and quality of life) compared with standard care.
- 1.3 Spinal cord stimulation should be provided only after an assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with spinal cord stimulation devices, including experience in the provision of ongoing monitoring and support of the person assessed.
- 1.4 When assessing the severity of pain and the trial of stimulation, the multidisciplinary team should be aware of the need to ensure equality of access to treatment with spinal cord stimulation. Tests to assess pain and response to spinal cord stimulation should take

into account a person's disabilities (such as physical or sensory disabilities), or linguistic or other communication difficulties, and may need to be adapted.

- 1.5 If different spinal cord stimulation systems are considered to be equally suitable for a person, the least costly should be used. Assessment of cost should take into account acquisition costs, the anticipated longevity of the system, the stimulation requirements of the person with chronic pain and the support package offered.
- 1.6 People who are currently using spinal cord stimulation for the treatment of chronic pain of ischaemic origin should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

2 Clinical need and practice

- 2.1 Pain that persists for more than several months, or beyond the normal course of a disease or expected time of healing, is often defined as chronic. This pain becomes a significant medical condition in itself rather than being a symptom. Chronic pain can affect people of all ages, although in general, its prevalence increases with age. Estimates of the prevalence of this condition in the UK vary from less than 10% to greater than 30% depending on the specific definition of chronic pain used. Chronic pain is accompanied by physiological and psychological changes such as sleep disturbances, irritability, medication dependence and frequent absence from work. Emotional withdrawal and depression are also common, which can strain family and social interactions.
- 2.2 Neuropathic pain is initiated or caused by nervous system damage or dysfunction. Neuropathic pain is difficult to manage because affected people often have a complex history with unclear or diverse causes and comorbidities. Neuropathic conditions include failed back surgery syndrome (FBSS) and complex regional pain

syndrome (CRPS). People with FBSS continue to have back and/or leg pain despite anatomically successful lumbar spine surgery. It is not easy to identify a specific cause of neuropathic pain and people with FBSS may experience mixed back and leg pain. CRPS may happen after a harmful event or period of immobilisation (type I) or nerve injury (type II). Pain and increased sensitivity to pain are the most significant symptoms and are present in almost all people with CRPS. Other symptoms can include perceived temperature changes, weakness of movement and changes in skin appearance and condition.

2.3 Ischaemic pain is caused by a reduction in oxygen delivery to the tissues, usually caused by reduction in blood flow because of constriction of a vessel (vasospasm) or its obstruction by atheroma or embolus. Ischaemic pain is commonly felt in the legs or as angina, but can occur anywhere in the body. Ischaemic pain conditions include critical limb ischaemia (CLI) and refractory angina (RA). CLI is characterised by a reduction of blood flow to the legs and can lead to gangrene, an increased risk of limb loss and a marked increase in mortality. CLI is also characterised by rest pain (which may be felt as a burning sensation), non-healing wounds and/or tissue necrosis. RA may be defined as the occurrence of frequent angina attacks that are not controlled by optimal drug and/or revascularisation therapy, with the presence of coronary artery disease, making percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery unsuitable.

2.4 The goal of treatment for chronic pain is to make pain tolerable and to improve functionality and quality of life. It may be possible to treat the cause of the pain, but usually the pain pathways are modulated by a multidisciplinary approach (described as conventional medical management [CMM] in this document). This

may include pharmacological interventions such as non-steroidal anti-inflammatory drugs, tricyclic antidepressants, anticonvulsants, analgesics and opioids. Non-pharmacological interventions, such as physiotherapy, acupuncture, transcutaneous electrical nerve stimulation and psychological therapies, can also be a part of CMM. For some chronic pain conditions there may also be condition-specific treatments; for example, people with FBSS may have a repeat operation. People with chronic pain may continue to experience pain despite CMM, and complete relief is rarely achieved.

3 The technology

3.1 Spinal cord stimulation (SCS) is a treatment for chronic pain that is usually considered after standard treatments (such as those listed in section 2.4) have failed. SCS modifies the perception of neuropathic and ischaemic pain by stimulating the dorsal column of the spinal cord. SCS is minimally invasive and reversible. A typical SCS system has four components.

- A neurostimulator that generates an electrical pulse (or receives radio frequency pulses) – this is surgically implanted under the skin in the abdomen or in the buttock area.
- An electrode(s) implanted near the spinal cord either surgically or percutaneously (the latter via puncture, rather than through an open surgical incision, of the skin).
- A lead that connects the electrode(s) to the neurostimulator.
- A remote controller that is used to turn the neurostimulator on or off and to adjust the level of stimulation.

3.2 Neurostimulators may be either implantable pulse generators (IPGs), which use either a non-rechargeable or a rechargeable internal battery, or radio frequency devices, which receive energy in the form of radio frequency pulses from an external device powered

by a rechargeable battery. Devices are not specific to pain conditions. However, SCS systems will have different longevities dependant on a person's pain patterns, stimulation power required and body area involved. Therefore the choice of SCS system will depend on these factors as well as preferences of the individual person and the clinician.

