

Protocol and methods of NAP5



Jaideep J Pandit



Tim M Cook

HEADLINE

5.1 NAP5 employed a novel methodology to approach the problem of AAGA: a nationwide network of local coordinators across all the UK National Health Service hospitals (and separately in Ireland) reported all new patient reports of AAGA to a central database using a system of monthly anonymised reporting over a calendar year. The database collected the details of the reported event, anaesthetic and surgical technique and any sequelae. These reports were categorised into mutually exclusive groups by a multidisciplinary panel, using a formalised process of analysis. The main categories were those reports judged Certain/probable (Class A), Possible (B), Sedation (C), ICU (D), Unassessable (E), Unlikely (F), Drug Errors (G) and Statement Only (SO). The degree of evidence to support the categorisation was also defined for each report. Patient experience and sequelae were categorised using current tools or modifications of such. This methodology is compared with previous methods used to address the problem of AAGA, and its potential strengths and limitations discussed. The NAP5 methodology should form an important means to assess new reports of AAGA in a standardised manner, especially for the development on an ongoing database of case reporting.

BACKGROUND

- 5.2 Several studies into AAGA use the methodology of a Brice questionnaire (Brice et al., 1970) and consistently establish an incidence for AAGA of 1–2:1,000 (e.g. Avidan et al., 2008 & 2011). It is also suggested that there is a potentially severe impact, with high rates of post-traumatic stress disorder (PTSD) reported (Bruchas et al., 2011).
- 5.3 However, it is apparent that the methodology used to study AAGA influences the results that can be obtained. For example, a method that uses Brice questioning of patients, but administered twice over a 48-hour period (as in a study by Pollard et al. as part of a quality improvement program) yields a much lower incidence of 1:14,500 (Pollard et al., 2007). Mashour et al. (2013) reported that different methodologies can yield different incidences for AAGA.
- 5.4 There are, overall, several methodologies employed in studying the problem of AAGA or, the differences in large part related to the specific research question being addressed. Amongst these are: case series, randomised or non-randomised controlled trials, and data registries.
- 5.5 An example of a *case series* is the paper of Blussé van Oud-Alblas et al. (2009) who questioned 928 consecutive paediatric patients for AAGA using a Brice questionnaire repeated three times over a month. Their aim was to ascertain an incidence and look for common patterns that may emerge in the elicited reports. Other types of case series examine only the patients reporting AAGA, to focus on common themes or on the psychological impact (Moerman et al., 1993; Samuelsson et al., 2007).

- 5.6 *Non-randomised* studies usually seek to establish the incidence of AAGA or ascertain influential factors. For example, Sebel et al., (2004) reports on a prospective cohort study in just under 20,000 patients that sought to establish an incidence (using Brice interview repeated twice over a week) and used multivariate logistic regression to identify possible contributory factors.
- 5.7 *Randomised* study designs usually seek to assess the impact of an intervention (such as preventative treatment or monitoring) to reduce incidence of AAGA (Avidan et al., 2009). For example the impact of BIS monitoring was examined by the B-Aware trial of Myles et al. (2004). An example of a randomised study examining the impact of a prophylactic treatment is that of Wang et al. (2013).
- 5.8 *Data registries* are, at the simplest level, a collection of case details stored and then analysed by later interrogation (Klein et al., 2014). Small scale registries may be assembled by referral from colleagues (Moerman et al., 1993) or advertisement (Schwender et al., 1998). The ASA Awareness Registry (<http://depts.washington.edu/asaccp/projects/anesthesia-awareness-registry>) was hitherto probably the largest database. Started in October 2007, it is a system of direct access, self-registration by patients. To date, in seven years, it has collected ~278 subjects (~40 per year), about one-third of whom in fact received sedation and not general anaesthesia (Kent et al., 2013). By definition, this methodology is self-selected (or colleague-selected) and so subject to biases.
- 5.9 Mapped against these previous methodologies, that of NAP5 seems unique.

