

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Report for Guidance Executive

Review of DG6: Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M

This guidance was issued in November 2012.

The review date for this guidance is November 2015.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Recommendation

Transfer the guidance to the 'static guidance list'.

That we should consult on the proposal.

A list of the options for consideration and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Original objective of guidance

To assess the clinical and cost effectiveness of BIS, E-Entropy and Narcotrend for assessing depth of anaesthesia in individuals undergoing general anaesthesia

3. Current guidance

Adoption recommendations

- 1.1. The use of electroencephalography (EEG)-based depth of anaesthesia monitors is recommended as an option during any type of general anaesthesia in patients considered at higher risk of adverse outcomes. This includes patients at higher risk of unintended awareness and patients at higher risk of excessively deep anaesthesia. The Bispectral Index (BIS) depth of anaesthesia monitor is therefore recommended as an option in these patients.

- 1.2. The use of EEG-based depth of anaesthesia monitors is also recommended as an option in all patients receiving total intravenous anaesthesia. The BIS monitor is therefore recommended as an option in these patients.
- 1.3. Although there is greater uncertainty of clinical benefit for the E-Entropy and Narcotrend-Compact M depth of anaesthesia monitors than for the BIS monitor, the Committee concluded that the E-Entropy and Narcotrend-Compact M monitors are broadly equivalent to BIS. These monitors are therefore recommended as options during any type of general anaesthesia in patients considered at higher risk of adverse outcomes. This includes patients at higher risk of unintended awareness and patients at higher risk of excessively deep anaesthesia. The E-Entropy and Narcotrend-Compact M monitors are also recommended as options in patients receiving total intravenous anaesthesia.
- 1.4. Anaesthetists using EEG-based depth of anaesthesia monitors should have appropriate training and experience with these monitors and understand the potential limitations of their use in clinical practice.

Patients who are considered at higher risk of unintended awareness during general anaesthesia include patients with high opiate or high alcohol use, patients with airway problems, and patients with previous experience of accidental awareness during surgery. The risk of unintended awareness is also raised by the use of concomitant muscle relaxants. Older patients, patients with comorbidities and those undergoing certain types of surgery are also considered at higher risk of unintended awareness. This is because they are at greater risk of haemodynamic instability during surgery. In these patients, lower levels of anaesthetic are often used to prevent adverse effects on the cardiovascular system and these levels can be inadequate.

Patients who are considered at higher risk of excessively deep levels of anaesthesia include older patients, patients with liver disease, patients with a high body mass index (BMI), and patients with poor cardiovascular function.

Patients receiving total intravenous anaesthesia are not considered at higher risk of adverse outcomes from general anaesthesia than patients receiving inhaled anaesthesia. The use of EEG-based depth of anaesthesia monitors has been recommended in patients receiving total intravenous anaesthesia because it is cost effective and because it is not possible to measure end-tidal anaesthetic concentration in this group.

Research recommendations

7.1. The Committee encourages further research as described in section 6.13 but has made no specific research recommendations. This is because, although there is uncertainty about many aspects of depth of anaesthesia monitoring (as described in section 6), the Committee considered that the current evidence base suggests depth of anaesthesia monitoring offers clinical benefits. Given the many complications in undertaking research in this area of anaesthesia, the Committee considered that the current uncertainty in the evidence base does not justify a potentially long delay in the uptake of what is likely to be a beneficial technology to the NHS and, particularly, to patients.

4. Rationale

No significant changes to the care pathway or the technologies have been identified since the publication of diagnostics guidance 6. Further, no evidence has been found through the updated literature searches that will materially impact the recommendations made in diagnostics guidance 6. It is therefore proposed that this guidance is placed on the static guidance list.

5. Implications for other guidance producing programmes

No overlaps have been identified.

6. New evidence

The search strategy from the original diagnostics assessment report was re-run in Medline, Medline in process, Cochrane Database, DARE, HTA database, CRD York, NHS Economic Evaluations Database, EMBASE, and EconLit. References from January 2011 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. To capture new evidence and information which has become available since diagnostics guidance 6 was issued, the searches of bibliographic databases was supplemented with searches focussing on systematic reviews, guidance and background information including company details.

Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked intended use for their technology. Specialist Committee Members for this guidance topic were also consulted and asked to submit any information regarding changes to the technology, the evidence base and clinical practice. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

Since the publication of NICE diagnostics guidance 6 in November 2012 there have been minor software changes in two of the technologies covered by the guidance and no changes to CE marking.