- 3.3 Fourteen SCS devices manufactured by three companies have received European approval to market (CE marking) and are available in the UK. List prices for SCS systems are not publicly available, but the Association of British Healthcare Industries (ABHI) provided indicative SCS equipment costs: a mid-range price based on the average cost of each of the manufacturer's best-selling product, a lower cost based on the average cost of each manufacturer's least expensive product, and an upper cost based on the average cost of the most expensive product. The prices supplied were: SCS system including neurostimulator, controller and charger, if applicable, but excluding leads £9282 (range £6858 to £13,289); and leads £1544 (range £928 to £1804) or £1136 (range £1065 to £1158) for surgical or percutaneous implantation, respectively. Device and component prices may vary in different settings because of negotiated procurement discounts.
- 3.4 Boston Scientific manufactures a rechargeable IPG (Precision SC-1110). The device is CE marked as an aid in the management of chronic intractable pain.
- 3.5 Advanced Neuromodulation Systems manufactures seven devices. Four are non-rechargeable IPGs (Genesis IPG 3608, Genesis XP 3609, Genesis XP Dual 3644 and Genesis G4), one is a rechargeable IPG (Eon), and two are radio frequency systems consisting of an implant with external rechargeable power (Renew 3408 and Renew 3416). The devices are CE marked as

aids in the management of chronic intractable pain of the trunk and/or limbs.

- 3.6 Medtronic manufactures six devices. Four are non-rechargeable IPGs (Synergy, Synergy Versitrel, Itrel 3 and Prime ADVANCED) and two are rechargeable IPGs (Restore ADVANCED and Restore ULTRA). The devices are CE marked as aids in the management of chronic intractable pain of the trunk and/or limbs, peripheral vascular disease, or refractory angina pectoris.
- 3.7 Further details of contraindications, implant requirements and potential complications can be found in the implant manual for each SCS component.
- 3.8 For FBSS, the British Pain Society (BPS) suggests that SCS may be an alternative to a repeat operation or increased opioid use. For CRPS, the BPS suggests that SCS may be considered after pharmacotherapy and nerve blocks have been tried but have not provided adequate pain relief. It is acknowledged that SCS is not suitable for everyone with chronic pain, and that it should be used only as part of a multidisciplinary team approach with other therapies and a strategy for rehabilitation. Re-intervention may be necessary to replace the SCS device because of complications (component failures, lead position or implant-related adverse events such as infection) or when the power source is depleted. Ongoing care of patients is also required, which includes 24-hour availability for the investigation and management of potentially serious problems.
- 3.9 People selected for SCS normally have a stimulation trial to determine suitability for permanent implantation of a neurostimulator. This usually involves implanting the electrode(s) and leads with a temporary external device, which is used to mimic the effects of an implanted neurostimulator. A stimulation trial will

assess tolerability (for example, of the stimulation sensation or the stimulation device) and the degree of pain relief likely to be achieved with full implantation.

4 Evidence and interpretation

The Appraisal Committee (appendix A) considered evidence from a number of sources (appendix B).

4.1 *Clinical effectiveness*

4.1.1 The Assessment Group included 11 randomised controlled trials (RCTs) in their systematic review of clinical effectiveness. Three of these trials included people with neuropathic pain and eight trials included people with ischaemic pain. The devices used in all the trials were non-rechargeable IPG SCS systems produced by Medtronic.

Neuropathic pain conditions

4.1.2 Two RCTs investigated the effect of SCS on the treatment of FBSS. One trial (PROCESS) compared SCS in combination with CMM with CMM alone. The other trial compared SCS in combination with CMM with repeat operation in combination with CMM. Follow-up in the PROCESS trial was at 6 and 12 months, and in the other trial at 6 months and after a mean of 2.9 years. The primary outcome in both studies was the proportion of people who had 50% or greater pain relief.

4.1.3 The PROCESS trial reported that SCS had a greater effect than CMM in terms of the proportion of people experiencing 50% pain relief at 6 months (48% and 9% in the SCS and CMM groups, respectively, $p < 0.001$) and 12 months (34% and 7% in the SCS and CMM groups, respectively, $p = 0.005$). The other trial also reported a statistically significant benefit in terms of those experiencing 50% pain relief, favouring SCS in comparison with

repeat operation (39% and 12% in the SCS and repeat operation groups, respectively, $p = 0.04$). In the PROCESS trial, opioid use did not differ significantly between the two groups (56% and 70% using opioids in the SCS and CMM groups, respectively, $p = 0.20$). However, the other trial reported that SCS resulted in a significantly greater number of people reducing or maintaining the same dose of opioids when compared with repeat operation (87% and 58% in the SCS and repeat operation groups, respectively, $p = 0.025$). In the PROCESS trial the SCS group showed a significantly greater improvement in function compared with the CMM group for mean change in functional ability as measured by the Oswestry Disability Index. The other trial reported no statistically significant differences between SCS and repeat operation for pain related to daily activities or neurological function. The PROCESS trial measured health-related quality of life (HRQoL) using the Short Form-36 (SF-36) and reported statistically significant benefits favouring SCS across all domains of the SF-36, except for 'role-physical'.

