# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

# Overview

# Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin

The overview is written by members of the Institute's team of technical analysts. It forms part of the information received by the Appraisal Committee members before the first committee meeting. The overview summarises the evidence and views that have been submitted by consultees and evaluated by the Assessment Group, and highlights key issues and uncertainties. To allow sufficient time for the overview to be circulated to Appraisal Committee members before the meeting, it is prepared before the Institute receives consultees' comments on the assessment report. These comments are therefore not addressed in the overview.

A list of the sources of evidence used in the preparation of this document is given in Appendix A.

## 1 Background

### *1.1 The condition*

Chronic pain is pain that persists for more than 3 months or beyond the normal course of a disease or expected time of healing. This persistent pain becomes a significant disease in itself rather than being a symptom. 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 cause strain on family and social interactions.

Chronic pain may affect people of all ages. In general, the prevalence of chronic pain increases with age, and is higher among women and people with physically strenuous occupations. Estimates of the prevalence of this condition in the UK vary

from less than 10% to greater than 30% depending on the definition of chronic pain used.

This appraisal includes chronic pain that is either neuropathic or ischaemic in origin. Neuropathic pain is initiated or caused by nervous system damage or dysfunction. The pathophysiology is complex, multifactorial and poorly understood. Neuropathic pain is difficult to manage because affected people often present with complex natural history, unclear or diverse aetiologies, and comorbidities. 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.

Neuropathic pain conditions include failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). FBSS refers to a condition in which people continue to have back and/or leg pain despite anatomically successful lumbar spine surgery. A specific cause of neuropathic pain is not easily identifiable and people with FBSS may experience mixed back and leg pain. CRPS is a disabling disorder characterised by pain, and sensory-motor and autonomic symptoms. CRPS may occur following a noxious event or period of immobilisation (type I) or nerve injury (type II). Pain and increased sensitivity to pain are the most important symptoms and are present in almost all people with CRPS. Signs and symptoms can include sensory (such as intense pain), autonomic (such as temperature changes), motor (such as weakness) and dystrophic (skin changes) difficulties.

Ischaemic pain conditions include critical limb ischaemia (CLI) and refractory angina (RA). CLI is characterised by a reduction of blood flow to the lower limbs. Local phenomena, such as prolonged muscle spasm, can occur, which can be extremely painful. Poor oxygenation, autonomic and biochemical responses can lead to gangrene, an increased risk of limb loss and a marked increase in mortality. People with CLI may experience rest pain (which may be felt as a burning sensation), non-healing wounds and/or tissue necrosis. RA is defined as the occurrence of frequent angina attacks uncontrolled by optimal drug and/or revascularisation therapy, which

significantly limits daily activities, with the presence of coronary artery disease rendering percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG) unsuitable.

## *1.2 Current management*

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 more usually the pain pathways are modulated by a multidisciplinary pain management programme, which can include pharmacological treatments (such as non-steroidal anti-inflammatory drugs; tricyclic anti-depressants; anti-convulsants; the application of local analgesics, anaesthetic (including nerve blocks used in an attempt to reduce pain transmission from a group of nerves) or neurolytic agents; β blockers or opioids, non-pharmacological interventions (such as physiotherapy, acupuncture or transcutaneous electrical nerve stimulation) and psychological therapies (such as cognitive behavioural therapy). The management programme may be referred to as conventional medical management (CMM).

Treatment pathways may be specific to a condition (see the Association of British Healthcare Industries [ABHI] cross-industry joint submission, sections 1.4–5). For example, pharmacotherapy is the favoured treatment for neuropathic pain, but nerve blocks may also be considered. People with FBSS may undergo re-operation. For ischaemic conditions, the preferred treatment is revascularisation (for angina, this includes CABG and percutaneous myocardial revascularisation [PMR]; for CLI, percutaneous angioplasty or distal grafting). However, not everyone is eligible for this intervention and so people with angina who are likely to receive a spinal cord stimulation (SCS) device are those with refractory angina unsuitable for revascularisation. In CLI amputation is often considered. Despite a variety of treatments, people can continue to experience distressing and disabling symptoms. In studies of pharmacological treatments, people whose pain severity is not reduced by 30% or greater are commonly considered to experience a suboptimal response.

Spinal cord stimulation (SCS) is a treatment for chronic pain that would usually only be considered after the more conservative treatments have failed. The British Pain Society (BPS) suggests that, for indications strongly supported by evidence, SCS may be considered when simple first-line therapies are insufficient[1]. For indications such as FBSS, the BPS suggests that SCS may present an alternative to re-operation or opioid use. For CRPS, the BPS suggests that SCS may be considered after pharmacotherapy and nerve blocks have been tried and found to provide inadequate pain relief. It is acknowledged that people with chronic pain vary in their suitability for treatment with SCS and that the technology should be used in the context of a pain management programme in parallel with other appropriate therapies and a strategy for rehabilitation.

## 2 The technologies

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:

1. 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.
2. Electrode(s) that are implanted near the spinal cord implanted either surgically or percutaneously (via puncture, rather than open surgical incision, of the skin).
3. A lead that connects the electrode(s) to the neurostimulator.
4. A remote controller that is used to turn the stimulator on or off and to adjust the level of stimulation.

Neurostimulators may be either implantable pulse generators (which may 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

[1] http://www.britishpainsociety.org/SCS_2005.pdf

powered by a rechargeable battery). Neurostimulators transmit low voltages through the lead to the spinal cord or specific peripheral nerves. The precise mechanism of pain modulation is not fully understood, but it is thought to involve direct and indirect inhibition of pain signal transmission. It is also thought that, for ischaemic pain, SCS gives an additional benefit of increasing microcirculatory blood flow.

People selected for SCS will usually undergo a stimulation trial. The trial involves implantation of the electrode(s) and leads, but use of a temporary, external pulse generator, which is intended to mimic the effects of an implanted device. The criteria for a successful trial are tolerability and pain relief (of a minimum of 50% achieved across a minimum of 80% of painful areas of the body). Permanent implantation, however, may still follow in some cases where these criteria are not fulfilled.