6.1.1. Bispectral Index (BIS) (Covidien)

There have been minor software updates to facilitate connectivity to electronic medical records, but no algorithm-related changes have been made since 2012 and no physical changes to the equipment.

6.1.2. E-Entropy module (GE Healthcare)

There have been no changes to E-Entropy since the guidance was published in November 2012.

6.1.3. Compact M (Narcotrend)

The algorithm used in the Narcotrend Compact M monitor has been extended to include 2 new parameters, Sharp Transient Intensity (STI) and Reduced Power Alpha Beta (RPAB). These parameters provide additional information on the patient's state. The algorithm also now includes special classification algorithms which detect and take into account the developmental state of the EEG in the first year of a person's life. This may allow use of the Narcotrend Compact M monitor in patients younger than 2 years old. A new patient lead with 4 electrodes (instead of 5 electrodes) for 2-channel recordings has also been developed. Narcotrend is equipped with artefact detection algorithms to exclude segments contaminated with artefact from further analysis. A new additional software version has been included in the Narcotrend Compact M monitor and is adapted to detect artefacts in the EEG in intensive care unit conditions that may be generated by the patient through eye movement or muscle activity, or by an external source such as mains or power line interference. This software is for use in intensive care units (ICU) ■

6.1.4 Costs

The table below details the acquisition cost for the depth of anaesthesia monitors quoted in the DAR and the acquisition cost quoted by the companies in 2015.

	Acquisition cost (excluding VAT)		Sensor cost, per patient (excluding VAT)	
	DAR (2012)	Manufacturers (2015)	DAR (2012)	Manufacturers (2015)
Bispectral Index (BIS)	4,687.50 ^a	3,640	17.75 ^b	13.54

E-entropy	5,352	5,352	8.68 ^c	7.2 ^d
Narcotrend-Compact M	8,572 – 11,998 ^e	11,000 ^f	0.56 ^g	█

^a average across manufacturer's price of £4,350 (BIS Vista) and £5,025 (BIS Vista bilateral)
^b average across manufacturer's price of £14.50 per patient (£362.50 for box of 25 sensors, 1 sensor per patient for Vista module) £21 per patient (£210 for box of 10 sensors, 1 sensor per patient for Vista bilateral module)
^c based on manufacturer's price of £217 for box of 25 sensors (1 sensor per patient)
^d based on manufacturer's price of £180 for box of 25 sensors (1 sensor per patient)
^e range of prices quoted, dependent on model
^f current estimated mean price (ex VAT) in the UK
^g based on manufacturer's price of £0.14 per sensor (3 required for 1-channel recording and 5 required for 2-channel recording)

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6.2. Additional technologies

No new technologies since the publication of guidance have been identified.

6.2.1. Devices licenced to use BIS

At the time of guidance production, there were 9 companies which had licenses to use the Bi-spectral Index (BIS) algorithm either built into their proprietary monitor or as an additional module. Because of consolidation in the market, 2 of these companies no longer exist. Mindray acquired Datascope and Dixtal Medical is now a subsidiary of Phillips. The remaining companies holding licences are: Draeger Medical, Germany; GE Healthcare, UK; Mennen Medical, Israel; Mindray, China; Nihon Kohden, Japan; Phillips Healthcare, Netherlands; and Spacelabs Health Care, USA. Some of these companies also produce patient monitoring systems that may include depth of anaesthesia monitoring.

6.2 Clinical practice

There has been no change in the diagnostic and care pathway since publication of diagnostics guidance 6.

The Royal College of Anaesthetists states that the obstetric patient undergoing rapid sequence induction for caesarean section has a higher risk of accidental awareness during general anaesthesia (Royal College of Anaesthetists 2015). This was a finding from the 5th National Audit Project (NAP5) (Pandit and Cook 2014). The audit also estimated incidence of patient reports of accidental awareness was around 1 in 19,000 anaesthetics, but with neuromuscular blockade there was a much high risk of

around 1 in 8000 compared with 1 in 136,000 without it. Two thirds of episodes occurred at induction of or emergence from anaesthesia.