- 4.1.4 One RCT investigated the effect of SCS in combination with physical therapy compared with physical therapy alone for the treatment of type I CRPS. The people in this trial were followed up at 6, 24 and 60 months. The primary outcome was change in pain intensity from baseline.
- 4.1.5 This trial reported that SCS in combination with physical therapy was more effective than physical therapy alone in reducing pain, measured as mean change on a visual analogue scale (0–10 cm) at 6 months (–2.4 cm and 0.2 cm, respectively, $p < 0.001$) and at 2 years (–2.1 cm and 0 cm, respectively, $p = 0.001$), but not at 5 years (–1.7 cm and –1.0 cm, respectively, $p = 0.25$). No statistically significant differences were identified between the SCS and physical therapy groups for improvement in time taken to perform tasks using the affected hand or foot. There were also no

statistically significant differences for HRQoL at 6 months (percentage change in HRQoL: 6% in the SCS group and 3% in the physical therapy group, $p = 0.58$) or 2 years (7% in the SCS group and 12% in the physical therapy group, $p = 0.41$).

- 4.1.6 A subgroup analysis of this trial, which included only those people who received their allocated treatment, reported that SCS in combination with physical therapy was more effective than physical therapy alone in reducing pain, measured as mean change on a visual analogue scale at 5 years (−2.5 cm and −1.0 cm, respectively, $p = 0.06$).

Ischaemic pain conditions

- 4.1.7 Four RCTs investigated the effect of SCS on the treatment of CLI. Of these, two trials compared SCS in combination with CMM with CMM alone, one trial compared SCS in combination with oral analgesics with oral analgesics alone, and the fourth trial compared SCS in combination with prostaglandin E1 and standard wound care with prostaglandin E1 and standard wound care alone. In one trial the follow-up was at 6, 12, 18 and 24 months. In the other three trials there was a single follow-up at least 12 months after SCS. The primary outcome for all four trials was rate of limb salvage. One trial also included pain relief as a co-primary outcome.
- 4.1.8 Two of the trials reported pain relief outcomes; neither reported statistically significant differences between the intervention and control groups. Using a visual analogue scale (0–10 cm), one trial reported a mean reduction in pain of 2.45 cm for the SCS group and 2.61 cm for the CMM group at 18 months. The same trial reported medication outcomes: SCS was more effective than CMM in reducing use of analgesics at 6 months ($p = 0.002$), but not at 18 months ($p = 0.70$).

- 4.1.9 All four trials reported limb survival or amputation rates, but none reported statistically significant differences between groups. At 24 months, one trial reported 52% limb survival in the SCS group and 46% in the CMM group ($p = 0.47$). Another trial reported six major amputations in the SCS group and nine major amputations in the CMM group at 24 months. In one trial at 12 months, 16% of people in the SCS group had undergone a major amputation compared with 20% in the prostaglandin E1 group. One trial reported a borderline statistically significantly lower amputation rate for SCS compared with analgesics when categorising amputations by 'none', 'moderate' or 'major' ($p = 0.05$). One trial reported the results for a subgroup of people with intermediate skin microcirculation before treatment. In this subgroup, there was a non-significant trend towards lower amputation rate in the SCS group at 18 months follow-up. One trial assessed HRQoL. There was no statistically significant difference between the SCS and CMM groups (mean score on the Nottingham Health Profile at 18 months was 35 in the SCS group and 34 in the CMM group).
- 4.1.10 Four RCTs investigated the effect of SCS on the treatment of angina. One trial compared SCS with no SCS device implanted, one trial compared SCS with an implanted but inactive SCS system, one trial compared SCS with CABG, and one trial compared SCS with percutaneous myocardial revascularisation. All four trials recruited people with RA for whom revascularisation procedures were unsuitable or for whom it was considered that revascularisation would not improve prognosis. The follow-up was approximately 6 weeks in two trials and 1 year or more in the other two trials. In three trials, the primary outcome was exercise capacity. In one trial, the primary outcome was frequency of angina attacks.

- 4.1.11 One trial reported pain outcomes. This trial reported no statistically significant difference between SCS and inactive stimulator in terms of pain relief (measured as mean reduction on a visual analogue scale [0–10 cm]: 1.1 cm versus 0.2 cm, respectively). Three trials measured nitrate consumption. Two of these trials reported statistically significant benefits favouring SCS over no SCS device (median weekly nitrate consumption 1.6 and 8.5, respectively, $p < 0.05$) or an inactive SCS device (change in nitrate consumption –48% and 27%, respectively, $p = 0.03$). One of the trials found no statistically significant difference between SCS and CABG for short-acting nitrates but a statistically significant difference favouring CABG over SCS for long-acting nitrates ($p < 0.0001$).
- 4.1.12 Three trials reported frequency of angina attacks. Two of these reported a statistically significant difference favouring SCS when compared with no SCS (median number of angina attacks a week: 9.0 and 13.6, respectively) or inactive SCS (number of angina attacks a day: 2.3 and 3.2, respectively). One trial reported no statistically significant difference between SCS and CABG for mean number of angina attacks a week (4.4 and 5.2, respectively).
- 4.1.13 All four trials reported functional outcomes such as exercise duration or workload capacity. Two studies reported a statistically significant difference favouring the use of SCS when compared with inactive SCS (mean exercise duration in seconds: 533 and 427, respectively, $p = 0.03$) and no SCS (exercise duration in seconds: 827 and 694, respectively, $p < 0.03$). Another trial reported no statistically significant difference between the SCS and percutaneous myocardial revascularisation groups for exercise duration (mean exercise duration in minutes: 7.08 and 7.12, respectively, $p = 0.466$).
- 4.1.14 All four trials reported HRQoL outcomes. One trial reported that HRQoL (daily and social activity scores) was more improved by

SCS than no SCS at 6–8 weeks ($p < 0.05$). The other three trials did not identify any statistically significant differences in HRQoL outcomes.

