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5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors†‡

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Editor's key points

- This paper describes the main findings of NAP5, on accidental awareness during anaesthesia.
- The incidence of accidental awareness during general anaesthesia, spontaneously reported by the patient was estimated to be roughly 1:19 000.
- The risk factors included female sex, younger adults, obesity, previous awareness, emergencies, and use of neuromuscular blockers.

We present the main findings of the 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia (AAGA). Incidences were estimated using reports of accidental awareness as the numerator, and a parallel national anaesthetic activity survey to provide denominator data. The incidence of certain/probable and possible accidental awareness cases was ~1:19 600 anaesthetics (95% confidence interval 1:16 700–23 450). However, there was considerable variation across subtypes of techniques or subspecialities. The incidence with neuromuscular block (NMB) was ~1:8200 (1:7030–9700), and without, it was ~1:135 900 (1:78 600–299 000). The cases of AAGA reported to NAP5 were overwhelmingly cases of unintended awareness during NMB. The incidence of accidental awareness during Caesarean section was ~1:670 (1:380–1300). Two-thirds (82, 66%) of cases of accidental awareness experiences arose in the dynamic phases of anaesthesia, namely induction of and emergence from anaesthesia. During induction of anaesthesia, contributory factors included: use of thiopental, rapid sequence induction, obesity, difficult airway management, NMB, and interruptions of anaesthetic delivery during movement from anaesthetic room to theatre. During emergence from anaesthesia, residual paralysis was perceived by patients as accidental awareness, and commonly related to a failure to ensure full return of motor capacity. One-third (43, 33%) of accidental awareness events arose during the maintenance phase of anaesthesia, mostly due to problems at induction or towards the end of anaesthesia. Factors increasing the risk of accidental awareness included: female sex, age (younger adults, but not children), obesity, anaesthetist seniority (junior trainees), previous awareness, out-of-hours operating, emergencies, type of surgery (obstetric, cardiac, thoracic), and use of NMB. The following factors were not risk factors for

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- The paper offers strategies to prevent accidental awareness during general anaesthesia.

accidental awareness: ASA physical status, race, and use or omission of nitrous oxide. We recommend that an anaesthetic checklist, to be an integral part of the World Health Organization Safer Surgery checklist, is introduced as an aid to preventing accidental awareness. This paper is a shortened version describing the main findings from NAP5—the full report can be found at http://www.nationalauditprojects.org.uk/NAP5_home.

Keywords: accidental awareness; awareness; National Audit Project

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The 5th National Audit Project (NAP5) of the Royal College of Anaesthetists (RCoA) and the Association of Anaesthetists of Great Britain and Ireland (AAGBI) concerned accidental awareness during general anaesthesia (AAGA). It commenced its phase of prospective data collection on June 1, 2012, and completed it on May 31, 2013.[1–3] Two of its stated aims included estimating an incidence of reports of AAGA and determining risk factors. The methodology is described in an accompanying paper[4] and together with its activity survey[5] makes NAP5 the largest and most comprehensive study on AAGA and its risk factors ever undertaken.

Perhaps the most common tool used to establish the incidence of AAGA has been the Brice and colleagues[6] interview, conducted immediately after anaesthesia and often repeated up to three times over up to a month. Over several decades, the incidence appears to have consistently reported to be ~1–2:1000 general anaesthetics.[7–12] It has been reported to be higher in obstetric (1:384),[13] cardiac (1:43),[14] and paediatric (1:135)[15] anaesthesia. However, some studies do report a much lower incidence (1:14 560),[16] but these have been criticized for using a modified Brice interview within 48 h of anaesthesia and not repeating it.[17]

The NAP5 Baseline Survey reported an incidence for patient reports of AAGA of ~1:15 000, similar to the findings of Pollard and colleagues.[16] A similar survey conducted in Ireland, using as denominator an estimate of anaesthetic activity that was conducted in parallel,[18] reported a similarly low incidence (1:23 000).[19] These surveys suffer from potential limitations, including failure of patients to report the event, memory of the anaesthetist for the incident, bias, and also possible systems failures preventing the anaesthetists being made aware of the report.[20]

Incidence apart, previous studies have addressed risk factors for AAGA. Certain types of surgery (e.g. cardiac, obstetric), female sex,[21 22] higher ASA physical status,[21 23 24] and obesity[25–27] are all implicated. The notion of an intrinsic, possibly genetic, resistance to anaesthesia has also been raised, with up to 11% of patients with AAGA having a previous history[8 27] and an important minority of AAGA cases having no apparent cause.[9 28]

In this context, NAP5 was able to address questions of both the incidence of reports of AAGA and risk factors for these.

Methods

The methods are described in the accompanying paper.[4] For the analysis of risk factors, we compared the relative frequencies of features in AAGA reports with the frequency of those in the NAP5 activity survey.[5] Psychological aspects, the impact of human factors, quality of care and preventability, cases arising after sedation, and issues of consent and medico-legal aspects are discussed in a separate paper.[29] Data are quoted with 95% Poisson confidence intervals (CIs),[30] and χ^2 testing reserved for some comparisons of certain/probable AAGA frequencies (the most complete data set).