The Association of Anaesthetists of Great Britain and Ireland (AAGBI) has published draft recommendations for standards of monitoring during anaesthesia and recovery, with publication of the final guidelines expected in the journal *Anaesthesia* in 2016. The AAGBI considered that the data from depth of anaesthesia monitors may provide an additional source of information on the patient's condition; however, it was also considered that the efficacy of depth of anaesthesia monitors in correctly predicting accidental awareness during general anaesthesia or correctly predicting an adequate level of anaesthesia, remains inconsistent and of debate. The following recommendations regarding depth of anaesthesia monitors were made:

- Depth of anaesthesia (DOA) monitoring is recommended when neuromuscular blockade is used in combination with total intravenous anaesthesia technique (TIVA).
- DOA monitoring should commence before induction and be continued until after full emergence from anaesthesia.
- Transfer of patients receiving TIVA and neuromuscular blockade presents difficulties in monitoring DOA, because portable battery powered DOA monitors are not widely available. Such devices may come to the market in the future and their efficacy evaluated.
- End-tidal anaesthetic vapour monitoring is an acceptable alternative to DOA monitoring when volatile anaesthetic drugs are used.
- The isolated forearm technique (IFT) is another technique to monitor DOA, although experience is very limited.

6.3 New studies

For evidence on the clinical effectiveness of the technologies, 14 studies are included in this report: 11 studies on BIS, 2 studies on E-Entropy, 1 study on Narcotrend. No relevant studies were identified relating to cost effectiveness and quality of life.

6.3.1. Bispectral Index (BIS) -Covidien

Time to extubation

Vance et al. (2014) conducted a randomised controlled trial (RCT) to determine whether BIS-guided anaesthesia (trigger for BIS>60) improves time to extubation compared to anaesthesia guided by minimum alveolar concentration (MAC) in patients (n=294) undergoing elective coronary bypass grafting, valve replacements,

and bypass plus valve replacements. Patients were randomly assigned to receive either BIS-guided anaesthesia alerts (n=131) or MAC-guided anaesthesia alerts (n=163). Valid data on extubation time were available for 247 (number of patients from each group unclear) of the 294 patients. Median time to extubation was 307 (interquartile range (IQR) 215 to 771) minutes in the BIS group and 323 (IQR 196 to 730) minutes in the MAC group (p=0.61). Median length of intensive care unit (ICU) stay was 54 (IQR 29 to 97) hours in the BIS group and 70 (IQR 44 to 99) hours in the control group (p=0.11). There was no difference between the groups in postoperative hospital length of stay, with a median time of 6 days (IQR 5 to 8) in each group (p=0.69). The authors concluded that, the use of intraoperative BIS monitoring during cardiac surgery did not change time to extubation, ICU length of stay or hospital length of stay.

Bresil et al. (2013) studied the effects of using BIS monitoring on time to extubation and on the quantity of anaesthetics. A total of 157 patients of different age groups undergoing elective ear, nose, and throat surgery were randomly allocated into either the BIS group (n=79) or the total intravenous anaesthesia group with propofol and remifentanyl according to conventional clinical practice (n=78). Children aged 1–3 years in the BIS group had a longer time to extubation compared with controls (p=0.04). In terms of amount of propofol administered, patients aged 12–17 years in the BIS group received higher maintenance infusion rates of propofol compared with controls (p=0.02). In terms of total amount of remifentanyl administered, no significant difference in the weight adjusted amount of remifentanyl administered is observed between the BIS and control groups of the different age groups. No significant difference for these outcome variables was evidenced in the other age groups. The authors concluded that BIS monitoring for guidance of propofol-remifentanyl anaesthesia did not result in reduced consumption of anaesthetics and did not reduce time to extubation in adult and children compared with conventional practice.

Villafranca et al. (2013) conducted a randomised controlled trial (RCT) to assess whether BIS-guided anaesthesia would result in earlier tracheal extubation compared with end-tidal anaesthetic concentration (ETAC)-guided anaesthesia in fast-track cardiac surgery patients. A total of 751 patients undergoing elective cardiac surgery involving cardiopulmonary bypass were randomly allocated to BIS group (n=374) and ETAC group (n=376). Time to tracheal extubation was not significantly different between the groups (odds ratio 1.04, 95% CI 0.88–1.23, p=0.643). There was no significant difference between the groups in either the number of patients who used the anaesthetic drugs or the dose of the anaesthetic drugs. The authors concluded that compared with management based on ETAC, anaesthetic management based on BIS guidance does not strongly increase the probability of earlier tracheal extubation in patients undergoing fast-track cardiac surgery. The decision to extubate the trachea is more influenced by patient characteristics and perioperative course than the assignment to BIS or ETAC monitoring.