METHODS

- 5.10 The methodology of NAP5 is similar to, and builds upon, that used for NAP3 and NAP4 (Cook et al., 2009 & 2011a and b).
- 5.11 The NAP5 project was approved by the National Information Governance Board (NIGB) in England and Wales, and Patient Advisory Groups in Scotland and Northern Ireland. The National Research Ethics Service (NRES) confirmed it to be a service evaluation and waived the requirement for formal ethical approval. The project has the endorsement of all four Chief Medical Officers of the UK. In March 2013, NIGB was abolished and its functions taken over by the Confidentiality Advisory Committee of the NHS Health Research Authority (HRA). This deals with approvals for the handling of patient-identifiable information across the NHS.
- If such information is required, then approvals are required under Section 251 of its governance procedures. NAP5 re-submitted the relevant information to the HRA and the latter confirmed that, since no patient-identifiable information was used, no section 251 application was necessary.
- 5.12 Each of 329 UK hospital centres volunteered a Local Co-ordinator (LC), a consultant anaesthetist who provided the main link between the central NAP5 team and their hospital. Because some LCs covered more than one hospital as part of an NHS Trust (or Board in Scotland) there were 269 LCs.
- 5.13 In parallel, in Ireland 41 Local Co-ordinators volunteered to provide the link between the NAP5 team and all the 46 public hospitals. The NAP5 project in Ireland has received approval from the Department of Health and was endorsed by the Health Service Executive (HSE) National Quality and Patient Safety Directorate. The requirement for ethical approval in Ireland was waived.
- 5.14 There were three phases to NAP5:
- A Baseline Survey conducted in early 2012 and relating to the calendar year 2011, to ascertain anaesthetist knowledge of reports of AAGA, and certain baseline data related to anaesthetic practice (monitoring) and staffing.
 - The core project which ran from 1 June 2012 to 31 May 2013.
 - An Activity Survey to provide denominator data for the key findings of interest, conducted between 26 November and 3 December 2012 in Ireland and 9 and 16 Sept 2013 in the UK.
- 5.15 The UK and Irish Baseline Surveys have been published in full (Pandit et al., 2013a and b). The UK and Irish Activity Surveys are also published (Jonker et al., 2014a and b).
- 5.16 LCs were provided with detailed information which can be viewed at www.nationalauditprojects.org.uk/NAP5_home. In brief, they were asked to develop local multidisciplinary networks across their centres, encompassing all surgical and medical specialties, nursing and paramedical services, and psychiatric and psychology units. On a monthly basis each LC was required to provide the central NAP5 team with a 'return' indicating the number of reports of AAGA received that month. Where no reports were received the LCs returned a 'nil' report; this was based on the UK obstetric surveillance system (Knight, 2007).
- 5.17 Information about the project was also disseminated at intervals to their members by the Royal College of General Practitioners, the Royal

College of Psychiatrists and national societies of psychological practitioners. Publications in general medical journals also helped highlight the project to professionals (Pandit & Cook, 2013).