Results

A total of 300 reports of AAGA were made to NAP5 in the reporting period June 1, 2012, to May 31, 2013, of which 141 (47%) were considered to be certain/probable or possible (Table 1; see accompanying paper for categorization of AAGA reports).[4] There was a marked under-representation of children, a slight over-representation of younger/middle-aged adults, and an under-representation of the elderly (Fig. 1A). There was also a preponderance of women (91, 65%). Over three times as many obese patients experienced AAGA than generally undergo anaesthesia (Fig. 1B), but ASA grades were equivalently represented (Fig. 1C).

By speciality (Fig. 2), the striking result was the marked over-representation in obstetrics (a 10-fold difference) and cardiothoracics (2.5-fold difference). Two specialities appear under-represented: orthopaedics/trauma/spine (~1.5-fold difference) and plastics (a five-fold difference).

Two-thirds of certain/probable and possible reports were related to the dynamic phases of anaesthesia: induction of

Table 1 Reports of accidental awareness during general anaesthesia by class, and those in whom NMB was used. Values are number (proportion). N/A, not applicable or data not available; *the proportion of those not N/A

Class	Reports	NMB used
Certain/probable	110 (37%)	107 (97%)
Possible	31 (10%)	24 (77%)
Sedation	32 (11%)	N/A
Intensive care	6 (2%)	6 (100%)
Unassessable	19 (6%)	N/A
Unlikely	12 (4%)	N/A
Swaps/drug error	20 (7%)	17 (85%)
Statement only	70 (23%)	N/A
Total	300	156 (93%)*

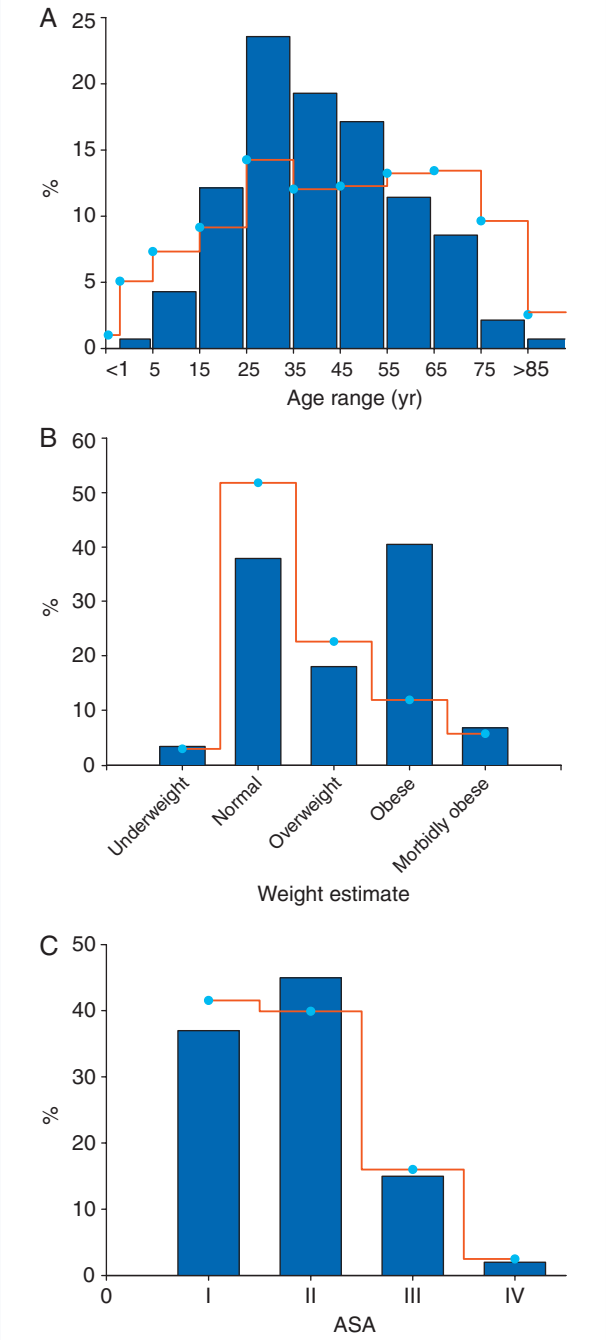

Fig 1 Certain/probable and possible accidental awareness during general anaesthesia cases (shaded bars), compared with patient characteristic distribution from the activity survey (dots with lines) of (A) age, (B) body habitus, and (C) ASA physical status.

anaesthesia [59 (47%)] and emergence [23 (18%)], compared with during maintenance [43 (34%)]. In nine cases, AAGA was judged to occur during multiple phases, and in seven cases, the panel was unable to judge.

The main features of anaesthetic practice in the AAGA cases compared with those in the activity survey are shown in Figure 3.

Neuromuscular block (NMB) appeared far more commonly in the AAGA reports (93% of reports) than its use in the activity survey (46% of anaesthetics). Notably, a nerve stimulator was used after a non-depolarizing neuromuscular blocking drug (NBD) had been administered much less frequently in AAGA cases (9%) compared with the activity survey (38%). Similarly, reversal of non-depolarizing NBDs was less common in AAGA cases (48%) than in the activity survey (68%). Thus, the combination of using NBDs, not monitoring their effect, and not reversing it, seemed to incur a risk for AAGA.