Postoperative complications / side-effects

Whitlock et al. (2014) conducted a secondary analysis of a RCT to determine whether there was a difference in postoperative delirium between patients randomised to BIS-guided or end-tidal anaesthetic concentration (ETAC)-guided protocols. Of the 337 consecutive patients (18 years of age or older who were undergoing elective surgery) included in the RCT, 310 were considered for inclusion in the analysis. The postoperative delirium incidence in the BIS group was lower than that in the ETAC group (18.8% compared with 28.0%); however, the difference was not statistically significant (odds ratio 0.60, 95% CI 0.35-1.02, $p=0.058$). Low average volatile anaesthetic dose, intraoperative transfusion, ASA physical status, and EuroSCORE were found to be independent predictors of postoperative delirium. The authors concluded that randomisation to the BIS or ETAC-guided protocols did not decrease postoperative delirium in this patient population, but the results remain consistent with previous findings suggesting that BIS guidance decreases delirium after major surgery. The authors suggested a large randomised study was needed to confirm the results. The mechanism by which EEG guidance could decrease delirium requires elucidation. The average ETAC during anaesthetic maintenance, intraoperative units of packed red blood cells administered, EuroSCORE and ASA physical status were significant independent predictors of postoperative delirium in a cardiothoracic surgical population. Some of these factors may be modifiable, and they may be usefully incorporated into clinical screens to identify patients who are at increased risk of delirium after cardiac and thoracic surgery.

Chan et al. (2013) tested the effect of BIS monitoring on postoperative cognitive dysfunction (POCD) in patients aged 60 years or older, undergoing elective non-cardiac major surgery. A total of 921 patients were randomly assigned to either BIS-guided anaesthesia ($n=462$) or routine care anaesthesia ($n=459$). Patients, surgeons, and all research staff were blinded to the treatment identity. BIS-guided anaesthesia reduced propofol delivery by 21% and that for volatile anaesthetics by 30% when BIS was maintained between 40 and 60 during surgery. There were significantly fewer patients with delirium in the BIS group compared with routine care (15.6% compared with 24.1%, $p=0.01$). Cognitive performance was similar between groups at 1 week after surgery. Patients in the BIS group had a significant lower rate of POCD at 3 months compared with routine care (10.2% compared with 14.7%, $p=0.02$). The authors concluded that BIS-guided anaesthesia reduced anaesthetic exposure and decreased the risk of POCD at 3 months after surgery. For every 1000 elderly patients undergoing major surgery, anaesthetic delivery titrated to a range of BIS between 40 and 60 would prevent 23 patients from POCD and 83 patients from delirium.

Radtke et al. (2013) conducted a RCT to determine whether monitoring depth of anaesthesia influences the incidence of postoperative delirium. A total of 1277 patients aged 60 years or older who were planned for surgery in general anaesthesia

(expected to last at least 60 minutes) were randomly allocated to receive either BIS-guided anaesthesia (n=593) or anaesthesia where the BIS monitor value was concealed and only the signal quality indicator was visible (n=600). Of these patients, 575 from the BIS-guided group and 580 from the BIS-blinded group were included in analysis. Postoperative delirium occurred in 95 patients (16.7%, 95% CI 13.87–19.96%) in the BIS-guided group compared with 124 patients (21.4%, 95% CI 18.24–24.90%) in the control group (p=0.036). There was no significant difference between the two groups in anaesthetic drug usage. There was also no significant difference between the two groups in terms of postoperative length of stay, incidence of POCD on 7th postoperative day, incidence of POCD on 90th postoperative day, and incidence of death.

Fritz et al. (2013) conducted a subgroup analysis based on data from two previous RCTs to assess whether a BIS-based anaesthetic protocol was superior to an end-tidal anaesthetic concentration (ETAC)-based protocol in decreasing recovery time and postoperative complications. The population in the trials was adult patients at high risk of intraoperative awareness who underwent surgery with general anaesthesia using a potent volatile anaesthetic agent. The sub-group analysis included those who were observed in the post-anaesthesia care unit but were not subsequently admitted to the ICU (n=2958, including 1474 in the BIS group and 1484 in the ETAC group). The BIS cohort was not superior in time to readiness for post-anaesthesia care unit discharge (hazard ratio, 1.0; 95% CI 1.0–1.1), time to achieve an Aldrete score of 9–10 (hazard ratio, 1.2; 95% CI 1.0–1.4), ICU length of stay (hazard ratio, 1.0; 95% CI 0.9–1.1), incidence of postoperative nausea and vomiting (absolute risk reduction, –0.5%; 95% CI –5.8 to 4.8%), or incidence of severe postoperative pain (absolute risk reduction, 4.4%; 95% CI –2.3 to 11.1%). The authors concluded that, in patients at high risk of awareness, the BIS-guided protocol was not superior to an anaesthetic concentration-guided protocol in time needed for postoperative recovery or in the incidences of common postoperative complications.