- 5.18 Initially, no public announcement or media exposure was actively sought, in case this altered the normal manner in which patients made reports of AAGA. However, publication of the Baseline papers in April 2013 was accompanied by widespread media attention (see www.bbc.co.uk/news/health-21742306 and www.dailymail.co.uk/news/article-2292532/Study-reveals-153-patients-wake-anaesthesia.html as examples).
- 5.19 Any person wishing to file a report of AAGA on behalf of themselves or another person could do so, or could contact an LC using an online list. Equally, LCs could contact each other to exchange information securely (e.g. if a patient presented to one hospital having had an experience of AAGA at another). The architecture of the secure website (see <http://nap5.org/>) meant that the NAP5 Panel had no knowledge of these exchanges, or who was filing the report.
- 5.20 In order to file a report of AAGA, the LC (or other person) needed login details to the secure site provided by the administrative arm of the NAP5 central team. A short set of screening questions was used to filter inadmissible reports, and later on review, some reports that had been filed were deemed inadmissible. To be reportable, a report of AAGA had to:
- Be a situation where the patient (or their representative or carer) made a statement that they had been *aware for a period of time when they expected to be unconscious*. Thus, a complaint of 'pain' or 'anxiety' alone was inadmissible, as was a desire to have been less conscious (as opposed to unconscious) during a procedure.
 - Be a *first report* of AAGA made to the healthcare system.
 - Be a first report made between 00.00hrs on 1 June 2012 and 23.59.59hrs on 31 May 2013; regardless of when the actual event occurred. Thus an operation that led to AAGA many years ago, but was not reported until, say, October 2012 was potentially admissible. A report made on 1 June 2013 about an operation that occurred on 31 May 2013 was, however, inadmissible.
 - Be a report that related to a specific surgical or medical intervention in which anaesthesia care was provided. 'Anaesthesia care' is interpreted in the broadest sense, ranging from monitored anaesthesia care (i.e. where the anaesthetist is on standby for purposes of resuscitation) through sedation to general anaesthesia, given by any type of practitioner.
- (e) Relate to care undertaken in a public hospital.
- We therefore aimed to capture all new patient reports of AAGA irrespective of whether the patient's perception of the event was accurate.
- 5.21 For cases deemed to meet inclusion criteria, login details and a password were issued. The reporter was required to change this password on first accessing the website. Once access information was released to an individual, the NAP5 team had no access to information during report submission but merely received notification of when the website was first accessed and when the form was completed, to enable progress to be monitored. The website was secure and encrypted.
- 5.22 Where there was uncertainty as to whether a case met the inclusion criteria, the reporter was directed to discuss this with the NAP5 Moderator, Dr David Smith, a consultant anaesthetist with expertise in the topic and clear knowledge of the inclusion criteria. The NAP5 moderator was entirely independent of the NAP5 project team and had no contact with the review Panel throughout the project.
- 5.23 The secure reporting site asked for details of the case and the conduct of anaesthesia, so LCs were advised to file the report after reviewing the case notes. No patient identifiable data was requested and prompts on the secure site ensured that all potentially identifiable data were removed. Once completed and closed, the website forwarded the report electronically to the NAP5 Clinical Lead. A demonstration of all the questions asked can be viewed as a demonstration at <http://nap5.org/>. To further guarantee anonymity the NAP5 Clinical Lead had no link indicating who had originally filed the report, and no method of determining this.
- 5.24 On a monthly basis, the NAP5 Panel met for a full day to review and discuss all submitted reports. The Panel had access to several types of information in performing the review: first, the full patient report on the secure website. Second, a case summary prepared by the NAP5 Clinical Lead. The Panel used these to review cases in a structured manner (see below). The Panel also created a standardised output form to help provide a summary of categorisation, and spreadsheet output combining

data from all submitted reports for quantitative analysis of the dataset (e.g. age range, weight, agents used, etc).

- 5.25 Each report was first reviewed by a minimum of four Panel members. These first review groups populated the structured review output form. Definitions of all classifications were available to all Panel members at each meeting. Several small groups reviewed simultaneously in this way. The report then underwent second review by a larger group formed of the combined small groups, typically 12-16 members. Each report and its output were presented and this was further reviewed and moderated. At each meeting some reports were intentionally reviewed by pairs of small groups before large group review as a form of 'internal control'.
- 5.26 In performing reviews the Panel was repeatedly cautioned about 'outcome bias' (where knowledge of the poor outcome can lead to a retrospective harsh judgement) (Caplan et al., 1991); 'hindsight bias' (an exaggerated belief that a poor outcome would have been predicted) (Henriksen et al., 2003); and 'groupthink' (where groups make irrational decisions given a subconscious desire to agree with

Small group review by a minimum of four reviewers was the first phase of review



others) (Turner & Pratkanis, 1998). The two stage review process was specifically designed to address the latter bias.

- 5.27 Reports were classified by *type of report* (Table 5.1) and separately classified by *degree of evidence* (Table 5.2). Reports were given only one classification of type and evidence (i.e. all were mutually exclusive).

Table 5.1. Classification into types of report

Class A: Certain/probable AAGA. A report of AAGA in a 'surgical setting' in which the detail of the patient story was judged consistent with AAGA, especially where supported by case notes or where report detail was verified independently.

Class B: Possible AAGA. A report of AAGA in a 'surgical setting' in which details were judged to be consistent with AAGA or the circumstances might have reasonably led to AAGA, but where otherwise the report lacked a degree of verifiability or detail. Where the panel was uncertain whether a report described AAGA, the case was more likely to be classified as Possible rather than excluded.

(For the purpose of the final numerical analysis, it was decided to group Certain/probable and Possible cases together; numerical analysis showed this did not change the overall conclusions of the report).

Class C: Sedation. A report of AAGA where the intended level of consciousness was sedation.

