It is often said that every good study starts with a good question. The question and hypothesis then determine the methods, which determine the results on which the conclusions are based. It seems simple, but when it comes to research about anaesthesia, defining the research question can often be tricky, particularly when it comes to the issue of accidental awareness during general anaesthesia (AAGA). In 1991, Christof Koch, an eminent neuroscientist, wrote that he believed consciousness to be a ‘prescientific concept’ and ‘to evaluate the anesthetic monitoring of consciousness, we must first agree about which defined phenomena are to be regarded as evidence for consciousness during the operation’. This sage observation, which is as applicable today as it was in 1991, is not only relevant to monitoring of consciousness during anaesthesia, but also to post hoc evaluation of possible cases of unintended return of consciousness and awareness during anaesthesia.

In the absence of agreed definitions on the phenomena regarded as evidence for unintended return of consciousness during surgery, and also the absence of any method of differentiating consciousness and unconsciousness with 100% sensitivity and specificity, researchers have so far tended to focus on recall of intraoperative events as evidence of intraoperative events. In this issue of the British Journal of Anaesthesia (and jointly in Anaesthesia), Pandit and colleagues report and discuss the methodology used in the 5th National Audit Project (NAP5) on AAGA, along with some of the results pertinent to this methodology. It is clear that a huge, multi-disciplinary collaborative effort was required to develop and implement this methodology. The level of coordination of the efforts of a large team, and the 100% response rates of local coordinators are impressive. Admirable too is the application of standard tools and techniques in the analysis and classification of reports of AAGA.

How should we evaluate the choice of methodology, and eventually also the results of the study (the latter are published in a separate article)? An important first step is to return to the research question, and to evaluate whether the methods are appropriate to the question, and more importantly, to establish whether the question is appropriate for the problem being addressed.

The NAP5 research question is not explicitly stated in the methodology article, but clearly, an estimate of the incidence of AAGA was an important subsection. Working backwards from the described methods, we assume that in this regard the research question underlying the NAP5 study was: ‘During the space of 1 year, how many patients spontaneously inform a hospital healthcare worker or other person that at some point in their life they have experienced AAGA?’ For this question, the methodology of the NAP5 study is well chosen and appropriate. It is probably safe to say that in almost all cases where a patient complained of awareness, this led to appropriate action which also resulted in the filing of a report onto the NAP5 website. As mentioned too, the methodology for filtering and further processing of filed reports appears structured, highly professional, and transparent.

How appropriate is this research question for the problem being addressed? For patients undergoing anaesthesia for surgery, our intention, and also our informal ‘contract’ with them, is that they will be unconscious and thus unaware of events occurring during surgery. In its broadest sense then, the problem we need to address is the problem of accidental awareness during general anaesthesia.
return of consciousness during intended general anaesthesia, but we agree with other authors that intraoperative awareness is a ‘spectrum of brain states’ with a spectrum of consequences.1–6

Patients who complain spontaneously represent one subset of a portion of this spectrum—that is, those patients who experienced an episode of awareness that they were later able to remember and chose to report. For a study of the incidence of other anaesthetic complications, such as pain or nausea and vomiting, it would be inconceivable to only focus on the patients who complained spontaneously during the perioperative period. We thus need to ask ourselves some important questions. First, of all cases of AAGA that occurred in the UK and Ireland during the study period, what proportion could the NAP5 methodology have detected? Secondly, is it sufficient to only focus on these cases?

Figure 1 comprises a Venn diagram illustrating qualitatively four possible contingencies with regard to anaesthesia: no awareness, AAGA, AAGA with subsequent recall, and AAGA with recall followed by a spontaneous complaint. Given the strong amnestic effects of subhypnotic doses of most hypnotic agents used for anaesthesia, it is evident that absence of recall is certainly not evidence of absence of intraoperative return of consciousness. Studies using the isolated forearm technique (IFT) suggest that ~42% of patients undergoing general anaesthesia with muscle relaxation will respond to command (IFT) suggest that ~42% of patients undergoing general anaesthesia with muscle relaxation will respond to command on one or more occasions during surgery.6 The majority of patients who respond to these commands have no subsequent explicit recall of intraoperative events. As there remains no consensus on the phenomena regarded as evidence for consciousness, or unconsciousness, the significance of this state of responsiveness not associated with subsequent recall is uncertain and is still being debated.6–9

Anaesthetists seldom observe responses to command in anaesthetized but non-paralysed patients. This leads us to wonder whether the ischaemic arm pain caused by the IFT, but in an area remote from the operative site, is sufficient to cause a degree of arousal that will maintain responsiveness to commands but without causing the patient undue distress (since he will have been pre-warned about this pain) and without leading to a return of memory function. This is especially likely considering the low anaesthetic doses administered in some of these studies.10–13 Another possibility is that the neuromuscular blocking agents, or muscle relaxation itself, may alter activity in neuronal pathways in a way that results in a greater likelihood of ‘connected consciousness’ without spontaneous responsiveness, than in non-paralysed patients.