Specialist care is required after implantation of the SCS device as part of the pain management programme and to monitor pain relief, tolerability, device and implant status. Re- intervention may be required 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. Battery life estimates vary, as do manufacturer product warranties. For example, in the implant manual for the Precision IPG (supplied by Advanced Bionics), projections for battery longevity are from 9.7 to 11.3 years. Clinical advice (obtained by the Assessment Group) indicated an average device longevity of 10 years.

According to information received from ABHI, 14 SCS devices have received European approval to market (CE Marking) and are currently available in the UK (table 1). SCS devices are not specific to pain conditions and the same model of neurostimulator can be used to treat a variety of chronic pain conditions. The choice of SCS system will depend on the needs and preferences of the individual person, taking into consideration pain patterns, power and coverage needs, as well as the clinician’s preference. Table 3, appendix B lists the indications for use of available SCS devices.

**Table 1 Neurostimulators available in the UK**

| Manufacturer | Name of product | Power supply | List price (£) |
|---|---|---|---|
| Advanced Bionics, a division of Boston Scientific | Precision SC-1110 | Rechargeable IPG | [redacted] [redacted]AG |
| Advanced Neuromodulation Systems, a division of St Jude Medical | Genesis IPG (3608) | Non-rechargeable IPG | [redacted] |
| | Genesis XP (3609) | Non-rechargeable IPG | [redacted] |
| | Genesis XP Dual (3644) | Non-rechargeable IPG | [redacted] |
| | Genesis G4 | Non-rechargeable IPG | [redacted] |
| | Eon | Rechargeable IPG | [redacted] |
| | Renew (3408) | Radio frequency | [redacted] |
| | Renew (3416) | Radio frequency | [redacted] |
| Medtronic | Synergy EZ | Non-rechargeable IPG | [redacted]AG |
| | Synergy Versitrel | Non-rechargeable IPG | [redacted]AG |
| | Itrel 3 | Non-rechargeable IPG | [redacted]AG |
| | Prime ADVANCED | Non-rechargeable IPG | [redacted]AG |
| | Restore ADVANCED | Rechargeable IPG | [redacted]AG |
| | Restore ULTRA | Rechargeable IPG | [redacted] |

AG, price data obtained by Assessment Group; IPG, implantable pulse generator; List price, listed selling price (supplied by manufacturers) for SCS system, comprising neurostimulator and control equipment (and radio frequency transmitter in the case of RF systems); Non-rechargeable, non-rechargeable internal battery; Radio frequency, transcutaneous passage of pulses by radio frequency system, powered by rechargeable external source; Rechargeable, rechargeable internal battery.

SCS is available in approximately 20–30 centres in the UK and about 1000 SCS implantations and 300 re-interventions are undertaken each year (Neuromodulation Society of UK and Ireland estimates). There are differences between centres in whether surgery is offered as a day case, whether electrodes are implanted surgically or percutaneously, and whether test stimulation is routinely conducted before permanent implantation of SCS systems.

# 3 The evidence

## *3.1 Clinical effectiveness*

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. In addition, the Assessment Group identified nine systematic reviews relevant to the appraisal. Study selection differed from the ABHI submission in that the Assessment Group included one additional RCT of CLI; however, three studies of RA were excluded owing to the absence of relevant data or crossover design. The characteristics of the trials included in the assessment report are summarised in table 4, appendix C and results in table 5, appendix C. All 11 RCTs used non-rechargeable implantable pulse generator (IPG) SCS systems produced by Medtronic.

### 3.1.1 Clinical effectiveness of SCS systems for the treatment of FBSS

Two RCTs (PROCESS and North) investigated the effect of SCS on the treatment of FBSS. The intervention in both trials was SCS combined with CMM, but the comparators differed. In the PROCESS trial, SCS and CMM was compared with CMM alone. In the North trial, SCS and CMM was compared with re-operation and CMM. The follow-up in the PROCESS trial was at 6 and 12 months, whereas that in the North trial was at 6 months and after a mean of 2.9 years. The primary outcome in both studies was the proportion of people whose pain relief was reduced by 50% or greater.

The PROCESS trial reported that SCS and CMM had a greater effect than CMM in terms of the proportion of people experiencing pain relief at both 6 months (p value < 0.001) and 12 months (p < 0.01). The North trial also reported a statistically significant benefit favouring SCS in comparison with re-operation (p < 0.05). In the PROCESS trial opiate use did not differ significantly between the two groups (p = 0.20), but the North trial reported that SCS resulted in a significantly greater (p = 0.025) number of people reducing or maintaining the same dose of opiates when compared with re-operation. The PROCESS trial reported that SCS was more effective than CMM in improving functional ability as measured by the Owestry Disability Index (p < 0.001). The PROCESS trial also measured health-related quality of life (HRQoL) using the Short form-36 (SF-36) and identified statistically significant benefits (p < 0.02) favouring SCS across all domains of the SF-36 except for 'role physical' (p = 0.12). The North trial reported no statistically significant differences between SCS and re-operation for pain related to daily activities or neurological function.

### 3.1.2 Clinical effectiveness of SCS systems for the treatment of CRPS

One RCT (Kemler) investigated the effect of SCS in combination with physical therapy (PT) compared with PT alone for the treatment of CRPS (type 1). The follow-up was at 6, 24 and 60 months. The primary outcome was change in pain intensity from baseline.

This trial reported that SCS plus PT was more effective than PT alone in reducing pain at 6 months (p < 0.001) and at 2 years (p = 0.001), but not at 5 years (p = 0.25). SCS plus PT was also statistically significantly more effective in terms of patients' Global Perceived Effect of treatment (patients 'much improved' at 6 months p ≤ 0.01 and at 2 years p ≤ 0.001). No statistically significant differences were identified between the SCS and PT groups for improvement in functional ability of affected hand or foot, and for HRQoL at either 6 months or 2 years.