Class D: ICU: A report of AAGA from a patient in, or under the care of an intensive care unit, who underwent a specific procedure during which general anaesthesia was intended.

Class E: Unassessable. A report, where there was simply too little detail submitted to make any classification possible.

Class F: Unlikely. Details of the patient story were deemed unlikely, or judged to have occurred outside of the period of anaesthesia or sedation.

Class G: Drug error and miscellaneous. This was originally used as a miscellaneous category to be reviewed at the end of the data collection period. In fact, this class rapidly filled with syringe swaps and drug errors, with only three remaining other cases.

Statement Only. A patient statement describing AAGA, but for which there were no case notes available to verify, refute or examine that claim further. This was often because the case was historical.

Table 5.2 Classification by degree of evidence

Evidence A: high. Where the report was (or could easily be) confirmed – or refuted – by other evidence.

Evidence B: circumstantial. Where the report was supported only by clinical suspicion or circumstance. For example, poor record keeping or chaotic, rapidly changing clinical scenarios may have led the Panel to conclude that there were circumstances that could have led to AAGA.

Evidence C: plausible. Where other evidence (e.g. case notes) were available, but this did not shed further light on the matter.

Evidence D: unconfirmed/unconfirmable. This was generally applied to the Statement Only cases where there was no evidence other than the patient report.

Evidence E: implausible. This was generally applied to Statement Only reports where there was no evidence other than the patient story and where this was judged implausible.

- 5.28 The *phase of anaesthesia/surgery* when the AAGA event occurred was recorded:
- (d) **Pre-induction** (drug errors occurring before intended anaesthesia).
 - (b) **Induction** at or after induction, before surgery.
 - (c) **Maintenance** during surgery.
 - (d) **Emergence** after surgery was complete but before full emergence.
 - (e) **Other** (uncertain time).
- 5.29 Induction was defined as from the start of induction of anaesthesia; maintenance from the start of incision or procedure, and emergence from when the last dressing, intervention or examination took place. Emergence reports extended to any time after the end of surgery, where the patient reported they were awake when they felt they should have been unconscious. Emergence therefore included cases where drug errors or failure to reverse neuromuscular blockade caused paralysis (and hence perceptions of AAGA) in the recovery period.
- 5.30 We classified *causality (contributory factors)* and *preventability*. Table 5.3 indicates the categories of causal/contributory factors considered. This is based on the NPSA contributory factors framework (at: www.nrls.npsa.nhs.uk/resources/?entryid45=75605).

Table 5.3. Contributory, causal or mitigating factors considered

Factors
Communication
Education and Training
Equipment/ resource factors
Medication
Organisation and strategic
Patient
Task
Team and social
Work and environment
Other
Unknown

- 5.31 We judged quality of care (i) leading up the reported event, and (ii) after the reported event. This was classified as ‘good’, ‘poor’, ‘good and poor’ or ‘unassessable’ based on consensus of the Panel, where possible making the judgement relevant to standards effective at the time of the report for historical cases.
- 5.32 The preventability of each case was classified as ‘yes’, ‘no’, or ‘uncertain’. In one sense, all cases of AAGA are by definition preventable simply by the administration of ‘more anaesthetic’ but this is of little value in judging practice. Preventability was therefore defined as where ‘had one or more avoidable actions or omissions outwith standard practice not occurred, AAGA would unlikely have arisen’.

- 5.33 The impact on the patient was classified in three ways:
- (a) Patient experience during the episode using the Michigan Awareness Classification Instrument (Mashour et al., 2010) (Table 5.4).
 - (b) Intra-operative cognitive state and the later psychological impact on the patient using the Wang classification (Wang et al., 2012) (Table 5.5).
 - (c) Severity of patient outcome, using a modification of the NPSA tool (NPSA, 2008) adapted specifically for NAP5 to be suitable for the predominantly psychological harm related to AAGA (Table 5.6). This was used to estimate the 'longer term' impact on the patient (i.e. as judged at the time they made the report).