Prevention of intraoperative awareness

Mashour et al. (2012) conducted a RCT to compare the efficacy of BIS monitor with anaesthetic concentrations on the prevention of intraoperative awareness with explicit recall in unselected surgical population. The study was terminated due to futility. A total of 21601 patients were enrolled in the study at the time of interim analysis, with a 97% recruitment rate. Of the study cohort, 18836 (87%) of the patients were available for post-operative interview assessing awareness at one month; 9460 patients were randomised to the BIS group and 9376 to the anaesthetic concentration group. At interim analysis the incidence of definite awareness was 0.12% (11/9376; 95% CI 0.07 to 0.21%) in the anaesthetic concentration group and 0.08% (8/9460; 95% CI 0.04 to 0.16%) in the BIS group (p=0.48). There was no significant difference between the two groups in terms of meeting criteria for

recovery room discharge or incidence of nausea and vomiting. The authors concluded that this negative trial could not detect a difference in the incidence of definite awareness or recovery variables between monitoring protocols based on either BIS values or anaesthetic concentration. By post hoc analysis, a protocol based on BIS monitoring reduced the incidence of definite or possible intraoperative awareness compared to routine care.

6.3.1.2 Bispectral Index (BIS) — Aspect Medical

Sargin et al. (2015) conducted a RCT to assess the effects of BIS on the haemodynamics and recovery profile in developmentally delayed paediatric patients undergoing dental surgery. Forty children having general anaesthesia maintained with 1-2 minimum alveolar concentration of sevoflurane in oxygen were randomised to either Group 1 (n=20) monitored by standard practice, or to Group 2 (n=20) monitored by BIS depth of anaesthesia monitor. Statistically significant reductions [difference in means (95% CI)] were observed in Group 2 when compared to Group 1 for: minutes to extubation (3.13 (1.66–4.60), $p < 0.001$); minutes to spontaneous ventilation (3.17 (1.79–4.54), $p < 0.001$); minutes to open eyes (3.97 (2.34–5.59), $p < 0.001$); post-anaesthesia care unit stay time in minutes (23.55 (18.08–29.01), $p < 0.001$); and for the Non-communicating Children's Pain Checklist score (0.60 (0.17–1.02), $p < 0.007$). The authors concluded that routine BIS monitoring may be beneficial for the recovery of developmentally delayed paediatric patients.

Kabukcu et al. (2014) investigated the effect of BIS monitoring on the amount of anaesthetic substance used, and the quality of anaesthesia in patients with persistent atrial fibrillation who would undergo cardioversion. The patients were randomised 1:1 to either Group 1 where the anaesthesia was performed following evaluation of the clinical condition and taking BIS values into consideration, or Group 2 where anaesthesia was based only on the clinical condition of the patient. BIS values were recorded for patients in Group 2, but the anaesthetists were kept blinded to these values. The differences between the groups were not statistically significant for all outcomes. The authors concluded that in the presence of an anaesthetist in the team, BIS monitoring does not contribute to determining of anaesthetic drug dosage and the depth and quality of anaesthesia in patients with persistent atrial fibrillation during cardioversion.

Shafiq et al. (2012) performed a quasi-randomised trial to evaluate the effect of BIS monitoring on isoflurane consumption during maintenance and recovery profile at the end of anaesthesia in an elderly Asian population. The primary outcome used for the power calculation was 'reduction in time to get orientation after discontinuation of the anaesthesia'. Statistically significant differences were observed for all outcomes, which include isoflurane use ($p = 0.001$), time to eye opening ($p = 0.0001$), time taken to extubate the patients ($p = 0.0001$), time taken by the patients to become ready for the shifting to recovery room ($p = 0.0001$), and post anaesthesia recovery score at arrival in recovery room ($p = 0.0001$). The authors of the study concluded that use of

BIS resulted in a 40% reduction of isoflurane use, reduction in time to open eyes and better recovery profiles in patients at the end of anaesthesia.