4.2 Cost effectiveness

4.2.1 A single joint submission was received from Boston Scientific, Neuromodulation Systems and Medtronic. This submission, which included an economic evaluation, was coordinated by the ABHI. The Assessment Group also developed their own economic evaluation. Both the manufacturers' and Assessment Group's models used a similar structure.

The manufacturers' submission

4.2.2 The submission received from the manufacturers evaluated the cost effectiveness of SCS for the treatment of neuropathic pain and modelled both FBSS (SCS with CMM compared with either CMM alone or repeat operation in combination CMM) and CRPS (SCS with CMM compared with CMM alone). Ischaemic pain conditions were not modelled. The model included two-stages: a decision tree for short-term treatment with SCS (first 6 months), followed by a Markov process for SCS treatment from 6 months to 15 years. Probabilities of events were based on data from the RCTs of FBSS and CRPS. The time frame in the second stage of the model was based on an observational study that investigated clinical predictors of outcomes for people using SCS systems over a 15-year period. Treatment success was defined as 50% or greater reduction in pain.

4.2.3 Health-state utilities were based on the EQ-5D. Utility values were assumed to be the same for both FBSS and CRPS, and were based on the FBSS PROCESS trial. The baseline utility value for all patients was 0.168 (no pain reduction). Other stages were valued at optimal pain relief (0.598), optimal pain relief and

complications (0.528), suboptimal pain relief (0.258), and suboptimal pain relief and complications (0.258).

- 4.2.4 In the base case, the cost of an SCS device was £9282. This cost was described in the submission as the average cost of the best-selling device from each manufacturer. In the base case, device longevity was set to 4 years, after which the neurostimulator was replaced. Other costs associated with FBSS and CRPS were taken from the PROCESS trial.
- 4.2.5 For FBSS, the model produced an incremental cost-effectiveness ratio (ICER) of £9155 per quality-adjusted life year (QALY) gained when SCS in combination with CMM was compared with CMM alone. A comparison of SCS and CMM with repeat operation and CMM produced an ICER of £7954 per QALY gained. For CRPS, the model produced an ICER of £18,881 per QALY gained for SCS and CMM compared with CMM. Sensitivity analyses demonstrated that the model was sensitive to assumptions about device longevity and device cost.
- 4.2.6 Further data were provided by the ABHI on behalf of the manufacturers that included utility data collected in the CRPS trial. Health-state utilities were based on the EQ-5D. The baseline utility value for all patients was 0.16 (no pain reduction). Other stages were valued at optimal pain relief (0.61), optimal pain relief and complications (0.56), suboptimal pain relief (0.23), and suboptimal pain relief and complications (0.18). Using the CRPS utility data, the model produced an ICER of £16,088 per QALY gained for SCS compared with CMM. The SCS device cost used was £9000 and the device longevity was 4 years.

Assessment Group's economic evaluation of neuropathic pain

- 4.2.7 The Assessment Group developed a two-stage model, comprising a decision tree to 6 months with a Markov process extending to

15 years. Both FBSS and CRPS conditions were modelled using data from the two trials of FBSS and the trial of CRPS. For FBSS, SCS in combination with CMM was compared in the model with CMM alone, and with repeat operation in combination with CMM (the latter is referred to in the remainder of the document as 'repeat operation'). For CRPS, SCS in combination with CMM was compared with CMM alone. Patients entered into the second stage of the model in the same health state that they were assigned to at the end of the first 6 months (in the first stage of the model). The time frame was based on an observational study that investigated clinical predictors of outcomes for people using SCS systems over a 15-year period.

- 4.2.8 The effect of SCS was assumed to continue over the time horizon of the model except for an annual withdrawal rate from SCS of 3.24% per annum, assumed to be because of gradual loss of pain control. This figure was from a longitudinal observational study. Complications (after 6 months) were assumed to be at a rate of 18% per annum and no complications were assumed to occur in the CMM only groups. In the base case, device longevity was set to 4 years and explored in sensitivity analyses.
- 4.2.9 The Assessment Group used cost data from a range of published sources including the 'British national formulary' (BNF), the Personal Social Services Research Unit (PSSRU) and published studies. In the Assessment Group base case, the combined cost of a neurostimulator and control system was lower than that used in the submission from the manufacturers. This cost reflected a mid-range of device prices obtained, commercial in confidence, in a survey of manufacturers conducted by the Assessment Group. The Assessment Group also provided sensitivity analyses for a broad range of device costs, ranging from £5000 to £15,000. The Assessment Group's base-case results are not described in this

document. Instead, the Assessment Group's sensitivity analyses using a device cost of £9000 are presented, which is similar to the £9282 presented in the submission from the manufacturers.