Table 5.4. Michigan Awareness Classification Instrument (from Mashour et al. 2010). An additional designation of D is applied where the report described distress during the experience (e.g. fear, suffocation, sense of impending death, etc)

Class A cases (%)	
Class 0	No AAGA
Class 1	Isolated auditory perceptions
Class 2	Tactile perceptions (with or without auditory)
Class 3	Pain (with or without tactile or auditory)
Class 4	Paralysis (with or without tactile or auditory)
Class 5	Paralysis and pain (with or without tactile or auditory)

Table 5.5. Wang classification of intra-operative cognitive states (Wang et al., 2012)

Grade	Intra-operative state		Immediate post-operative state	Late post-operative state (>1 month)	Descriptor
0	Unconscious	No signs; no response to command	No recall	No recall	Adequate anaesthesia
1	Conscious	Signs/response to command	No recall	No recall or emotional sequelae	Intra-operative wakefulness with obliterated explicit and implicit memory
2	Conscious; word stimuli presented	Signs/response to command	No explicit recall, implicit memory for word stimuli	No explicit recall; implicit memory for word stimuli but no emotional sequelae	Intra-operative wakefulness with subsequent <i>implicit memory</i>
3	Conscious	Signs/response to command	No recall	PTSD/nightmares but no explicit recall	Intra-operative wakefulness with implicit emotional memory
4	Conscious	Signs/response to command	Explicit recall with or without pain	Explicit recall but no emotional sequelae	Awareness but resilient patient
5	Conscious	Signs/response to command	Explicit recall with distress and/or pain	PTSD/nightmares with explicit recall	Awareness with emotional sequelae

Table 5.6. Original NPSA classification of harm caused by a patient safety incident (from www.nrls.npsa.nhs.uk/resources/collections/seven-steps-to-patient-safety/?entryid45=59787) (column 2), and the modified NPSA classification including psychological impact on the patient devised for use in NAP5

Severity	NPSA – original definitions of harm (NPSA, 2008)	Revised definitions for NAP5
0	No harm occurred	No harm occurred
1	Required extra observation or minor treatment and caused minimal harm	Resolved (or likely to resolve) with no or minimal professional intervention. No consequences for daily living, minimal or no continuing anxiety about future healthcare
2	Resulted in further treatment, possible surgical intervention, cancelling of treatment, or transfer to another area, and which caused short term harm	Moderate anxiety about future anaesthesia or related healthcare. Symptoms may have some impact on daily living. Patient has sought or would likely benefit from professional intervention
3	Caused permanent or long term harm	Striking or long term psychological effects that have required, or might benefit from professional intervention or treatment: severe anxiety about future healthcare and/or impact on daily living. Recurrent nightmares or adverse thoughts or ideations about events. This may also result in formal complaint or legal action (but these alone may not be signs of severity)
4	Caused death	Caused death

(Modification by Ms Helen Torevell, NAP5 Panel member)

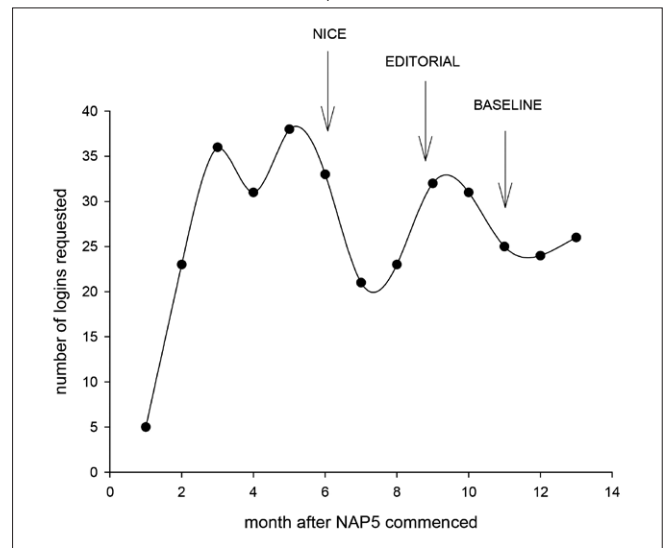
Small group review was followed by second review in a large group to moderate output from the first review