6.3.2. E-Entropy

A single-centre RCT (El Hor et al., 2013) recruited 55 patients (and reports data on 50) and assessed whether M-Entropy (previous name of E-Entropy) monitoring is associated with reduced sevoflurane uptake in patients undergoing major abdominal surgery. Patients with an American Society of Anaesthesiologists score of II–III, older than 18 years who were scheduled for elective laparoscopic rectosigmoidectomy (surgery for more than 2 hours) were eligible for inclusion. Surgical time was longer in M-Entropy monitoring group than standard care (161 min [134–193] vs. 135 min [109–157], $P = 0.03$). The authors considered shorter surgery times in the control group as a confounding factor with regard to the sevoflurane consumption and compared total sevoflurane uptake data between the two groups using the duration of surgery as a covariant. Sevoflurane uptake per hour was lower in M-Entropy monitoring group than standard care group. (5.2 ± 1.4 ml/h vs. 3.8 ± 1.5 ml/h, $P = 0.0012$).

Jiahai et al. (2012) study investigated whether the use of entropy monitoring (module not specified) reduces aesthetic dosage for patients undergoing during off-pump coronary artery bypass graft (OPCAB) surgery. This single site 2 arm RCT comprised 70 patients. In the first arm entropy values were visible to the anaesthetist (the entropy group) and in the second arm entropy values while collected were not available to the anaesthetist during surgery (the control group). In the first arm the anaesthetist titrated propofol infusion rate to maintain a State Entropy (SE) value of 45 to 55. Sufentanil infusion was adjusted so that the difference between Response Entropy (RE) and State Entropy would remain within 10 U. In the control arm propofol and sufentanil infusions were adjusted mainly based on the hemodynamic responses and clinical signs of deep or inadequate anaesthesia. Consumption of anaesthetics was lower in the entropy group (13.6 ± 3.5 propofol (mg/kg); 8 ± 3.2 sufentanil ($\mu\text{g/kg}$)) than the control (19.2 ± 4.2 propofol (mg/kg); 7.3 ± 2.4 sufentanil ($\mu\text{g/kg}$)) ($p < 0.05$).

6.3.3 Narcotrend-Compact M

Jiang et al. (2013) investigated the clinic effectiveness, safety and feasibility of using the Narcotrend monitor for evaluating depth of anaesthesia in infants with congenital heart disease (CHD) aged between 5 and 10 months undergoing cardiac surgery. This was a single-site RCT with two arms. In the first arm the depth of anaesthesia was monitored with the Narcotrend monitor ($n=40$). In the second arm the depth of anaesthesia was controlled according to experience (standard care) ($n=40$). Primary outcomes were total dose of sedative (Midazolam), analgesic (Fentanyl) and muscle relaxant (Vecuronium bromide), and time to extubation and recovery. The

Narcotrend arm compared to standard care arm required lower doses of sedative, analgesic and muscle relaxant ($p < 0.05$), and had shorter times to extubation and recovery. The authors of the study reported that the Narcotrend arm was more stable for mean arterial pressure and heart rate ($p < 0.05$). It also reported a significant difference ($p < 0.05$) for intra-operative awareness and breathings (values not provided).

7. Summary of new evidence and implications for review

Since the publication of diagnostics guidance 6, no significant changes have occurred to the depth of anaesthesia monitors included in the guidance. A number of additional devices have been licensed to use BIS.

There has been no change in the diagnostic and care pathways since publication of diagnostics guidance 6. The 5th National Audit Project (NAP5) of The Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland estimated incidence of patient reports of accidental awareness was around 1 in 19,000 anaesthetics, but with neuromuscular blockade there was a higher risk of around 1 in 8000 compared with 1 in 136,000 without it. Two thirds of episodes occurred at induction of, or emergence from anaesthesia.

The Association of Anaesthetists of Great Britain and Ireland (AAGBI) has published draft recommendations for standards of monitoring during anaesthesia and recovery, including depth of anaesthesia monitoring (final recommendations due to be published in 2016) (Association of Anaesthetists of Great Britain & Ireland 2016). However, it was also considered that the efficacy of depth of anaesthesia monitors in correctly predicting accidental awareness during general anaesthesia or correctly predicting an adequate level of anaesthesia, remains inconsistent and of debate.