### 3.1.3 Clinical effectiveness of SCS systems for the treatment of CLI

Four RCTs investigated the effect of SCS for the treatment of CLI. Of these, two trials (ESES, Suy) compared SCS and CMM with CMM alone, one trial (Jivegard) compared SCS and peroral analgesics with peroral analgesics alone and the fourth trial (Claeys) compared SCS and prostaglandin E1 (PGE1) with PGE1 alone. The follow-up was at 6, 12, 18 and 24 months for ESES, and at 12, 18, 24 months for Claeys, Jivegard and Suy, respectively. The primary outcome for all four trials was rate of limb salvage.

Two of the trials (ESES, Jivegard) reported pain relief outcomes; neither reported statistically significant differences between groups. One trial (ESES) reported medication outcomes. In this trial SCS was shown to be more effective than CMM in reducing use of analgesics (Medication Quantification Scale) at 6 months ($p = 0.002$), but not at 18 months ($p = 0.70$). All four trials reported limb survival or amputation rates. At 24 months the ESES trial reported no statistically significant differences for amputations or limb survival ($p = 0.47$). The Suy trial reported no statistically significant differences ($p = 0.42$) between SCS and CMM groups in terms of amputation rate and neither did the Claeys trial. The Jivegard trial reported a borderline statistically significant ($p = 0.055$) difference between SCS and analgesics when categorising amputations by ‘none’, ‘moderate’ or ‘major’, with fewer major amputations occurring in the SCS group. A non-significant trend towards lower amputation rate (at 18 months) in the SCS group was identified for a subgroup of people in the ESES trial with intermediate skin microcirculation. One trial (ESES) measured HRQoL. This trial reported no statistically significant differences between the SCS and CMM groups.

### 3.1.4 Clinical effectiveness of SCS systems for treatment of angina

Four RCTs investigated the effect of SCS for the treatment of angina. Each differed in the comparison studied. SCS was compared with no SCS device implanted (DeJongste), an implanted but inactive SCS system (Hautvast), CABG (ESBY) or PMR (SPiRiT). The DeJongste, Hautvast and SPiRiT trials recruited people with RA who were unsuitable for revascularisation procedures and ESBY recruited people in

whom revascularisation was not considered to improve prognosis. The follow-up was 6 weeks for Hautvast, 6–8 weeks for DeJongste; 6 and 58 months for ESBY, and 12 months for SPiRiT. In the DeJongste, Hautvast and SPiRiT trials the primary outcome was exercise capacity. In the ESBY trial the primary outcome was frequency of angina attacks.

One trial reported pain outcomes (Hautvast). This trial reported no statistically significant difference between SCS and inactive stimulator in terms of pain relief measured as mean reduction in visual analogue scale (VAS). Three trials measured nitrate consumption. Two of these trials (DeJongste and Hautvast) reported statistically significant benefits favouring SCS over either no SCS device or an inactive SCS device ($p < 0.05$ and $p = 0.03$, respectively), while one of the trials (ESBY) 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 ($p < 0.0001$).

All four trials reported functional outcomes, either frequency of angina attacks or the outcomes of exercise tests. Two trials (DeJongste, Hautvast) reported a statistically significant difference favouring SCS in comparison with either no SCS or inactive SCS for frequency of angina attacks, exercise duration and time to angina. The ESBY trial reported no statistically significant differences between SCS and CABG in number of angina attacks a week. The SPiRiT trial reported no statistically significant differences between SCS and PMR groups for either exercise duration ($p = 0.466$) or time to angina ($p = 0.191$) at 12 months follow-up. The ESBY trial reported that CABG was more effective than SCS in increasing maximum workload capacity ($p = 0.02$), although the SCS device was switched off during this comparison. All four trials reported HRQoL outcomes. DeJongste 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.

### 3.1.5 Adverse effects of treatment

SCS device-related complication rates varied across trials. Such complications were usually minor and included electrode migration, lead fracture, loss of paraesthesia, dural puncture and infection. Across the 14 trials, the percentage of implantations requiring surgery to resolve a device-related complication, including device removals, ranged from 0% to 38%. Differences in these rates may have been due to follow-up period, populations recruited or clinical settings. Across all trials, out of a total of 403 people who had implantations, four (1%) device removals were reported, all of these because of infection.

### 3.1.6 Summary

Trial data suggest that SCS is effective for the relief of neuropathic pain in FBSS and CRPS. There may be additional benefits of treatment with SCS for HRQoL and functional ability in FBSS. SCS was not shown to be more statistically significantly effective than other therapies in the treatment of CLI apart from resulting in a lower use of analgesics in the SCS group compared with the CMM group up to 6 months after starting treatment. There may be a subset of people with CLI that would benefit from SCS, but the AR reports that no definitive conclusions can be drawn because of limitations in study methodology. SCS is reported to be effective at reducing some angina symptoms when compared with either no SCS device or an inactive SCS device.

## *3.2 Cost effectiveness*

The ABHI submission included a *de novo* economic evaluation. The Assessment Group identified one economic evaluation in their systematic review and reviewed this along with the ABHI submission. In addition, the Assessment Group developed their own economic evaluation.

### 3.2.1 Published economic evaluations

The one economic evaluation that satisfied the Assessment Group's inclusion criteria (Taylor and Taylor, 2005) reported the cost effectiveness of SCS and CMM compared with CMM for the treatment of FBSS. The evaluation included a two-stage

model comprising a decision tree assessing costs and outcomes to 2 years and a Markov model extending assessment to a lifetime. Costs were derived from a Canadian centre and translated to the UK context (at 2003 prices). The base-case estimate of incremental cost effectiveness for SCS in comparison with CMM at 2 years was £33,053 per additional quality-adjusted life year (QALY) gained. One-way sensitivity analyses gave a range of estimates of incremental cost effectiveness from £21,908 to £45,816 per additional QALY gained. In the lifetime analysis, it was found that SCS was dominant (cost less and accrued more benefits) in both base-case and one-way sensitivity analyses.

### 3.2.2 The economic evaluation submitted by ABHI

The ABHI submission included a two-stage model comprising a decision tree for the short-term treatment with SCS (first 6 months) and a Markov process for SCS treatment from 6 months to 15 years. This structure was based on the Taylor and Taylor (2005) model. The model estimated the cost effectiveness of SCS for neuropathic pain and modelled both FBSS and CRPS conditions. Ischaemic pain conditions were not modelled.