NAP5 CASE REVIEW AND NUMERICAL ANALYSIS

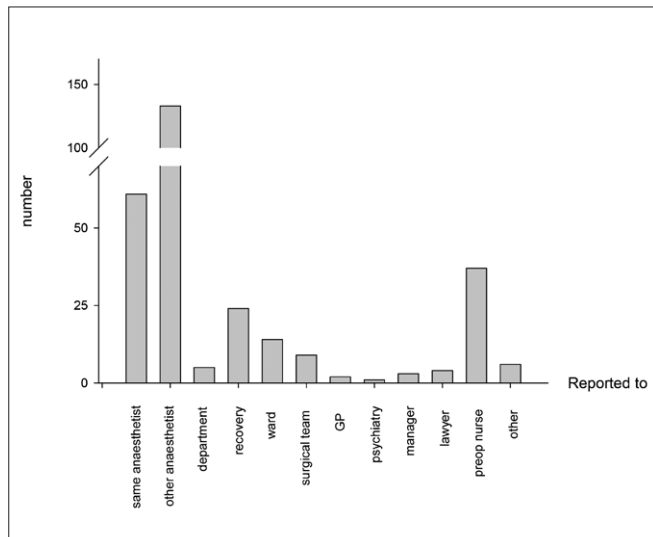
- 5.34 The results and analysis of reports of AAGA is presented in the remainder of this Report. This chapter presents only the results relating to the methodology itself.
- 5.35 Regular responses were received from all 269 UK LCs on a monthly basis (100% response rate). Of these, 108 LCs consistently filed zero returns for the whole data collection period (i.e. the hospitals covered by 108 LCs received no reports of AAGA in the year). There were no security breaches of the website, de-anonymisation of patient reports, or technical problems related to data collection. In Ireland, regular responses were received from each of 41 Irish LCs, 31 of whom submitted a nil return for the whole period.
- 5.36 A total of 471 requests from both UK and Ireland were received by the NAP5 team for login details to access the website. After screening, including consultation with the NAP5 Moderator where indicated, 341 were judged admissible and logins issued. However, 20 LCs did not use their logins, leaving 321 reports filed. Guidelines from the National Institute for Health and Care Excellence (NICE) on electronic depth of anaesthesia monitoring and criticisms thereof (Pandit & Cook, 2013b) were published in November 2012 and February 2013 respectively; the Baseline Survey (Phase 1) of NAP5 was published, with considerable media attention, in March 2013 (Pandit et al., 2013a and b). None of these appeared to influence the request rate for logins to the website (Figure 5.1).

Figure 5.1. The monthly request rate for logins to secure website per month. NAP5 commenced on 1 June 2012; the arrows show the times when relevant NICE guidance (NICE, 2012) and an associated editorial (Pandit & Cook, 2013b) and the NAP5 Baseline Survey (Pandit et al., 2013a and b) were published



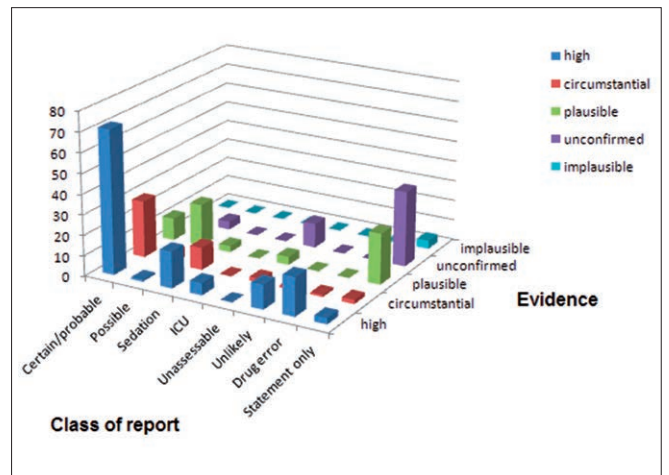
- 5.37 In the majority (98%) of reports, an LC was involved in submission to the NAP5 website, either alone or with another anaesthetist. In 7 reports, an anaesthetist who was not an LC filed the report alone.
- 5.38 A majority (95%) of reports were made spontaneously by the patient. Otherwise, reports were made by the patient to a friend, who reported it to an anaesthetist (one case), in a legal letter of claim (one case), where the anaesthetist suspected AAGA and initiated the discussion with the patient (six cases), by a carer or relative (eight cases).
- 5.39 Figure 5.2 shows to whom the report was first made. In the majority of cases (66%) the same anaesthetist who provided care, another anaesthetist, or the anaesthetic department received the report. It was also common for pre-operative nurses to receive a first report of AAGA (i.e. before a subsequent operation; 21%). Statement Only cases were generally reported to another anaesthetist or to the pre-operative nursing staff (presumably because most of these were historical cases, there was unlikely opportunity to report to the same anaesthetist that administered care).