The majority of new studies looked at the Bispectral Index (BIS) - Covidien. Three studies [Vance et al. (2014), Bresil et al. (2013) and Villafranca et al. (2013)] looked at time to extubation using BIS. None of the studies reported differences between time to extubation between patients monitored by BIS and patients in the control groups. Four studies looked at post-operative side effects using BIS. There was some evidence that monitoring with BIS reduced volume of anaesthetic used and post-operative delirium and reduced volume of anaesthetic used [Chan et al. (2013), Radtke et al. (2013)]; however, other studies showed no significant difference [Whitlock et al. (2014), Fritz et al. (2013)]. Mashour et al. (2012) could not detect a difference in the incidence of definite awareness or recovery variables between monitoring protocols based on either BIS values or anaesthetic concentration; however, post hoc analysis, a protocol based on BIS monitoring reduced the incidence of definite or possible intraoperative awareness compared to routine care.

Three studies used Bispectral Index (BIS) – Aspect Medical. Sargin et al. (2015) showed a significant improvement in recovery time for developmentally delayed

children undergoing dental surgery when their anaesthesia was monitored by BIS. Kabukcu et al. (2014) showed that BIS monitoring did not make any statistical difference to drug dosage and depth and quality of anaesthesia in patients with persistent atrial fibrillation during cardioversion. Shafiq et al. (2012) showed a 40% reduction in anaesthetic used, a reduction in time to opening of eyes and an improvement in recovery profiles in Asian patients using BIS monitoring.

Two studies were identified that used Entropy monitoring. El Hor et al. (2013) showed lower anaesthetic consumption per hour in patients monitored using E-Entropy. Jiahai et al. (2012) showed a reduction in anaesthetic use in patients monitored using Entropy_monitoring.

Jiang et al. (2013) showed that lower doses of sedative, analgesic and muscle relaxant, and shorter extubation and recovery in infants undergoing cardiac surgery using Narcotrend-Compact M monitoring.

In conclusion, the evidence base and clinical environment has not changed to an extent that is likely to have a material effect on the adoption recommendations in the existing guidance; it is therefore suggested that the guidance is transferred to the static list.

8. Implementation

No new implementation information has been identified.

9. Equality issues

No new equality issues have been identified since the publication of the guidance.

GE paper sign off: Carla Deakin, 2 February 2016

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Appendix 1 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

Options	Consequence	Selected – ‘Yes/No’
Standard update of the guidance	A standard update of the Diagnostics Guidance will be planned into NICE’s work programme.	No
Accelerated update of the guidance	An accelerated update of the Diagnostics Guidance will be planned into NICE’s work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:

Options	Consequences	Selected – ‘Yes/No’
Transfer the guidance to the ‘static guidance list’	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.	Yes
Produce a technical supplement	A technical supplement describing newer versions of the technologies is planned into NICE’s work programme.	No
Defer the decision to review the guidance to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Diagnostics Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

[Caesarean section](#) (2011) NICE guideline 132

[Sedation in under 19s: using sedation for diagnostic and therapeutic procedures](#) (2010) NICE guideline 112

In progress

[Post-traumatic stress disorder \(PTSD\)](#) (2005) NICE guideline 26. It was decided that this guideline should be updated in June 2015.

[The safe use and management of controlled drugs.](#) NICE guideline. Publication expected March 2016

Registered and unpublished trials

Trial name and registration number	Details
UMIN000012145 A comparison of bispectral index and entropy during sevoflurane anesthesia induction, in normal children and children with cerebral palsy	Observational Complete 4th April 2014. Results not yet published.
NCT02240368 Performance Evaluation of the Depth of Anesthesia Monitors in Pediatric Surgery	Prospective cohort Completed November 2014. Results not yet published.
NCT02174913 Awakening in Spine Surgery: A Comparison Between Clinical Signs and Bispectral Index	Randomised, double-blinded, parallel assignment December 2015
NCT02382445 Anesthesia Depth Increases the Degree of Postoperative Dementia, Delirium, and Cognitive Dysfunction (BIS & Dementia)	Randomised, double-blinded, parallel assignment December 2015
NCT02586441 Evaluation of EEG With Respect to the Change of Depth of Anesthesia During General Anesthesia	Open-label single group assignment November 2017

Trial name and registration number	Details
CTRI/2015/05/005809 Bispectral index guided harmonisation of anaesthesia induction and tracheal intubation procedures: a randomised control study	Randomised, parallel group trial Unclear

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