Of the anaesthetic induction agents, thiopental, etomidate, midazolam, and ketamine were over-represented in AAGA cases. Thiopental was used in only 3% of anaesthetic inductions, but was implicated in 23% of AAGA reports; an almost eight-fold difference. Fewer cases overall were conducted with the other three agents, making them subject to greater variation in estimates, so these data should be interpreted with caution.

Of the maintenance agents, the volatile anaesthetic agents appeared in AAGA cases in broad proportion to their general use, although sevoflurane was somewhat under-represented. Total i.v. anaesthesia (TIVA), including all methods of administration, appeared over-represented (18% in AAGA cases, but 8% overall; a greater than two-fold difference).

EEG-based depth of anaesthesia monitoring was used only occasionally, but more commonly in the AAGA reports (4.3%) than in the general population of anaesthetics (2.8%).

An analysis of the 110 certain/probable reports of AAGA (those with the most complete data set) identified the following additional factors as also being over-represented: out-of-hours operating ($P<0.0001$), urgent/emergency surgery ($P<0.0001$), and junior staff ($P=0.003$). The following factors were not associated with AAGA: race ($P=0.42$), ASA physical status ($P=0.23$), and use of nitrous oxide ($P=0.26$).

Incidences

The activity survey indicated that there were ~2 800 000 cases of general anaesthesia in the year studied. Several incidences can be calculated depending on which types of cases are included or excluded (Table 2). We discounted the sedation cases (an incidence for which is given in an accompanying paper),[29] unassessable and unlikely reports, and the statement-only cases, but included the drug-swap cases and those in the intensive care unit (ICU), which left 167 cases. This yielded an incidence of patient reports of AAGA ~1:17 000 (95% CI 1:14 300–19 500) general anaesthetics. If drug swaps (leading to brief awake paralysis but actually occurring before anaesthesia) were excluded, we were left with 147 cases and an incidence of 1:18 800 (95% CI 1:16 000–22 300). The incidence of certain/probable and possible accidental awareness cases was ~1:19 600 anaesthetics (95% CI 1:16 700–23 450). Both the number and the estimated incidence were remarkably close to the estimate from the NAP5 baseline survey of 153 cases and 1:15 000, respectively.[2] If we had included all unassessable and statement-only cases as if they were also accurate reports of AAGA, then this gives a 'pessimistic incidence' of 1:12 000 (95% CI 1:10 600–13 760).

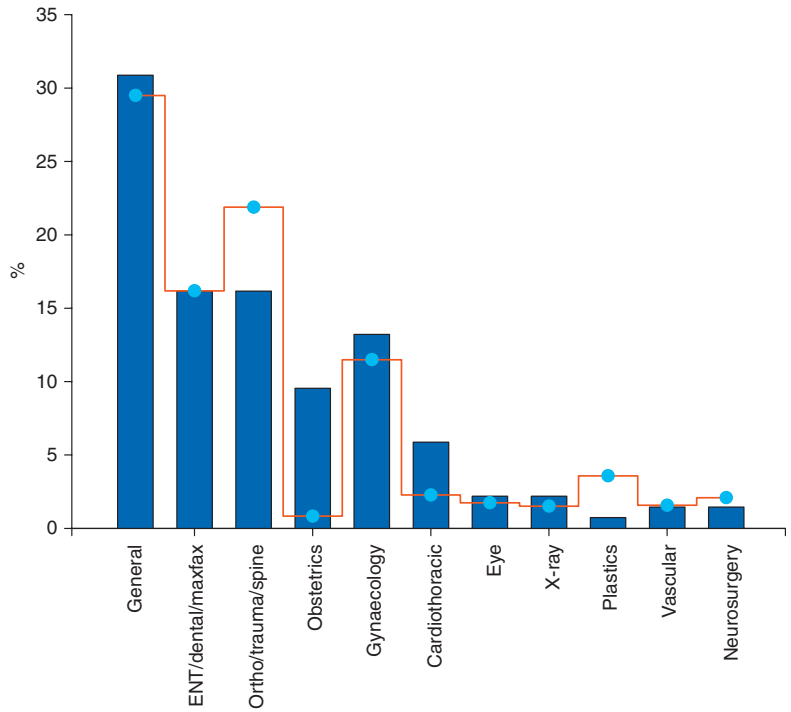

Fig 2 Certain/probable and possible accidental awareness during general anaesthesia cases by speciality (bars) compared with distribution in the activity survey (dots and line). Three cases in bariatric and transplant surgery have been omitted as they were not specified in the activity survey. ENT, ear, nose, throat; maxfax, maxillofacial surgery; ortho, orthopaedic surgery; eye, ophthalmology; X-ray, radiology; general surgery includes urology and other specialities not listed.