- 4.2.10 Health-state utilities were based on the EQ-5D and, in contrast to the manufacturers' model, differed between FBSS and CRPS. Utility data were obtained from the PROCESS trial for FBSS and a cross-sectional survey that investigated the burden of neuropathic pain for a range of conditions, including CRPS. In the model, the baseline utility value for FBSS for all patients was 0.168 (no pain reduction). Other stages were valued at optimal pain relief (0.598), optimal pain relief and complications (0.528), suboptimal pain relief (0.258), and suboptimal pain relief and complications (0.258). For CRPS, the baseline utility value for all patients was 0.16 (no pain reduction). Other stages were valued at optimal pain relief (0.67), optimal pain relief and complications (0.62), suboptimal pain relief (0.46), and suboptimal pain relief and complications (0.41).
- 4.2.11 For FBSS, the ICERs for SCS in combination with CMM, when assuming device longevity of 4 years and using a device price figure of £9000, were £10,480 per QALY gained compared with CMM alone and £9219 per QALY gained compared with repeat operation.
- 4.2.12 Results were sensitive to device longevity and price. At a device price of £9000, the ICERs for SCS in combination with CMM were less than £20,000 per QALY gained for device longevity of 3 years or longer, when compared with CMM alone or with repeat operation. At device longevity of 4 years, the ICERs for SCS in combination with CMM were less than £20,000 per QALY gained for a device price up to £13,000 when compared with CMM alone, and for a device price up to £15,000 when compared with repeat operation.

- 4.2.13 For CRPS, SCS in combination with CMM compared with CMM alone, when assuming device longevity of 4 years and using a device price of £9000, produced an ICER of £32,282 per QALY gained.
- 4.2.14 Results were sensitive to device longevity and cost. At a device price of £9000 the ICERs for SCS in combination with CMM compared with CMM alone were less than £20,000 per QALY gained for device longevity of 5 years or longer. At longevity of 4 years, the ICERs were less than £30,000 per QALY gained for device prices up to £8000, and less than £20,000 per QALY gained for device prices up to £6000.
- 4.2.15 The Assessment Group model – using utilities from the CRPS trial (as in section 4.2.6), a device cost of £9000 and device longevity of 4 years – produced an ICER of £16,596 per QALY gained for SCS compared with CMM.

Assessment Group's economic evaluation of ischaemic pain

- 4.2.16 The Assessment Group did not carry out an economic analysis of CLI, but explored the cost effectiveness of SCS for the treatment of RA using an alternative modelling approach. A threshold analysis was presented based on a mathematical model that incorporated data from a prospective observational study. This study compared the outcomes for CABG, PCI and CMM in groups of people for whom treatment with CABG, PCI or both (CABG and PCI) would be appropriate. Data for costs were taken from the BNF, the PSSRU and a study of outcomes in people who underwent revascularisation using CABG, PCI or both. Utility data were also identified in this study, which were reported after 6 years of follow-up. The time horizon of the model was 6 years.
- 4.2.17 The threshold analysis was presented as additional QALYs that would be needed for SCS to be cost effective at different levels of

willingness to pay. In these analyses, it was assumed that survival in the SCS and comparator groups (CABG, PCI and CMM) was similar. The average minimum utility required for SCS to be cost effective at £20,000 and £30,000 per QALY gained, assuming similar survival, was then calculated. For each comparator (CABG, PCI and CMM), three scenarios were modelled based on groups of people for whom CABG, PCI or either revascularisation procedure would be clinically appropriate.

4.2.18 Results of the analysis indicated that, for people who are suitable for treatment with:

- PCI: SCS dominates CABG (less costly and accrued more benefits). The expected utility values in the SCS intervention must be at least 0.6650 and 0.6504 when compared with PCI, and at least 0.6620 and 0.6384 when compared with CMM, for ICERs of £20,000 or £30,000 per QALY gained or less, respectively.
- CABG: the expected utility values in the SCS intervention must be at least 0.6218 and 0.6203 when compared with CABG, at least 0.6001 and 0.5884 when compared with PCI, and at least 0.6321 and 0.6103 when compared with CMM, for ICERs of £20,000 or £30,000 per QALY gained or less, respectively.
- CABG and PCI: the expected utility values in the SCS intervention must be at least 0.5687 and 0.5624 when compared with PCI, and at least 0.5657 and 0.5657 when compared with CMM, for ICERs of £20,000 or £30,000 per QALY gained or less, respectively. Compared with CABG, SCS dominates.

4.3 Consideration of the evidence

4.3.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of SCS for the treatment of chronic pain, having considered evidence on the nature of the condition

and the value placed on the benefits of SCS by people with chronic pain, those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources.

- 4.3.2 The Committee considered the pathways of care for people with chronic pain and the potential place of SCS in such pathways. The Committee heard from clinical specialists and the patient expert about patient referral and access to specialist pain services and patient experiences with SCS. In addition, the Committee heard about the use of SCS in UK clinical practice, including the application of BPS guidelines. It heard that BPS guidelines provide a general guide to the pathway of care, but that people have to be managed flexibly depending on their condition. The Committee appreciated that, to ensure a flexible approach and individualisation of treatments, people with chronic pain conditions are managed using a multidisciplinary team approach, with consideration given to the full range of treatments offered as part of their care. In addition, the Committee recognised that these treatments may vary for different chronic pain conditions because of their different presentation and management. The Committee concluded that it was necessary for people with chronic pain conditions to be managed by a multidisciplinary team experienced in the provision of ongoing monitoring and support of the person assessed for SCS.
- 4.3.3 The Committee discussed the use of a trial of stimulation before the permanent implantation of an SCS device, as had been carried out in the relevant clinical trials. The Committee heard from the clinical specialists that a trial of stimulation was normally, but not always, used before permanent implantation. The Committee heard that there could be benefits from a trial of stimulation, because it could help to identify people who would benefit from the complete procedure and gave people the opportunity to experience what