In the model, treatment success was defined as 50% or greater reduction in pain, with an alternative scenario of 30% pain relief modelled as a sensitivity analysis. The cycle length was 3 months and complications arising were assumed to be resolved within one cycle. Utility and cost data were assumed to be the same for both FBSS and CRPS, and were both based on the FBSS PROCESS trial. An average price for the SCS system (neurostimulator, controller and charger, if applicable) of £9282 plus lead costs of £1544 (surgical) or £1136 (percutaneous) was used, with a range given in the submission of £6858–13,289 for SCS systems and £928–1804 and £1065–1158 for surgical and percutaneous leads, respectively. Based on clinical advice it was assumed that percutaneous leads were used in 70% of patients. Health state utilities were based on the EQ-5D, 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; suboptimal pain relief and complications 0.258. In the base-case, device longevity was set to 4 years.

The FBSS modelling included two scenarios. The first was a comparison of SCS and CMM with CMM alone, the second was a comparison of SCS and CMM with re-operation. Probabilities of events were based on the North and PROCESS trials. Assuming device longevity of 4 years, the estimate of incremental cost effectiveness for SCS and CMM compared with CMM alone was £9155 per additional QALY gained. For the comparison of SCS and CMM compared with re-operation, the estimate of incremental cost effectiveness was £7954 per additional QALY gained.

The CRPS modelling compared SCS and CMM with CMM alone using probabilities based on data from the trial by Kemler. Assuming device longevity of 4 years, the estimate of incremental cost effectiveness for SCS and CMM compared with CMM alone was £18,881 per additional QALY gained.

### 3.2.3 Assessment Group's economic evaluation of neuropathic pain

The Assessment Group developed their own model, following the approach adopted previously by ABHI and Taylor and Taylor (2005). The two-stage model comprised a decision tree to 6 months with a Markov process extending to 15 years. Treatment success was defined as 50% or greater reduction in pain.

The Assessment Group modelled both FBSS and CRPS conditions. For FBSS the decision tree used event data from the PROCESS and North trials to compare SCS and CMM with CMM alone, and SCS and CMM with re-operation. For CRPS the decision tree used event data from the Kelmer trial that compared SCS and CMM with CMM alone. In the decision tree, one of four health states (optimal pain relief or suboptimal pain relief, either with or without complications) was possible, as for the ABHI model. Modelled patients entered the second-stage model in the state assigned in the first-stage model. In the Markov model, one of four states was possible for CRPS (optimal pain relief, suboptimal pain relief, no pain relief or death) and an additional health state (no pain relief following re-operation) was incorporated into the FBSS model. 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. Complications (after 6 months) were

assumed to be at a rate of 18% per annum and withdrawal from SCS was assumed to be at a rate of 3.24% per annum, mainly because of gradual loss of pain control. No complications were assumed to occur in the CMM (without SCS) groups. In the base-case device longevity was set to 4 years and explored in sensitivity analyses.

The Assessment Group opted not to use costs from the PROCESS trial as included in the ABHI model because these were not publicly available at the time of assessment. The Assessment Group used cost data from the British national formulary (BNF, medication); Personal Social Services Research Unit (PSSRU; GP visits); retrospective analysis on SCS complications (trial stimulation, implantation, complications and device explanation/failed trial stimulation) and national statistics (population death rates). Proportions for drug therapy use for CMM were taken from PROCESS, with relevant costs taken from the BNF. Non-drug costs were based on PSSRU costs and an economic evaluation of acupuncture for the treatment of lower back pain. In the base-case, the average combined cost of a neurostimulator and control system was £[redacted], reflecting a mid-range of equipment prices obtained by the Assessment Group.

Health state utilities were based on the EQ-5D and in contrast to the ABHI model differed between FBSS and CRPS. Utility data were obtained from PROCESS for FBSS and a cross-sectional survey that investigated the burden of neuropathic pain for CRPS. Utility values for each possible health state are shown in table 2.

**Table 2 Health state utility values used in the model**

| Health state | Utility value | |
|---|---|---|
| | FBSS | CRPS |
| Optimal pain relief (without complications) | 0.598 | 0.67 |
| Optimal pain relief with complications | 0.528 | 0.62 |
| Suboptimal pain relief (without complications) | 0.258 | 0.46 |
| Suboptimal pain relief with complications | 0.258 | 0.41 |
| No perceived pain reduction | 0.168 | 0.16 |

FBSS, failed back surgery syndrome; CRPS, complex regional pain syndrome.

### Estimates of incremental cost effectiveness for FBSS

The estimate of incremental cost effectiveness for SCS and CMM compared with CMM alone was £7996 per additional QALY gained. In a scenario where SCS and CMM was compared with re-operation, the estimate of incremental cost effectiveness was £7043 per additional QALY gained. Results were sensitive to device longevity and price (see appendix C, tables 7 and 8). Sensitivity analyses that held the device price constant and changed the assumptions about device longevity suggested that in both scenarios the incremental cost-effectiveness ratios (ICER) would be less than £30,000 per QALY gained if device longevity was 2 or more years and less than £20,000 per QALY gained if device longevity was 3 years or longer. Sensitivity analyses which held device longevity constant (4 years as per the base-case) and changed the device price produced an ICER that was less than £20,000 per QALY gained with a device priced up to £13,000 for SCS and CMM compared with CMM and £15,000 for SCS and CMM compared with re-operation and CMM. For both comparisons the ICER was less than £30,000 per QALY gained for any device cost explored in the analyses (that is, £5000 to £15,000).

### Estimates of incremental cost effectiveness for CRPS

The estimate of incremental cost effectiveness for SCS and CMM compared with CMM alone was £25,095 per additional QALY gained. Results were sensitive to device longevity and cost (see table 9, appendix C). Sensitivity analyses that held the device price constant and changed the assumptions about device longevities (at the base-case price) suggested that if device longevity was 4 years or longer then the ICER would be less than £30,000 per QALY gained, and less than £20,000 per QALY gained if device longevity was 5 years or longer. Sensitivity analyses that held device longevity constant (as per the base-case) and changed the device price suggested the ICER was 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.