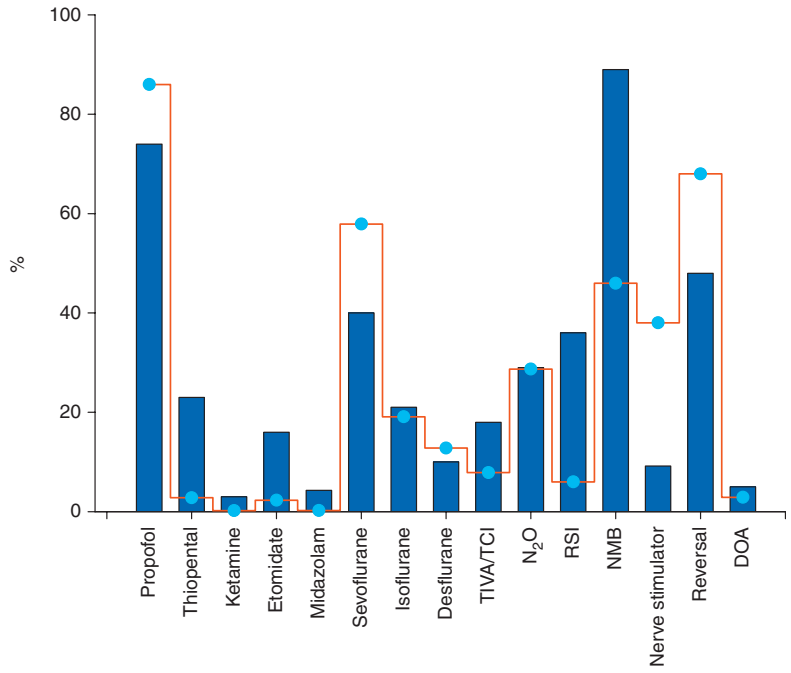

Fig 3 Representation of some components of anaesthesia practice in certain/probable and possible accidental awareness during general anaesthesia reports (bars) compared with distribution in the activity survey (dots and lines). Propofol in first bar refers to its use as an induction agent, as distinct from a later bar (TIVA) where its use is referred to for maintenance. TIVA, total i.v. anaesthesia; TCI, target-controlled infusion; N_2O, nitrous oxide; RSI, rapid sequence induction; NMB, neuromuscular block; DOA, specific depth of anaesthesia monitor.

Table 2 Estimated incidences for accidental awareness during general anaesthesia arising out of reports to NAP5 (rounded to nearest 100). Values are number or number (95% CI). *All login requests to NAP5 (i.e. artificially inflated estimate); †all certain/probable and possible cases, intensive care cases, and cases of syringe swaps or drug error. NMB, neuromuscular block

	Activity survey estimate; *n*	Incidence	Proportion
All patient reports (*n*=471)*	2 766 600	1:6000 (1:5370–6450)	0.017 (0.015–0.019)
Certain/probable, possible, unassessable and statement-only cases (*n*=230)	2 766 600	1:12 000 (1:10 600–13 760)	0.008% (0.007–0.009%)
Certain/probable only (*n*=111)	2 766 600	1:25 000 (1:20 800–30 400)	0.004% (0.003–0.005%)
Certain/probable and possible (*n*=141)	2 766 600	1:19 600 (1:16 700–23 450)	0.005% (0.004–0.006%)
NMB used† (*n*=155)	1 272 700	1:8200 (1:7030–9700)	0.012% (0.010–0.014%)
No NMB used† (*n*=11)	1 494 000	1:135 900 (1:78 600–299 000)	0.001% (0.0003–0.0013%)
During sedation by anaesthetists (*n*=20)	308 800	1:15 500 (1:10 300–25 700)	0.006% (0.004–0.010%)
Caesarean section (*n*=12)	8000	1:670 (1:380–1300)	0.150% (0.075–0.263%)
Cardiothoracic anaesthesia (*n*=8)	68 600	1:8600 (1:4300–23 000)	0.012% (0.004–0.023%)
Paediatric anaesthesia (*n*=8)	488 500	1:61 100 (1:30 500–163 000)	0.002% (0.001–0.003%)

Table 3 Estimated incidences for reported accidental awareness arising out of reports to NAP5 in Ireland. Values are number or number (95% CI). NMB, neuromuscular block. *All categories of AAGA. †All certain/probable and possible cases, and cases of syringe swaps or drug error. NMB, neuromuscular block

	Activity survey estimate (*n*)	Incidence	Proportion
All patient reports (*n*=11)*	219 700	1:20 000 (1:11 500–44 000)	0.005% (0.002–0.009%)
Certain/probable only (*n*=5)	187 000	1:37 400 (1:17 000–93 500)	0.003% (0.001–0.006%)
Certain/probable and possible (*n*=6)	187 000	1:31 200 (1:14 400–93 500)	0.003% (0.001–0.007%)
NMB used† (*n*=5)	77 115	1:15 500 (1:7010–38 600)	0.006% (0.003–0.014%)
No NMB used† (*n*=1)	109 885	1:110 000 (1:18 300–4 400 400)	0.001% (2.2×10^{-5}–0.005%)
During sedation by anaesthetists (*n*=1)	32 700	1:32 700 (1:6540–1 308 000)	0.003% (7.6×10^{-5}–0.015%)
Caesarean section (*n*=1)	17 400	1:17 400 (1:3500–696 000)	0.005% (1.4×10^{-4}–0.03%)
Cardiothoracic anaesthesia (*n*=1)	5200	1:5200 (1:1040–208 000)	0.02% (4.8×10^{-4}–0.096%)
Paediatric anaesthesia (*n*=1)	46 100	1:46 100 (1:9220–1 844 000)	0.002% (5.4×10^{-5}–0.011%)

The most pessimistic incidence of patient reports of suspected AAGA can be estimated assuming that all 471 original requests for logins were made on some positive grounds. This would give an overall incidence of no higher than 1:6000 (95% CI 1:5370–6450).