Taking into account the fact that most paralysed patients are not subjected to the IFT and that many patients are not paralysed at all during surgery, it is probably safe to assume that the overall incidence of AAGA is significantly <42%, but appreciably greater than the incidence of AAGA with recall. At present, there is no evidence that AAGA without explicit recall—shown as the grey zone in Figure 1—leads to subsequent psychological sequelae. Thus, although we may have failed in our intention to obliterate consciousness during surgery, it has recently been argued that this occurrence (represented by the grey area in Fig. 1) may be acceptable if not associated with distress, awareness of pain, or later recall.9 14

When put in a historical context, this suggestion is not as radical as it might seem. During Morton’s demonstration of ether administration for a surgical procedure in 1846, the patient, Gilbert Abbott, was ‘aware that the operation was proceeding’. Despite this, the demonstration was deemed to be successful. Oliver Wendell Holmes later wrote to Morton to suggest the term ‘anaesthesia’, derived from Greek, emphasizing the fact that the state thus described was associated with the absence of sensation of touch. Anaesthesia was proclaimed as a great advance as it was deemed to provide ‘Surgery without pain’. The emphasis on surgery without awareness only came later.

There are currently few circumstances in which one might regard awareness with subsequent explicit recall as acceptable, and thus it is important to consider what proportion of these patients the NAP5 methodology might (not) have detected. For a patient to have spontaneously reported a memory of awareness, several critical factors would have been required. The memory trace should have been present and accessible at the time of an interaction with an intermediary who might have reported it (a healthcare professional, relative), the patient would have had to have evaluated the validity and significance of the memory, and weighed up (albeit subconsciously) the many factors that might influence whether he/she would wish to discuss his memory with specific individuals and then finally do so. The latter requirement for several executive processes to occur and culminate in a decision to report a memory, spontaneously, or in response to a question is the reason why memory is sometimes described as a ‘behaviour’. There are thus many reasons why patients who experienced AAGA during the NAP5 study period may
not have spontaneously reported this to healthcare professionals during the perioperative period (some of these were discussed in an editorial accompanying NAP5 pilot data, and will only be briefly discussed here).\textsuperscript{15}

The first is the fact that the investigators relied on spontaneous reports of awareness, whereas it has been shown that routine postoperative interviews without structured questions will only detect \~{}20\% of cases of awareness with recall.\textsuperscript{16} Secondly, the time window in which patients might have had opportunities to report experiences of awareness to hospital staff was too short. From studies in which patients are prospectively repeatedly questioned over the space of several weeks, it appears that in many cases, patients only report a memory of awareness after a few weeks. In the case of the landmark Swedish study of awareness, of 18 cases of awareness (judged by a committee to be ‘definite’), only 11 would have been detected if there had only been a structured interview in the post-anaesthesia care unit; and of the 18 cases, five were detected for the first time at the final structured interview (7–14 days after surgery).\textsuperscript{17} Experts thus advise that structured interviews should be performed 1–4 weeks after surgery.\textsuperscript{17, 18, 19} The low incidence of AAGA (1:15 000) detected by the large prospective study performed by Pollard and colleagues\textsuperscript{20} was likely due to the fact that structured interviews were performed no later than 1–2 days after surgery, whereas another recent large study using repeated structured interviews showed an incidence of 1:1000 (19 cases of definite awareness among 18 836 unselected surgical patients).\textsuperscript{21}

In a survey of NHS activity during 2012–3, orthopaedic, general surgery, and gynaecological procedures formed the majority of surgical procedures [http://www.hscic.gov.uk/ (accessed 8 August 2014)]. For these procedures, the median lengths of stay were 3, 2, and 1 day(s), respectively. Thus, the majority of patients admitted during the NAP5 study would have been discharged home, and out of sight and contact with healthcare workers, before the key window of 1–4 weeks. Therefore, based on the experiences of Sandin and others,\textsuperscript{17, 19} at least 30\% of patients with AAGA would have been discharged home before their awareness memory was accessible to consciousness. Of the remaining 70\% of patients with AAGA, \~{}20\% would have been detected if no more than a routine postoperative visit, not containing a structured awareness questionnaire, had been performed. Clearly, patients with AAGA would have had other opportunities to report memories of AAGA during their admission, and great care was taken to maximize the chances any such reports would lead to an NAP5 report. Still, of the 70\% of cases of AAGA where the memory was already present during discharge, probably somewhere between 0\% and 80\% would have been missed, meaning that the NAP5 methodology could only hope to detect of the order of 14–70\% of AAGA cases.