Table 6, in appendix C, compares results of the ABHI economic evaluation with those produced by the Assessment Group.

### 3.2.4 Assessment Group economic evaluation of ischaemic pain

The Assessment Group did not complete an economic analysis of CLI, but was able to explore 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 (Griffin and colleagues, 2007) that compared the outcomes for CABG, PCI and CMM in groups of people who were identified as being appropriate for CABG, PCI or both CABG and PCI. Data for costs were identified from the BNF, PSSRU and Griffin (2007). Utility data were also identified from Griffin (2007), which reported utility values after 6 years of follow-up. The time horizon of the model was 6 years.

The threshold analysis was presented both in terms of additional survival (life years gained) and as additional quality-adjusted life years that would need to be associated with SCS for SCS to be cost effective at different levels of willingness to pay. In the latter analyses it was assumed that survival in the SCS and comparators (CABG, PCI and CMM) was similar. The average minimum utility required for SCS to be cost effective at £20,000 and £30,000 assuming similar survival was then calculated. For each comparator (CABG, PCI and CMM), three scenarios were modelled based on groups of people who were defined as clinically appropriate to receive CABG, PCI or either revascularisation procedure.

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 value 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 to CMM, for ICERs of £20,000 or £30,000 per QALY gained or less, respectively.

For people who are appropriate for 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.

For people who are appropriate for 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 to CABG, SCS dominates.

The Assessment Group highlighted the exploratory nature of these analyses and commented that because of the lack of published evidence concerning utility values and expected survival for SCS in the treatment of RA, the results of this threshold analysis should be interpreted carefully.

# 4 Issues for consideration

Evidence of clinical effectiveness is available for only a limited range of SCS devices (all trials used a Medtronic, non-rechargeable IPG) and trial results could not be combined in meta-analysis. Does the Committee consider that the evidence available is representative of the effectiveness of any particular SCS device or SCS devices as a technology group?

Studies that have investigated the clinical effectiveness of SCS for different pain conditions (such as FBSS, CRPS, CLI or RA) do not always show the same pattern of effects across outcomes, across studies and at different follow-up points. Does the Committee consider that the clinical effectiveness of SCS has been demonstrated for the different pain conditions?

For FBSS, the base-case estimates of incremental cost effectiveness provided by the ABHI and the Assessment Group are broadly comparable. For CRPS, the estimates of incremental cost effectiveness are less comparable, differing because of the utility data and the costs used. For CRPS, which utility and cost data does the Committee consider to be the most appropriate for use in the economic modelling?

The cost of SCS devices varies. In the economic analysis by the ABHI an average SCS system price of £9282 with a range given in the submission of £6858–13,289. In their base-case, the Assessment Group used a mid-range price for a SCS system

of £[redacted], and explored the impact on cost effectiveness of increasing and reducing this price. How can the Committee take into account the different device prices available? How do the different device prices affect the guidance on SCS devices?

As well as being sensitive to device cost, the economic models provided by ABHI and the Assessment Group are also sensitive to device longevity. In the base-case analysis for both economic models device longevity of 4 years was assumed. The Assessment Group's clinical advisers and implant manual submitted by Advanced Bionics indicated a device longevity of approximately 10 years. What does the Committee consider to be an appropriate assumption for device longevity?

Neither the ABHI submission nor the Assessment Group modelled the cost effectiveness of CLI. Therefore cost effectiveness analyses of SCS when used for CLI are unavailable. What conclusions can be drawn on the cost effectiveness of SCS for the treatment of CLI?

People with angina likely to receive an SCS device are those with RA characterised by the presence of coronary artery disease rendering PCI and CABG unsuitable. The cost effectiveness evidence includes comparisons of RA with PCI and CABG in people defined by their appropriateness for CABG and PCI. Does the Committee consider that the data source (Griffin and colleagues, 2007) used by the AG to populate the threshold analysis reflects an appropriate clinical scenario for people with RA? What do the Committee consider are appropriate assumptions about utility and survival in people with RA that are required to interpret the threshold analysis?

# 5 Ongoing research

Consultees recommended that outcome data should be recorded for every patient who receives a SCS device and that more data for other SCS indications (other than those examined in this appraisal) are required. The Assessment Group suggest good quality registers of SCS patients could address some of the outcomes not determined in the RCTs included in their assessment report.

# 6 Authors

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May 2008

# Appendix A. Sources of evidence considered in the preparation of the overview

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

- Simpson EL, Duenas A, Holmes MW and Papaioannou D, Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin, March 2008

B Submissions from the following organisations:

I Manufacturer/sponsors:

- Advanced Bionics
- Advanced Neuromodulation Systems
- Medtronic

II Professional/specialist and patient/carer groups:

- Action on Pain
- Back Care
- Pain Relief Foundation
- British Pain Society
- British Society of Rehabilitation Medicine
- Royal College of Anesthetists (Faculty of Pain Medicine)
- Neuromodulation Society of UK and Ireland
- Pain Concern
- Pain Relief Foundation
- Pelvic Pain Support Network Submission

# Appendix B: Indications for use

### Table 3 Indications for use for specific neurostimulator devices

| Manufacturer | Device name | Power, configuration | CE marked indications |
|---|---|---|---|
| Advanced Bionics | Precision SC-1110 | Rechargeable IPG | As an aid in the management of chronic intractable pain |
| Advanced Neuromodulation Systems (ANS) | Genesis IPG (3608)<br>Genesis XP (3609)<br>Genesis XP Dual (3644)<br>Genesis G4 | Non-rechargeable IPG | As an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with any of the following: failed back surgery syndrome, and intractable low back pain and leg pain |
| | Eon | Rechargeable IPG | As an aid in the management of chronic intractable pain of the trunk and/or limbs |
| | Renew (3408)<br>Renew (3416) | Radio frequency system (implant, with external rechargeable power) | As an aid in the management of chronic pain, intractable pain of the trunk and/or limbs |
| Medtronic | Synergy<br>Synergy Versitrel<br>Itrel 3<br>Prime ADVANCED | Non-rechargeable IPG | As an aid in the management of chronic, intractable pain of the trunk and/or limbs, peripheral vascular disease, or intractable angina pectoris |
| | Restore ADVANCED<br>Restore ULTRA | Rechargeable IPG | As an aid in the management of chronic pain, intractable pain of the trunk and/or limbs, peripheral vascular disease, or refractory angina pectoris |

Best practice in patient selection or contraindications for devices stipulates a test stimulation for patients before permanent implant.