There was a striking difference between the incidence of AAGA when no NBD was used (1:135 900) compared with when one was used (1:8200). The latter figure was very similar to the incidence for cardiothoracic surgery, where the use of NBD is commonplace, which might explain over-representation of this speciality in AAGA cases (Fig. 2). Another subgroup where NBDs are commonly used with notably high incidence is obstetrics (1:670). The estimate for AAGA in children (where the activity survey indicates NBDs were less often used), on the other hand, was very low.

In Ireland, there were 11 cases of AAGA reported, of which six were certain/probable or possible (Table 3), yielding broadly similar incidences, albeit with wider CIs, as the UK.

Discussion

Our main finding was that, similar to that of the NAP5 baseline surveys,[2 19] the overall incidence of patient reports of AAGA was very low, approximately one in 19 000 general anaesthetics. Even the most pessimistic estimate was one in 6000. We believe that this is important new information for anaesthetists and patients.

Of note, these figures are several orders of magnitude less common than the incidence consistently ascertained using the Brice interview, which may be as high as 1:600.[7–12] If we assume the Brice method to reveal the correct incidence, then it means that for every 40 patients who experience AAGA by Brice, just one will make a report, according to our data. The reasons for this marked disparity need fuller discussion. Methodological differences may be relevant, including inherent weaknesses in the Brice interview, *vs* weaknesses in the process of NAP5 data collection. The differences may also relate to the possible impact the AAGA had on the patient.

The theoretical reasons for not reporting an experience are diametrically opposed: either because it was so trivial that it simply does not warrant a report; or because the event was so traumatic that it is difficult or impossible to make a report.

Some support for the first interpretation may lie in the fact that the incidence of distress at the time of the event or psychological sequelae afterwards did not differ between cases reported early and late.[29] Also, in studies using the Brice interview, a low proportion (about one-third) of patients report pain or distress associated with their AAGA experience (i.e. the majority appear to make a neutral report).[7 8 31] This is similar to the proportion reporting distress in the NAP5 baseline survey,[2] but somewhat lower than the 50% we have reported.[29] Of relevance, Villafranca and colleagues[32] described a patient who responded positively to a Brice interview, but maintained that the experience was so trivial that he did not wish to discuss it further.

Yet, in some support of the second interpretation, a number of the statement-only cases in NAP5 clearly exhibited forms of phobic avoidance for decades after AAGA[4] (see also Chapter 25 of full report: http://www.nationalauditprojects.org.uk/NAP5Doc_NAP5_Baseline_Survey_in_the_UK). The relative proportion of relatively trivial *vs* relatively traumatic experiences in a Brice-positive cohort is unknown and warrants formal investigation.

Induction of anaesthesia and transfer to theatre

Accidental awareness around the time of induction of anaesthesia is not widely discussed in the literature. A previous review has suggested that three-quarters of cases of AAGA occur during surgery itself.[33 34] A novel finding of NAP5 is that the period from the start of induction of anaesthesia to the start of the surgical intervention, including induction of anaesthesia and transfer into theatre, is the time when AAGA most commonly occurred. About half of these reports involved cases categorized as urgent or emergency, and many of these involved rapid sequence induction, usually with thiopental. There were many cases where no opioid was used at induction of anaesthesia, particularly when conducted by a trainee, and failing to continue anaesthesia during difficult airway management attempts was judged contributory to AAGA in a number of cases.

These results suggest that more careful attention to dosing of induction agent is needed, along with a proper assessment that it has worked sufficiently well before NBDs are administered. In turn, this finding requires a fundamental reassessment of what is intended by rapid sequence induction of anaesthesia, or even how it is defined, since this was such a potent risk. Rapid sequence induction accounted for most occasions when thiopental was administered, and this combination appeared to be an important risk factor for AAGA. Relevant questions include: whether co-administration of opioids or other adjuncts lowers the risk of AAGA while still achieving the goals of rapid sequence induction; whether there is time to assess the effect of the induction agent and provide more if needed; whether the administration of the rapidly acting NBD can be delayed slightly to check the conscious level, even check the ease of bag-mask ventilation, or both,[35–38] itself a test of depth of anaesthesia; and whether thiopental should continue to have a place.

The high proportion of AAGA cases associated with failed, prolonged, or difficult airway management indicates an overlap between the findings of NAP4[39] and NAP5. Safe airway management should go hand-in-hand with appropriate delivery of anaesthetic to maintain unconsciousness.

Importantly, the gap between i.v. induction and commencement of inhalation anaesthesia, often associated with transfer of the patient from anaesthetic room to theatre, was identified as a major factor in many AAGA cases. We therefore propose that a formal checklist, to be integrated as an anaesthetic subcomponent of the World Health Organization (WHO) checklist, is trialled (Fig. 4).

Maintenance of anaesthesia

Previous studies of AAGA have focused on events during the maintenance phase of anaesthesia—during surgery itself. Ghoneim and colleagues[27] suggested that 75% of episodes of AAGA occurred during the maintenance phase.[33] However, only one-third of NAP5 cases fell into this category, and this is consistent with our baseline survey.[2] Many of these were in fact because of contributory factors at or after induction of anaesthesia, such as failure to turn on the vaporizer after transfer into theatre. Other contributory factors identified were deficiencies in end-tidal monitoring or in responding to monitored levels of end-tidal volatile agent, stopping delivery of the volatile agent too soon before the end of surgery, and using intentionally low doses.