stimulation would feel like. However, the Committee heard that trial stimulation results may be both false positive (that is, people may report a successful trial stimulation, but then do not benefit from permanent implantation of SCS) and false negative (that is, have an unsuccessful trial, but may benefit from permanent implantation) and be associated with increased costs because of the need for additional hospital attendances and also a possible increase in the risk of adverse effects such as infection. The Committee noted that the key trials and the economic modelling included people who had had a successful trial of stimulation. The Committee therefore considered, on balance, that it was appropriate that permanent implantation of an SCS device should follow only after a successful trial of stimulation. The trial should be undertaken as part of an assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with SCS devices.

- 4.3.4 The Committee noted that pain measuring at least 50 mm on a 0–100 mm visual analogue scale was an inclusion criterion in the clinical trials of SCS in neuropathic pain. It also noted that clinical trials of SCS in neuropathic pain specified that the person enrolled had experienced pain for at least 6 months after surgery (in one FBSS trial) or that their pain had not responded to CMM of 6 months duration (in the CRPS trial). Therefore, the Committee concluded that people considered for treatment with SCS should be assessed as experiencing a similar severity of pain and duration of CMM before being offered assessment for SCS. However, the Committee recognised that the criteria for the assessment of severity of pain and the trial of stimulation may not be appropriate for people with physical or sensory disabilities or for people with other linguistic or cognitive difficulties. The Committee concluded that healthcare professionals should take these factors into account. In these situations, modification of the testing procedure or alternative tests may be required.

4.3.5 The Committee examined the clinical-effectiveness evidence for SCS. The Committee noted that only a small number of clinical trials had been identified and that relatively small numbers of people were included in these studies. In addition, the Committee noted that the trials were limited to four chronic pain conditions: FBSS, CRPS, CLI and RA. The Committee recognised that neuropathic and ischaemic pain included a much larger range of pain conditions than those reflected in the evidence. Additionally, the Committee heard from clinical specialists that there was additional evidence on the use of SCS in larger numbers of people and a greater range of chronic pain conditions, but this was from observational studies and clinical experience. The Committee heard from clinical specialists that the different pain conditions did not need to be considered separately for the use of SCS. The Committee concluded that it should take into account other chronic pain conditions of neuropathic and ischaemic origin that were not reflected in the clinical trial data.

4.3.6 The Committee examined the evidence on the clinical effects of SCS in the treatment of FBSS and CRPS as examples of chronic pain of neuropathic origin. The Committee agreed that, for FBSS and CRPS, the evidence suggested that SCS was more effective in reducing pain than CMM. The Committee noted that, in the trial data initially reported for CRPS (section 4.1.5), the difference in pain relief was not sustained at the 5-year follow-up. However, the Committee recognised that this analysis included a number of people who had not had a successful trial of stimulation and had consequently, as per the trial protocol, not received an SCS device. The analysis had also excluded people in the control group who had subsequently received an SCS device. The Committee therefore considered a subgroup analysis (section 4.1.6) of only those people who had received an implant and considered that this analysis supported the likelihood of a maintenance of benefit. The

Committee accepted that there was some uncertainty about how the effects of pain treatments were sustained over time, but concluded that benefits could be sustained for at least up to 5 years in pain of neuropathic origin.

4.3.7 The Committee next considered the clinical effectiveness evidence for CLI and RA. It was aware that functional outcomes were important (as well as pain relief) as was reflected in the primary outcomes of the studies. The Committee noted that no studies had demonstrated statistically significant differences for pain outcomes, but that for RA the effect of SCS had been shown to be comparable to other treatments, such as CABG and PCI, for functional outcomes. In addition, the Committee considered that there was some evidence of reduced medication use from studies of RA. The Committee was aware that for CLI, non-randomised evidence suggested that there may be greater benefits from SCS for certain subgroups of people with low levels of peripheral oxygenation who demonstrated an increase in transcutaneous oxygen tension after stimulation is started. The Committee also noted comments from consultees that for people with CLI a meta-analysis of controlled trial data suggested that SCS may be associated with better limb survival. The Committee heard from clinical specialists that they accepted that the benefits of SCS for CLI and RA were less certain than for FBSS and CRPS. The Committee concluded that although the current limited evidence suggested that there may be additional benefits from SCS for CLI and RA in some subgroups of patients, there remained considerable uncertainty as to the extent of these benefits and whether these benefits may be generalised more widely.

4.3.8 The Committee examined the economic modelling that had been carried out for the appraisal. It noted that both the model by the Assessment Group and that submitted by the manufacturers had a

similar structure. However, the Committee was aware that the models differed in cost data and, for CRPS, the data on utilities that were used. The Committee noted that both models assumed there was some withdrawal from treatment but that the benefit from SCS was stable over 15 years. The Committee considered that there was some uncertainty about this assumption but accepted that current evidence suggested maintenance of effect. The Committee noted that serious adverse events had not been modelled in the SCS group, but were mindful of comments from consultees about the very low frequency of serious adverse events, and also that adverse events were not included in the CMM group. On balance, the Committee agreed that it was appropriate to consider the outputs from both models as well as sensitivity analyses produced by the Assessment Group.