Figure 5.2. Bar chart of to whom the report of AAGA was made. Department = anaesthetic department (e.g. by letter or telephone); GP = General Practitioner; Pre-op nurse = pre-operative nurse



- 5.40 Most of the Certain/probable reports, the Sedation and the Drug Error cases were associated with a strong level of evidence. Conversely the Unlikely and Statement Only cases with a weaker evidence base. For Possible cases the degree of evidence was variable see Figure 5.3.

Figure 5.3. Distribution of evidence base by class of report

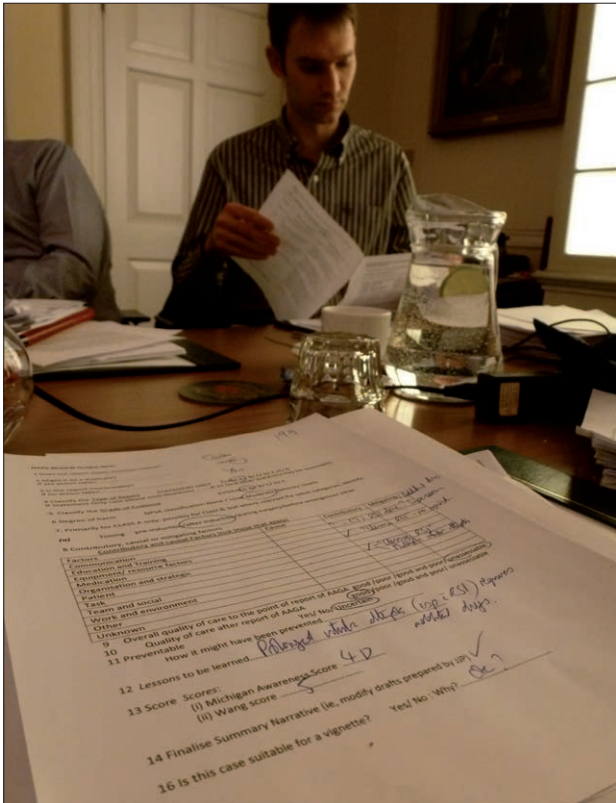


- 5.41 The Certain/probable and Possible reports (and those relating to Sedation, ICU or Drug Error) are discussed in later chapters, as are inadmissible reports, Unlikely reports and Statement Only reports.

DISCUSSION

- 5.42 The study architecture of NAP5 conforms to a registry, but one that is nationwide (separately for the UK and Ireland): NAP5 is therefore probably the first national survey of AAGA ever undertaken. Our method of assembling registry cases through LCs at each hospital appears unique to this topic (though identical to two previous NAPs). Several other features are important. It is a registry of *first reports* of AAGA and great care was taken to exclude reports made previously to the healthcare system. No active questioning of patients was required, but naturally, sometimes anaesthetists did question patients whom they suspected of having been aware. Reports elicited in this manner (6; 1.9%) were accepted as being part of routine clinical care rather than excluded as protocol-based interrogation.
- 5.43 It was the intention of the project that the AAGA reports remained anonymous, and the regulatory requirements imposed on NAP5 reinforced this necessity. Hence, the NAP5 Panel do not know the geographical source of the report, the identity of the LC who filed the report, or any patient, hospital or clinician identifiable details. If despite this case details provided in this Report appear recognisable to some readers, it is likely because they are very representative of not-infrequent occurrences (i.e. very few, if any, reports we received appeared unique).

All reports were reviewed in a structured manner with structured outputs



5.44 By relying on spontaneous reports we hoped to receive the most 'robust' reports; that is, those reports unprovoked by active questioning. We were confident that our team of LCs diligently scanned their hospitals on a regular basis, across departments actively searching for reports. The 100% response rate (including zero response) provides some evidence that this worked, and indeed reports were received from a variety of sources (Figure 5.2). Although we did obtain some reports from GPs and psychiatrists/psychologists, we cannot be certain that we did not miss any. The use of strictly defined categories of report was important in the project. We believe our methodology improved the likelihood of correct inclusion and exclusion of reports and made the nature of reports more explicit, adding to the robustness of the project. We have described those cases judged inadmissible or Unassessable here and in the Report to enable others to judge this. The relatively high proportion of Statement Only cases, and the strikingly long time intervals for their reporting, might also suggest a diligence of the system in detecting these otherwise long-unreported cases.