An important finding in cases of AAGA during surgery was that pain was more often a feature of the patient's experience than during other phases. Another important finding was that in 13 (26%) cases of AAGA during maintenance, no cause could be found, perhaps consistent with an innate resistance to the anaesthetic.

Emergence from anaesthesia

An important finding of NAP5 is that residual NMB during tracheal extubation or emergence from anaesthesia may be interpreted by patients as AAGA. Almost one-fifth of the reports to NAP5 occurred during emergence, most of which described experiencing the distress of paralysis.[29] Failure to use a nerve stimulator was judged causal or contributory in the majority of the reports. These cases highlight the fact that adverse outcomes were more often associated with the use of NBDs. Overall, AAGA was associated with the use of NBDs, failure to monitor their effects, and failure to reverse residual drug.

These findings have at least two very important implications. The first relates to our view of neuromuscular monitoring. Based on our results, we propose that a nerve stimulator should be regarded as a monitor of *motor capacity*. The train-of-four, or another suitable index, signifies obtunded motor capacity, which leads to distress if the patient is conscious. A full return of neuromuscular function as assessed by nerve stimulation is a necessary but not sufficient

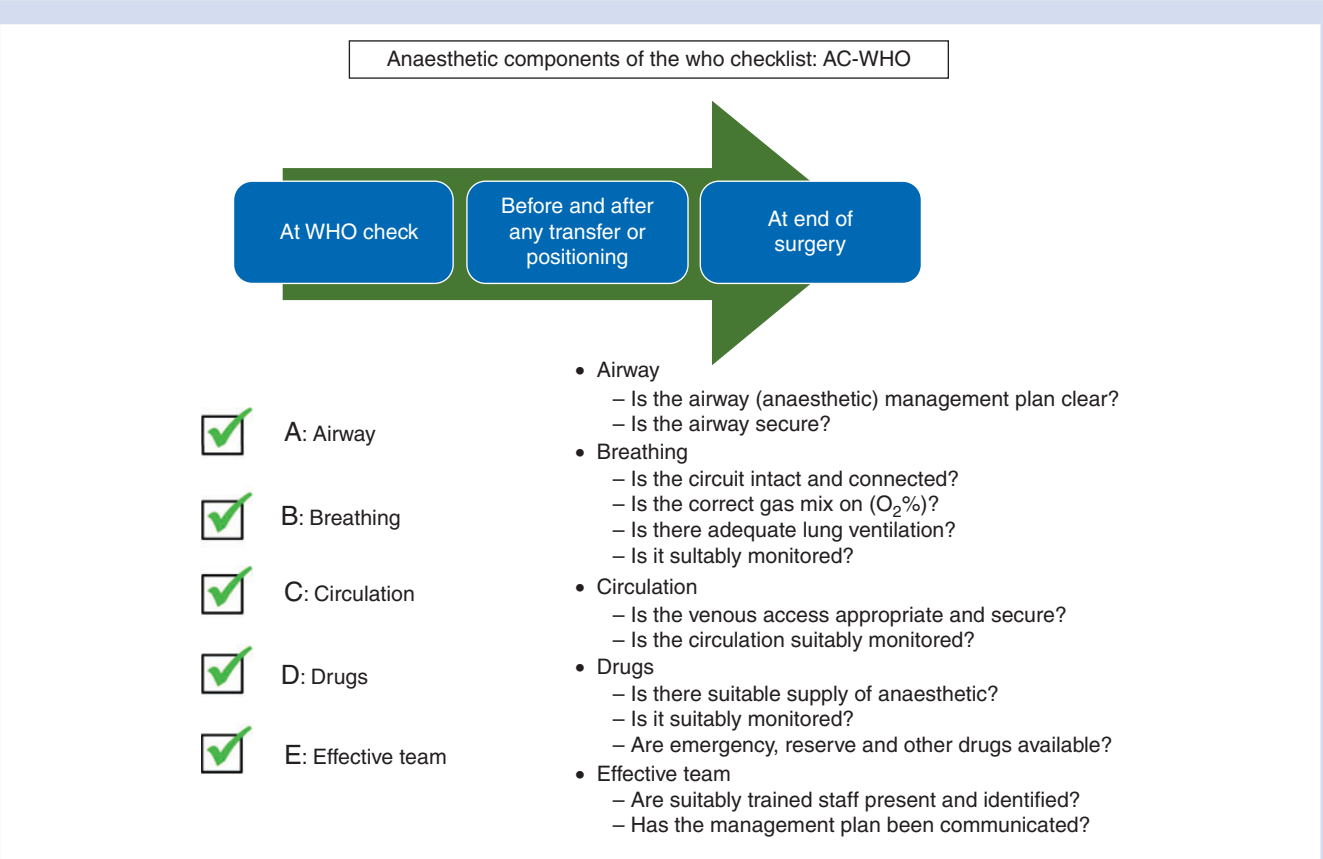

Fig 4 A proposed NAP5 anaesthesia component (AC) checklist of the World Health Organization checklist (NAP5 AC-WHO). The ABCDE check should be undertaken before commencing surgery (at the WHO surgical pause) and after each occasion the patient is moved.

condition for motor capacity. A patient in whom motor capacity has only just returned may still feel partially paralysed, and lack full muscle strength, and therefore can become distressed. Good understanding of this notion of motor capacity is fundamental to understanding the proper role of the nerve stimulator in anaesthetic practice.