IPG, implantable pulse generator.

# Appendix C: Summary of included studies

### Table 4 Summary of neuropathic pain trials

| Trial | Indication | Intervention | Comparator | Total number randomised | Data at follow-up | Primary outcome |
|---|---|---|---|---|---|---|
| PROCESS | Failed back surgery syndrome | SCS plus CMM | CMM | 100 | 6 and 12 months | Proportion of patients achieving at least 50% pain relief in the legs |
| North | Failed back surgery syndrome | SCS plus CMM | Re-operation plus CMM | 60 | 6 months, and mean 2.9 years | At least 50% pain relief plus patient satisfaction |
| Kemler | Complex regional pain syndrome type I | SCS plus physical therapy | Physical therapy | 54 | 6, 24 and 60 months | VAS pain intensity change from baseline |
| ESES | CLI | SCS plus CMM | CMM | 120 | 6, 12, 18 and 24 months | Limb salvage rates; pain relief |
| Suy | CLI | SCS plus CMM | CMM | 38 | 24 months | Limb salvage rates |
| Jivegard | CLI | SCS plus peroral analgesics | Peroral analgesics | 51 | 18 months | Limb salvage rates |
| Claeys | CLI | SCS plus Prostaglandin E1 | Prostaglandin E1 (PGE1) | 86 | 12 months | Limb salvage rates |

| Trial | Indication | Intervention | Comparator | Total number randomised | Data at follow-up | Primary outcome |
|---|---|---|---|---|---|---|
| DeJongste | Angina pectoris | SCS | No SCS | 17 | 6–8 weeks | Exercise capacity; HRQoL |
| ESBY | Angina pectoris | SCS | Coronary artery bypass surgery | 104 | 6 and 58 months | Angina attacks |
| SPiRiT | Angina pectoris | SCS | Percutaneous myocardial laser revascularisation | 68 | 12 months | Exercise capacity |
| Hautvas | Angina pectoris | SCS | Inactive stimulator | 25 | 6 weeks | Exercise capacity |

CLI, critical limb ischaemia; CMM, conventional medical management; HRQoL, health-related quality of life; SCS, spinal cord stimulation; VAS, visual analogue scale.

## Table 5 Summary of results from the included studies

| Trial | Pain | Medication | Function | Health related quality of life |
|---|---|---|---|---|
| **Failed back surgery syndrome** | | | | |
| **PROCESS** | VAS, % with ≥50% relief | Opioid, % using | ODI, Mean change | SF-36, change from baseline, **6 months** |
| | **6 months** **12 months** | **6 months** | **6 months** | PF RP BP GH Vit SoF RE MH |
| SCS + CMM | 48% 34% | 56% | 44.9 | 38.1 17.5 33.0 52.8 41.3 49.3 51.3 62 6 |
| CMM | 9% 7% | 70% | 56.1 | 21.8 8.0 19.5 41.3 31.1 33.5 29.5 50.1 |
| p value | **** ** | ns | *** | *** ns *** *** ** ** * ** |
| **North** | VAS, % with ≥50% relief | % decrease or stable medication | Self reported neurological function and work status | |
| | **Mean 2.9 years** | **Mean 2.9 years** | | |
| SCS + CMM | 39% | 87% | NR | |
| Reopern +CMM | 12% | 58% | NR | |
| p value | * | * | ns | |
| **Complex regional pain syndrome** | | | | |
| **Kemler** | VAS, mean change | | Mean improvement in seconds to perform task | Mean % change in health related quality of life |
| | **6 months 2 years 5 years** | | **6 months 2 years** | **6 months** **2 years** |
| SCS + PT | -2.4cm -2.1cm -1.7cm | | Hand 2 2<br>Foot -1 -3 | 6% 7% |
| PT | +0.2cm 0cm -1.0cm | | Hand -1 -5<br>Foot -1 -5 | 3% 12% |
| p value | *** *** ns | | ns ns<br>ns ns | ns ns |

VAS visual analogue scale, SF-36 short form 36, PF physical function, RP role physical, BP bodily pain, GH general health, Vit vitality, SoF social functioning, RE role emotional, MH mental health, SCS spinal cord stimulation, CMM conventional medical management, PT physical therapy, ns non significant

| Trial | Pain | Medication | Function | Health related quality of life |
|---|---|---|---|---|
| **Critical limb ischaemia** | | | | |
| **ESES** | VAS, mean change baseline | MQS, numbers of patients | Limb survival | NHP, Mean score |
| | **6 month 12 month 18 month** | **6 month 12 month 18 month** | **6 month 12 month 2years** | **6 month 18 month** |
| SCS + CMM | -1.35cm -1.94cm 2.45cm | 5 4 2 | 66% 60% 52% | 35 35 |
| CMM | -2.57cm -2.15cm 2.61cm | 12 6 0 | 68% 46% 46% | 34 34 |
| p value | ns ns ns | ** ns ns | ns ns ns | ns ns |
| **Suy** | | | Amputation (major), Nos. | |
| | | | **2 years** | |
| SCS + CMM | | | 6 | |
| CMM | | | 9 | |
| p value | | | ns | |
| **Jivegard** | VAS scale 0-100 | | Limb survival | |
| | | | **18 month** | |
| SCS + analgesics | NR | | 62% | |
| analgesics | NR | | 45% | |
| p value | ns | | ns | |
| **Claeys** | | | % of people undergoing amputation | |
| | | | Minor Major | |
| | | | **12 month 12 month** | |
| SCS+ PGE1 | | | 13% 16% | |
| PGE1 | | | 15% 20% | |
| p value | | | ns ns | |