5.45 However, the accuracy of our method in detecting all cases of AAGA relies upon the ability of the healthcare system to transmit the report to

anaesthetists: as Avidan and Mashour (2013a and b) previously commented, we may be 'under the rate, or under the radar'. The fact that the majority of reports were made to anaesthetists (Figure 5.2) does not exclude the possibility that reports were made to others but not transmitted to anaesthetists' and therefore, not detected by LCs. The type of report we obtained was at several removes from the source. That is, details were not obtained from the patient direct but rather mostly from an LC, who in turn had obtained information from a mixture of case notes and colleagues involved in the case. Furthermore, we did not have access to the medical records, but rather, the LC's version of what those records were. There was thus some inevitable loss of detail. On first principles, this potential loss of detail may have affected the reporting of sophisticated outcomes such as psychological detail more than it did objective details such as drugs administered, etc.

5.46 The alternative to a reliance on spontaneous reporting is to use active questioning. Although the Brice interview is commonly used in research, we cannot find any previous critique of it; its possible weaknesses appear to have gone unchallenged. It is often described as 'modified', but seems identically used in respect of its key questions to that originally described. For example it is not known if different questions, or an alternative sequence of questions, will elicit a different response rate. Studies using the Brice questionnaire often lack detail as to how the output of the questionnaire is interpreted, what (if any) other investigation of possible cases is undertaken and what criteria are used to confirm or refute AAGA. Therefore for any given group of patients administered the Brice instrument, it is not known what proportion of those initially indicating AAGA are (or would be) later judged by a review panel *not* to have Certain or Possible AAGA (and whether this proportion is consistent across studies). While it seems that up to three Brice interviews up to a month post-operatively yields the highest positive response rate for AAGA, it is not known if even more questioning yields higher (or lower) rates. Indeed, it would appear likely that several cases classified as 'Unassessable' or 'Unlikely' in NAP5 might in fact have been deemed as admissible AAGA if a Brice method alone had been used. Therefore, although methods relying on spontaneous reporting have their limitations, it is far from certain that Brice questioning should be regarded as the 'gold standard'.

- 5.47 The issue of what causes AAGA is important, but our methodology did not robustly address this: AAGA could be avoided or prevented by knowing its causes. However, the analysis of causality is complex. In one sense, it implies that one action (or inaction) directly leads to another event. This simplistic view does not always accommodate a need for several conditions to exist (no one of them alone sufficient) so that one event can lead to another. Nor does it encompass causality as a probabilistic analysis (i.e. as an event more or less likely to occur given certain conditions). In the analysis of medical practice in particular, the notion of 'contributory factors' is perhaps more meaningful than 'cause' (Pearl, 2000; Green, 2003) and we have adopted this in our analysis.
- 5.48 *The immediate cause* of AAGA is always 'inadequate anaesthesia'. However, the *root cause* (the event initiating the causal chain) can be something quite different (e.g., distraction, ignorance, etc) (Mashour, 2013). In a more pragmatic sense, causes of AAGA might be broadly summarised as:
- a failure or interruption of delivery of suitable concentrations of anaesthetic (e.g. through root causes of mechanical failure, human error or misjudgement); or
 - an inherent patient resistance to anaesthetic drugs (which may involve root causes of 'physiological' resistance such as due to anxiety or pain; or 'pharmacological' resistance, such as the presence of other drugs that increase anaesthetic dose requirements; or possibly genetic factors that make the patient less susceptible to anaesthetic effects).
- 5.49 If possibilities like this are to be investigated then an ongoing database of AAGA cases becomes necessary, as large cumulative databases are the only means to study relatively rare diseases or syndromes with a genetic basis (DoH, 2013). Moreover, a more direct clinical relevance of our methodology is that it offers a standardised means to investigate or analyse cases of AAGA as they arise in practice. Use of the classification scheme in the Tables would help standardise some of the terminology. The relevant anaesthetic organisations, working together with the appropriate national patient safety organisations should consider developing a means by which all incidents of AAGA are properly recorded and entered onto a permanent database, to allow for ongoing learning.

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