A second implication is for the planning of awake tracheal extubation. Patients should be informed in advance if there is a possibility or indeed if it is likely that they may wake up with a tube in their throat, and perhaps a temporary sensation of weakness or inability to move, or assisted breathing. In addition, full recovery from NMB should be confirmed both objectively using a nerve stimulator and clinically. During this period, continuous communication with the patient and verbal reassurance may mitigate any adverse recall of events.[40]

Neuromuscular block

NMB was greatly over-represented in the AAGA cohort compared with the activity survey, while the use of nerve stimulators and reversal agents were both under-represented (Fig. 3). The cases of AAGA reported to NAP5 were perhaps more accurately, and overwhelmingly, cases of *unintended awareness during neuromuscular block* (Table 1), a term that could, or should, be a subtitle to this NAP5 report. The high incidence of distress in this cohort is examined in the accompanying paper,[29] and it is clear that the sensation of paralysis has the capacity to cause great psychological harm, unless it is counteracted by general anaesthesia.

Reflecting on these reports of AAGA, it can be argued that one of the main purposes of general anaesthesia is to enable patients to tolerate the global paralysis required for some surgeries. More than pain, it would seem uncommon for conscious patients to tolerate complete paralysis. Important ways to reduce AAGA might therefore include avoiding or minimizing the use of NBDs and always using a nerve stimulator before allowing emergence from anaesthesia.

Syringe swaps and drug error

We have reported 17 cases of brief awake NMB as a result of drug errors that led to administration of an NBD to a patient who was not anaesthetized. Importantly, distress and longer term psychological impact was of greater severity than in any other class of AAGA.[29] There were numerous contributory factors: staff shortages, pressured environment, hospital policies for the storage and preparation of drugs, and distractions, commonly from other staff. Shortcomings in individual conduct involved a lack of vigilance and undue haste.

A sustainable solution may require industry to work with the speciality with respect to drug packaging and presentation, in order that the risk of drug misidentification may be minimized. Institutions and individual anaesthetists need to develop organizational and personal strategies, respectively, to avoid circumstances that increase the likelihood of error, especially where NBDs are involved. Where a drug error leading to accidental paralysis has occurred, there are three priorities: reassuring the patient that he/she is safe, induction of anaesthesia promptly to mitigate any continued adverse impact, and consideration of reversing NMB at an appropriate time guided by nerve stimulator monitoring.

Specific depth of anaesthesia monitoring

Depth of anaesthesia monitors feature little in our results. This may be because such monitors are very rarely used in the UK. The activity survey estimated that just 2.8% of all general anaesthetics involve the use of any form of depth of anaesthesia monitoring.[5] This is despite guidance from the National Institute for Health and Care Excellence,[41] a full year before the activity survey was conducted, notwithstanding some criticism.[42] The isolated forearm technique is even less frequently used, despite prominent debate in the literature.[43–46] The use of depth of anaesthesia monitors in Ireland is somewhat higher, 9% of all general anaesthetics,[18 19] but it is unknown if this pattern is mirrored in other countries.

There was an over-representation of the use of a depth of anaesthesia monitor in AAGA cases by 50%, superficially suggesting a lack of benefit. However, we do not know if they were used appropriately. Furthermore, these monitors appeared to be used selectively.[2 19] In the activity survey, these monitors were used in 1% of cases using volatile anaesthesia without NMB, but in 23% of cases using TIVA with NMB (Table 4). Of all the anaesthetic techniques, TIVA with NMB appears to confer the greatest (almost four-fold) risk of AAGA (Table 4). Furthermore, the data suggested a potential benefit of using depth of anaesthesia monitors with this last technique, but not especially for other anaesthetic techniques (Table 5). This crude analysis, however, does not take into account obesity, sex, or age as potentially influencing the selection of anaesthesia technique or monitoring. One implication of Tables 3 and 4 is that focusing on specific subgroups, such as TIVA with NMB, might yield the most unambiguous results in clinical trials of monitor efficacy.

Total i.v. anaesthesia

TIVA, which included target-controlled, manually controlled infusion, and fixed-rate infusions and also bolus techniques, were over-represented compared with the activity survey. Failure to deliver the intended dose of drug, for example, because of a problem with the i.v. cannula, resulted in a number of cases of AAGA. However, the greatest over-representation was for instances where a volatile technique was converted to TIVA for transfer of patients out of theatre (Table 6). Many of these cases occurred outside theatres and in circumstances where a volatile anaesthetic could not be delivered. In summary, the most common cause was the administration of an inappropri-

Table 4 Risk profile of different anaesthetic techniques for accidental awareness during general anaesthesia (AAGA). Proportions of anaesthetic technique as used in the activity survey (*n*, annual estimates, rounded up to nearest 100), compared with their representation in our cohort of certain/probable and possible AAGA cases. In the last column, a ratio of >1 indicates over-representation in the AAGA cohort; <1 indicates under-representation. Values are number (proportion). NBD, neuromuscular blocking drug; TIVA, total i.v. anaesthesia