VAS visual analogue scale, MQS medication quantification scale, NHP Nottingham health profile, SCS spinal cord stimulation, CMM conventional medical management, PGE1 Prostaglandin E1, ns non significant, NR not reported

| Trial | Pain/Symptoms | | Medication | Function: exercise duration | Health related quality of life | |
|---|---|---|---|---|---|---|
| **Refractory Angina** | | | | | | |
| **Hautvast** | VAS, Mean change | Angina attacks per day | Nitrate consumption, % change | mean seconds | LASA (cm) percentage change from baseline | |
| | **6 week** | **6week** | **6 week** | **6 week** | **6 week** | |
| SCS | -1.1cm | 2.3 | -48% | 533 | 15% | |
| Inactive stimulator | -0.2cm | 3.2 | 27% | 427 | 1% | |
| p value | ns | ** | * | * | ns | |
| **deJongste** | Angina attacks per week, Median | | GTN consumption median per week | mean seconds | ADL (median) | SAS (median) |
| | **6-8 week** | | **6-8 week** | **6-8 week** | **6-8 week** | **6-8 week** |
| SCS | 9.0 | | 1.6 | 827 | 20.6 | 2.10 |
| No SCS | 13.6 | | 8.5 | 694 | 1.25 | 1.39 |
| p value | * | | * | * | * | * |
| **ESBY** | Angina attacks per week, Median | | Nitrate, doses/week (all nitrate) | Maximum workload capacity | NHP | |
| | **6 months** | | **6 months** | **6 months** | **6 months** | |
| SCS | 4.4 | | 4.1 | 92.2 | NR | |
| CABG | 5.2 | | 3.1 | 99.0 | NR | |
| p value | ns | | short acting ns, long acting *** | * (favours control) | ns | |
| **SPiRiT** | | | | mean minutes | SF-36 | |
| | | | | **3 months** **12 months** | **3 and 12 months** | |
| SCS | | | | 7.33 7.08 | NR | |
| PMR | | | | 7.32 7.12 | NR | |
| p value | | | | * ns | ns | |

VAS visual analogue scale, LASA Linear Analogue Self Assessment, SCS spinal cord stimulation, CABG Coronary Artery Bypass Graft, PMR Percutaneous Myocardial Laser revascularization, GTN Glyceryl trinitrate, ADL daily activity score, SAS social activity score, NHP Nottingham health profile

**Table 6 Comparison of results between ABHI and Assessment Group model**

| | ABHI model | | | Assessment Group model | | |
|---|---|---|---|---|---|---|
| **50% pain threshold criteria** | **Cost difference** | **QALYs difference** | **ICER** | **Cost difference** | **QALYs difference** | **ICER** |
| **FBSS: SCS + CMM versus CMM alone** | | | | | | |
| Device longevity | | | | | | |
| Base-case: 4 years | £11,439 | 1.25 | £9155 | £10,035 | 1.26 | £7996 |
| 2 years | | | £30,285 | | | £26,755 |
| 7 years | | | £2745 | | | £2304 |
| >7 years | | | SCS + CMM dominates | | | SCS + CMM dominates |
| **FBSS: SCS + CMM versus re-operation** | | | | | | |
| Device longevity | | | | | | |
| Base case: 4 years | £10,651 | 1.34 | £7954 | £9430 | 1.34 | £7043 |
| 2 years | | | £26,445 | | | £23,536 |
| 7 years | | | £2362 | | | £2055 |
| >7 years | | | SCS + CMM dominates | | | SCS + CMM dominates |
| **CRPS: SCS + CMM versus CMM alone** | | | | | | |
| Device longevity | | | | | | |
| Base case: 4 years | £12,041 | 0.64 | £18,881 | £8775 | 0.35 | £25,095 |
| 2 years | | | £52,541 | | | £80,388 |
| 7 years | | | £8737 | | | £8591 |
| >7 years | | | SCS + CMM dominates | | | SCS + CMM dominates |

ABHI, Association of British Healthcare Industries; CLI, critical limb ischaemia; CMM, conventional medical management; CRPS, complex regional pain syndrome; FBSS, failed back surgery syndrome; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; SCS, spinal cord stimulation.

**Table 7 Assessment Group analysis of FBSS (SCS with CMM versus CMM alone): impact of device price and longevity on cost effectiveness**

| | Discounted ICER (£/QALY) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Device cost/ longevity (years)** | **£5000** | **£6000** | **£7000** | **£8000** | **£9000** | **£10,000** | **£11,000** | **£12,000** | **£13,000** | **£14,000** | **£15,000** |
| 1 | £42,054 | £49,179 | £56,304 | £63,429 | £70,554 | £77,679 | £84,804 | £91,929 | £99,054 | £106,179 | £113,304 |
| 2 | £16,380 | £20,160 | £23,940 | £27,719 | £31,499 | £35,279 | £39,059 | £42,838 | £46,618 | £50,398 | £54,178 |
| 3 | £6326 | £8796 | £11,265 | £13,735 | £16,205 | £18,674 | £21,144 | £23,614 | £26,083 | £28,553 | £31,023 |
| 4 | £2563 | £4542 | £6521 | £8500 | £10,480 | £12,459 | £14,438 | £16,418 | £18,397 | £20,376 | £22,356 |
| 5 | –£694 | £861 | £2416 | £3971 | £5526 | £7081 | £8636 | £10,191 | £11,746 | £13,301 | £14,856 |
| 6 | –£1181 | £311 | £1802 | £3294 | £4785 | £6277 | £7768 | £9260 | £10,751 | £12,243 | £13,734 |
| 7 | –£1630 | –£197 | £1236 | £2669 | £4103 | £5536 | £6969 | £8402 | £9835 | £11,268 | £12,701 |
| 8 | –£4260 | –£3170 | –£2079 | –£989 | £101 | £1192 | £2282 | £3372 | £4463 | £5553 | £6643 |
| 9 | –£4426 | –£3357 | –£2289 | –£1220 | –£151 | £918 | £1986 | £3055 | £4124 | £5192 | £6261 |
| 10 | –£4584 | –£3536 | –£2487 | –£1439 | –£391 | £657 | £1705 | £2753 | £3802 | £4850 | £5898 |
| 11 | –£4734 | –£3705 | –£2676 | –£1648 | –£619 | £410 | £1438 | £2467 | £3496 | £4524 | £5553 |
| 12 | –£4876 | –£3866 | –£2856 | –£1846 | –£836 | £174 | £1185 | £2195 | £3205 | £4215 | £5225 |
| 13 | –£5011 | –£4019 | –£3026 | –£2034 | –£1041 | –£49 | £944 | £1936 | £2928 | £3921 | £4913 |
| 14 | –£5140 | –£4164 | –£3188 | –£2213 | –£1237 | –£261 | £715 | £1690 | £2666 | £3642 | £4617 |