4.3.9 The Committee noted that there were a range of SCS systems available at different prices. The Committee heard from clinical specialists that one of the factors affecting the choice of device was the complexity of pain pattern and the extent of pain. For example, a person with a single painful limb may be expected to derive greater longevity from the same device than someone with a more complex pain pattern or greater body area affected. Clinical specialists suggested that device longevity may regularly exceed 4 years, even with a non-rechargeable device. The Committee therefore recognised that price and longevity may be interdependent and that longevity varies depending on an individual's pain characteristics.

4.3.10 The Committee considered the estimates of cost effectiveness for SCS in the treatment of FBSS. The Committee noted that the manufacturers' and Assessment Group's models produced similar estimates of the ICERs for the use of SCS compared with alternative treatments, and that these were less than £11,000 per

QALY gained for the base-case analyses. The Committee was persuaded that the use of SCS for the treatment of FBSS would be a cost-effective use of NHS resources.

4.3.11 The Committee examined the estimates of cost effectiveness for SCS in the treatment of CRPS. It noted that the Assessment Group's and the manufacturers' models had used different sources of utility data and that neither captured the utility of a person with CRPS accurately, as one source was a trial of FBSS and the other a wider survey of neuropathic pain conditions. The Committee noted the additional utility data (section 4.2.6) that had been provided by the ABHI on behalf of the manufacturers from the CRPS clinical trial. The Committee agreed that these utility data appropriately reflected a group of people with CRPS who may be treated with SCS and that these data should be considered as part of the appraisal. The Committee therefore examined an analysis completed using the Assessment Group's model (section 4.2.15) that included the utility data from the CRPS trial. It acknowledged that the results of analysis using these data produced an ICER of less than £17,000 per QALY gained when using a device price of £9000. The Committee was also mindful of consultee comments that device longevity may be greater than the 4-year period used in the economic modelling. The Committee recognised that increasing device longevity would further reduce the ICER. The Committee was therefore persuaded that the use of SCS for the treatment of CRPS would be a cost-effective use of NHS resources.

4.3.12 The Committee recognised that the economic modelling had only included FBSS and CRPS trial data and that these syndromes were part of a range of other neuropathic pain conditions. The Committee recognised that because of the limited evidence there was uncertainty about generalising the available data to other chronic neuropathic pain conditions. The Committee considered

carefully how the impact of chronic pain on HRQoL may vary between different conditions that produce neuropathic pain and whether SCS was equally effective across neuropathic pain conditions. The Committee was mindful of the lack of robust data on these two important factors, but was persuaded by clinical specialists that there was no evidence that different neuropathic pain conditions were significantly different in these respects. Consequently, the Committee was persuaded that, on balance, if people with severe pain of neuropathic origin were appropriately identified, that is, undergo an assessment by a specialist multidisciplinary team which included a successful trial of stimulation, then the evidence of benefit could be generalised. The Committee therefore concluded that the use of SCS should be recommended as a treatment option for all chronic pain conditions of neuropathic origin.

- 4.3.13 The Committee noted that the manufacturers had not provided an economic evaluation of the use of SCS for ischaemic pain, and that the Assessment Group had only been able to complete exploratory threshold analyses for RA because of limited availability of evidence. The Committee also noted the additional information provided by the ABHI on behalf of the manufacturers in response to the Assessment Group's threshold analysis. Examining the analyses for RA, the Committee considered that their relevance was limited as they were based on a population of people for whom treatment with CABG or PCI was suitable. However, these revascularisation techniques are often unsuitable for people with RA. The Committee concluded that although the clinical evidence suggested that there may be groups of people with RA and CLI who could benefit from SCS, there was insufficient evidence on survival and benefits in HRQoL, as well as on cost effectiveness. It therefore concluded that the use of SCS for the treatment of chronic pain of ischaemic origin could currently not be

recommended. However, acknowledging the possible benefit in some subgroups, the Committee recommended that the use of SCS for the treatment of chronic pain of ischaemic origin be subject to further research as part of a clinical trial.

- 4.3.14 The Committee was aware that there was a range of SCS devices available. The Committee heard from clinical specialists that, in clinical practice, they took into account factors such as the pattern of pain and the amount and intensity of stimulation required. The clinical specialists stated that for people with complex pain patterns, complex devices may be more appropriate as they could provide a more complete response to the pain and have a greater longevity, meaning that re-intervention is required less often. The Committee considered that rechargeable devices, although more costly than some non-rechargeable neurostimulators, may have greater longevity and that this may be particularly important for those people requiring a greater complexity or intensity of stimulation. However, the Committee concluded that if, after consultation between the responsible clinician and the patient, it was considered that more than one SCS system was likely to be equally appropriate, the least costly should be used. The Committee considered that assessment of cost should take into account acquisition costs, the anticipated longevity of the system, the stimulation requirements of the person with chronic pain and the support package offered.

5 Implementation

- 5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally

within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.

5.2 'Healthcare standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 that requires local health boards and NHS trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TAXXX). [NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.
- Costing report and costing template to estimate the savings and costs associated with implementation.
- Implementation advice on how to put the guidance into practice and national initiatives which support this locally.
- Audit support for monitoring local practice.