Should we be concerned about the patients who experienced AAGA with recall but who could not or might not have been detected by the NAP5 methodology? At present, the answer to this question is uncertain. The literature on the psychological consequences of awareness show conflicting results, with a range of reported incidences of severe consequences such as post-traumatic stress disorder.\textsuperscript{22–26} As always some of these differences may be attributable to differences in definition and in methodology.\textsuperscript{27} Nonetheless, most investigators would agree that patients who experienced marked distress have a high risk of significant psychological sequelae, particularly when the patient suffered pain, was unable to move because neuromuscular blocking agents had been administered, or both.

Inherent in the NAP5 methodology is the assumption that those who are distressed by an experience of AAGA will report it to an intermediary, either during or after their hospital admission. This is a critical assumption that may not be correct. In one study, 26 patients were interviewed in depth after having been identified as possible victims of awareness during a preoperative interview for a subsequent anaesthetic.\textsuperscript{22} Although almost all remembered being anxious or distressed during the episode, only 18 (70\%) reported their experience during their postoperative hospital stay, of whom only nine reported their experience to the anaesthetist responsible for their care during the episode. At present, any statements on the frequency of this scenario (postoperative distress as a result of AAGA, but failure to report the fact), and on the likely reasons, are speculative, but may include factors such as the patient being ignorant or uncertain of the significance of their memory, or fear of being disbelieved.

In summary then, NAP5 was designed to detect historical and new cases of AAGA associated with a spontaneous complaint or report to a healthcare worker (the blue centre of Fig. 1) during a perioperative episode. In essence, the methodology reported is appropriate for this goal. Our concerns mostly lie with the underlying research question. With regard to the historical cases, we can draw few conclusions about incidence and significance; and with regard to new cases of AAGA occurring during the study period, we should bear in mind that the NAP5 methodology\textsuperscript{1} is only likely to show us the ‘tip of the iceberg’. At present, with current knowledge, we cannot yet ignore the invisible part of the ‘iceberg’ which is likely to include a significant number of cases of AAGA with recall (represented by the green zone in Fig. 1), a proportion of which may result in severe psychological consequences. To determine how often this occurs, and what the cost might be for society and for the victims, other studies, with different methodology, are required.

**Declaration of interest**

A.R.A. is an editor and editorial board member of the *British Journal of Anaesthesia*.

**References**

During the 12-month catchment period, and the numerator 2,766,600 general anaesthetics administered in the UK in the UK to be 1:19,600. The denominator is the estimated 14 Pandit JJ. Acceptably aware during general anaesthesia: ‘dysanaesthesia’. Anesthesiology 2014; 69: 801–7
7 Russell IF. Fourteen fallacies about the isolated forearm technique, and its place in modern anaesthesia. Anesthesiology 2013; 68: 677–81
8 Sleigh J. The place of the isolated forearm technique in modern anaesthesia: yet to be defined. Anesthesiology 2013; 68: 995–1000
12 Russell IF. The ability of bispectral index to detect intra-operative wakefulness during total intravenous anaesthesia compared with the isolated forearm technique. Anesthesiology 2013; 68: 502–11
14 Pandit JJ. Acceptably aware during general anaesthesia: ‘dysanaesthesia’—the uncoupling of perception from sensory inputs. Conscious Cogn 2014; 27C: 194–212
15 Avidan MS, Mashour GA. The incidence of intraoperative awareness in the UK: under the rate or under the radar? Br J Anaesth 2013; 110: 494–7
25 Samuelsson P, Bruin L, Sandin RH. Late psychological symptoms after awareness among consecutively included surgical patients. Anesthesiology 2007; 106: 26–32

**NAP5: intraoperative awareness detected, and undetected**

K. O. Pryor* and H. C. Hemmings Jr
Department of Anaesthesiology, Weill Cornell Medical College, 1300 York Avenue, New York, NY 10065, USA
* Corresponding author. E-mail: kap9009@med.cornell.edu

In the main findings from the 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia (AAGA), presented in this issue of the *British Journal of Anaesthesia*, Pandit and colleagues report the overall incidence of AAGA in the UK to be 1:19,600. The denominator is the estimated 2,766,600 general anaesthetics administered in the UK during the 12-month catchment period, and the numerator the 141 patient self-reports of AAGA adjudicated to be certain, probable, or possible. Other estimates of incidence are provided, reflecting more stringent or relaxed definitions and evidentiary criteria for AAGA—but it is the value of 1:19,600 that the authors most emphasize, and that is likely to be the headline result as NAP5 is quoted in both the medical and non-medical press.