**Table 8 Assessment Group analysis FBSS (SCS with CMM versus re-operation): impact of device price and longevity on cost effectiveness**

| | Discounted ICER (£/QALY) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Device cost/ Longevity (yrs)** | **£5000** | **£6000** | **£7000** | **£8000** | **£9000** | **£10,000** | **£11,000** | **£12,000** | **£13,000** | **£14,000** | **£15,000** |
| 1 | £37,142 | £43,429 | £49,715 | £56,001 | £62,288 | £68,574 | £74,861 | £81,147 | £87,434 | £93,720 | £100,006 |
| 2 | £14,424 | £17,744 | £21,063 | £24,383 | £27,703 | £31,022 | £34,342 | £37,662 | £40,981 | £44,301 | £47,621 |
| 3 | £5,583 | £7749 | £9914 | £12,079 | £14,244 | £16,409 | £18,575 | £20,740 | £22,905 | £25,070 | £27,235 |
| 4 | £2283 | £4017 | £5751 | £7485 | £9219 | £10,953 | £12,687 | £14,421 | £16,156 | £17,890 | £19,624 |
| 5 | –£570 | £791 | £2153 | £3514 | £4876 | £6238 | £7599 | £8961 | £10,322 | £11,684 | £13,046 |
| 6 | –£997 | £309 | £1,615 | £2,921 | £4,227 | £5,533 | £6,839 | £8,145 | £9,451 | £10,757 | £12,063 |
| 7 | –£1389 | –£135 | £1120 | £2374 | £3629 | £4884 | £6138 | £7393 | £8648 | £9902 | £11,157 |
| 8 | –£3690 | –£2736 | –£1782 | –£828 | £126 | £1080 | £2034 | £2988 | £3943 | £4897 | £5851 |
| 9 | –£3836 | –£2900 | –£1965 | –£1030 | –£95 | £840 | £1775 | £2711 | £3646 | £4581 | £5516 |
| 10 | –£3974 | –£3056 | –£2139 | –£1222 | –£305 | £612 | £1529 | £2447 | £3364 | £4281 | £5198 |
| 11 | –£4105 | –£3204 | –£2304 | –£1404 | –£504 | £396 | £1296 | £2196 | £3096 | £3996 | £4896 |
| 12 | –£4229 | –£3345 | –£2461 | –£1578 | –£694 | £190 | £1074 | £1958 | £2841 | £3725 | £4609 |
| 13 | –£4347 | –£3479 | –£2611 | –£1742 | –£874 | –£5 | £863 | £1731 | £2600 | £3468 | £4336 |
| 14 | –£4460 | –£3606 | –£2752 | –£1899 | –£1045 | –£191 | £663 | £1516 | £2370 | £3224 | £4077 |

**Table 9 Assessment Group analysis CRPS (SCS with CMM versus CMM alone): impact of device price and longevity on cost effectiveness**

| | Discounted ICER (£/QALY) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Device cost/ Longevity (yrs)** | **£5000** | **£6000** | **£7000** | **£8000** | **£9000** | **£10,000** | **£11,000** | **£12,000** | **£13,000** | **£14,000** | **£15,000** |
| 1 | £128,240 | £149,618 | £170,996 | £192,375 | £213,753 | £235,131 | £256,509 | £277,888 | £299,266 | £320,644 | £342,022 |
| 2 | £49,988 | £61,063 | £72,137 | £83,212 | £94,287 | £105,362 | £116,437 | £127,512 | £138,586 | £149,661 | £160,736 |
| 3 | £20,335 | £27,505 | £34,675 | £41,846 | £49,016 | £56,187 | £63,357 | £70,528 | £77,698 | £84,868 | £92,039 |
| 4 | £9,374 | £15,101 | £20,828 | £26,555 | £32,282 | £38,010 | £43,737 | £49,464 | £55,191 | £60,918 | £66,646 |
| 5 | –£51 | £4435 | £8921 | £13,408 | £17,894 | £22,380 | £26,866 | £31,352 | £35,839 | £40,325 | £44,811 |
| 6 | –£1456 | £2845 | £7147 | £11,448 | £15,749 | £20,050 | £24,352 | £28,653 | £32,954 | £37,256 | £41,557 |
| 7 | –£2749 | £1382 | £5513 | £9644 | £13,775 | £17,906 | £22,037 | £26,168 | £30,299 | £34,430 | £38,561 |
| 8 | –£10,309 | –£7173 | –£4037 | –£902 | £2234 | £5370 | £8505 | £11,641 | £14,776 | £17,912 | £21,048 |
| 9 | –£10,784 | –£7711 | –£4639 | –£1566 | £1507 | £4580 | £7653 | £10,726 | £13,799 | £16,872 | £19,945 |
| 10 | –£11,236 | –£8223 | –£5210 | –£2196 | £817 | £3831 | £6844 | £9858 | £12,871 | £15,884 | £18,898 |
| 11 | –£11,666 | –£8709 | –£5752 | –£2795 | £162 | £3119 | £6076 | £9033 | £11,989 | £14,946 | £17,903 |
| 12 | –£12,074 | –£9170 | –£6267 | –£3364 | –£461 | £2442 | £5346 | £8249 | £11,152 | £14,055 | £16,958 |
| 13 | –£12,461 | –£9,609 | –£6757 | –£3904 | –£1052 | £1800 | £4652 | £7504 | £10,357 | £13,209 | £16,061 |
| 14 | –£12,829 | –£10,025 | –£7221 | –£4418 | –£1614 | £1190 | £3994 | £6797 | £9601 | £12,405 | £15,209 |