6 Recommendations for further research

6.1 Further research is recommended as follows:

- Comparative studies (preferably in the form of randomised controlled trials) to assess the use of SCS for the treatment of people with chronic pain of ischaemic origin. These studies

should be designed to generate robust evidence about the benefits of spinal cord stimulation (including pain relief, function and quality of life) compared with standard care.

- Observational research to generate robust evidence about the durability of benefits in the use of SCS for the treatment of people with chronic pain of neuropathic origin.

7 Related NICE guidance

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Low back pain: the acute management of patients with chronic (longer than 6 weeks) non-specific low back pain. NICE clinical guideline. Publication expected: May 2009.

8 Review of guidance

8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.

8.2 The guidance on this technology will be considered for review in November 2011.

David Barnett

Chair, Appraisal Committee

August 2008

Appendix A: Appraisal Committee members and NICE project team

A *Appraisal Committee members*

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice-chair. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Professor A E Ades

Professor of Public Health Science, Department of Community Based Medicine, University of Bristol

Dr Amanda Adler

Consultant Physician, Cambridge University Hospitals Trust

Ms Anne Allison

Nurse Clinical Adviser, Healthcare Commission

Dr Tom Aslan

General Practitioner, The Hampstead Group Practice, London

Professor David Barnett (Chair)

Professor of Clinical Pharmacology, Leicester Royal Infirmary

Dr Matt Bradley

Head of HTA and Business Environment, sanofi-aventis Ltd

Mrs Elizabeth Brain

Lay Member

Mr David Chandler

Lay Member

Simon Dixon

Reader in Health Economics, University of Sheffield

Mrs Fiona Duncan

Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool

Mr John Goulston

Chief Executive, Barking, Havering and Redbridge Hospitals NHS Trust

Mrs Eleanor Grey

Lay Member

Professor Philip Home (Vice Chair)

Professor of Diabetes Medicine, Newcastle University

Dr Vincent Kirkbride

Consultant Neonatologist, Regional Neonatal Intensive Care Unit, Sheffield

Dr Alec Miners

Lecturer in Health Economics, London School of Hygiene and Tropical Medicine

Dr Ann Richardson

Lay Member

Mrs Angela Schofield

Chairman, Bournemouth and Poole Teaching PCT

Mr Mike Spencer

General Manager, Facilities and Clinical Support Services, Cardiff and Vale
NHS Trust

Dr Simon Thomas

Consultant Physician and Reader in Therapeutics, Newcastle Hospitals NHS
Foundation Trust and Newcastle University

Mr David Thomson

Lay Member

B NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Ruaraidh Hill

Technical Lead

Zoe Garrett

Technical Adviser

Eloise Saile

Project Manager

Appendix B: Sources of evidence considered by the Committee

A The assessment report for this appraisal was prepared by the University of Sheffield, School of Health and Related Research (SchARR).

- Simpson EL et al. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin, March 2008

B The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD). Organisations listed in I and II were also invited to make written submissions and have the opportunity to appeal against the final appraisal determination.

I Manufacturer/sponsor:

- Boston Scientific UK & Ireland (Precision Implantable Pulse Generator [IPG] Model no. 1110)
- Advanced Neuromodulation Systems, UK Ltd (Genesis IPG [3608], Genesis XP [3609], Genesis XP Dual [3644], Genesis G4, EON Rechargeable Neurostimulation System, Renew [3408 and 3416])
- Medtronic Ltd (Synergy, Versitrel, Itrel 3, Restore Rechargeable Neurostimulation System)

II Professional/specialist and patient/carer groups:

- Association of Anaesthetists of Great Britain & Ireland
- Association of British Neurologists
- Back Care
- British Association of Spinal Surgeons
- British Heart Foundation
- British Pain Society
- Herpes Viruses Association & Shingles Support Society
- Multiple Sclerosis Society
- Pain Concern
- Pain Relief Foundation
- Pelvic Pain Support Network
- National Refractory Angina Centre
- Neuromodulation Society of the United Kingdom and Ireland

- Physiotherapy Pain Association
- Royal College of Anaesthetists
- Royal College of Nursing
- Royal College of Physicians – Cardiology Committee
- Society of British Neurological Surgeons
- Vascular Society

III Other consultees

- Barnsley PCT
- Department of Health
- Welsh Assembly Government
- Guy's and St Thomas Foundation Trust

IV Commentator organisations (did not provide written evidence and without the right of appeal)

- Association of British Healthcare Industries (ABHI)
- Department of Health, Social Services and Public Safety for Northern Ireland
- NHS Quality Improvement Scotland

C The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Professor Turo Nurmikko, Professor of Pain Science, Division of Neurological Science, University of Liverpool, nominated by Association of British Neurologists – clinical specialist
- Mr Eric Ballantyne, Consultant Neurosurgeon, NHS Tayside, nominated by NHS Quality Improvement Scotland – clinical specialist
- Mr Paul Eldridge, Society of British Neurological Surgeons. Surgery – clinical specialist
- Dr Diana E Dickson, Consultant in Pain Medicine, Independent Practice, nominated by Association of Anaesthetists of Great Britain and Ireland – clinical specialist

- Mrs Judy Birch, Volunteer Chief Executive, Pelvic Pain Support network, nominated by the Pelvic Pain Support Network – patient expert