	Activity survey (*n*=2 667 000) (%)	Cases of AAGA with NMB specified (*n*=118) (%)	Ratio of AAGA % to activity survey %
Volatile, no NBD	1 357 600 (51)	7 (6)	0.12
Volatile, NBD	1 095 100 (41)	90 (76)	1.86
TIVA, no NBD	95 200 (4)	3 (2)	0.68
TIVA, NBD	108 400 (4)	18 (15)	3.73

Table 5 Use of processed EEG monitoring in different types of general anaesthesia in the activity survey (*n*, annual estimates) and in the certain/probable and possible cases of AAGA. In the last column, a ratio of <1 indicates the use of the monitor may have a protective effect against AAGA, such that there is under-representation in the AAGA cohort; >1 indicates the reverse. Values are number (proportion). NBD, neuromuscular blocking drug; TIVA, total i.v. anaesthesia. *, zero numerator

	EEG monitoring in activity survey (%)	EEG monitoring in AAGA cases (%)	Ratio
All general anaesthetics (*n*=2 667 600)	73 600 (3)	6 (5)	1.82
Volatile agent, no NBD (*n*=1 357 600)	15 000 (1)	0	— *
Volatile agent, NBD (*n*=1 095 100)	38 300 (4)	3 (3)	0.94
TIVA, no NBD (*n*=95 200)	7400 (8)	1 (33)	4.27
TIVA, NBD (*n*=108 400)	25 400 (23)	2 (11)	0.47

Table 6 Techniques used to maintain anaesthesia where general anaesthesia was induced in an operating theatre or theatre anaesthetic room, and certain/probable and possible AAGA reported. In the last column, a ratio of >1 indicates over-representation in the AAGA cohort; <1 indicates under-representation. The totals (*n*) are for the activity survey reporting period and AAGA cases. TCI, target-controlled infusion; *counted as TIVA

	Total	AAGA	Ratio
Volatile agent	13 479 (93%)	112 (82%)	0.89
Propofol infusion TCI*	764 (5%)	14 (10%)	1.94
Propofol infusion not TCI	82 (0.6%)	2 (1.5%)	2.50
Intermittent boluses*	106 (0.7%)	1 (0.7%)	1.00
Both volatile agent and propofol infusion	48 (0.3%)	7 (5%)	17.0
Total	14 479	136	—

ately low-dose, fixed-rate infusion of propofol to patients in whom NBDs had been used.

Obstetric anaesthesia

We have confirmed that obstetric anaesthesia is a high risk for AAGA—it was the most markedly over-represented of all surgical specialities. The vast majority of obstetric cases occurred during Caesarean section. There was also an impression that general anaesthesia for Caesarean section involved many of the risk factors for AAGA identified elsewhere in NAP5. These included: rapid sequence induction of anaesthesia, omission of opioids at induction, almost always using thiopental and sometimes at inappropriately low doses; universal use of NBDs; difficult airway management; obesity; brief period between anaesthetic induction and start of surgery with little time for reinforcement of the i.v. induction dose with a volatile agent; and a high incidence of urgent/immediate surgery often performed out of hours, resulting in higher rates of non-consultant care.

Cardiothoracic anaesthesia and AAGA in cases from ICU

We have confirmed that cardiac anaesthesia is also high risk for AAGA. Most of the reports involved either brief interruption of drug delivery, caused by human error or technical problems, or the use of intentionally low doses of anaesthetic drugs in high-risk patients, such as those with cardiovascular instability. There were seven reports of cases of AAGA during anaesthetic interventions on ICU. There appeared to be underestimation of anaesthetic requirements in sick, hypotensive patients, usually using a low-dose propofol infusion. All patients received NBDs and experienced distress,[29] and most episodes were judged to be avoidable.

Paediatric anaesthesia

We identified AAGA to be much less common in children than in other series,[14] at ~1:60 000. Some reports of AAGA were received by parents but not transmitted further, although the reasons for this are unclear. Others were first reported decades after the event, and by patients who reported significant psychological distress as a consequence. We classed patients aged up to 16 yr old as children but just one case was reported by a patient aged <5 yr old. Differences in patient experience, memory formation, childhood perceptions, and parental attitudes may have contributed. Also notable are a much reduced use of NBDs in children—25% *vs* 50% in adults in the activity survey.[5] However, when made, children's reports of AAGA appeared to be as reliable as adults', and we emphasize that children should be believed and treated sympathetically.

Inherent resistance to anaesthetic agents

There was some evidence from our data of differential risk of AAGA with different anaesthetic agents (Fig. 3): increased risk with thiopental and reduced risk with sevoflurane compared with other volatile agents. Variation in the risk of AAGA with different anaesthetic agents and the potential for heterogeneity in coding for protein channels on which anaesthetic agents are likely to act provide some support for the idea of a genetic role in patients' susceptibility to anaesthetic agents, or, conversely, risk of AAGA. Some support for this comes from NAP5's finding that, in 25% of AAGA reports arising in the maintenance phase of anaesthesia, the cause was unexplained. Also, six patients of our cohort had previously experienced AAGA, and one appeared to have a family history of AAGA, suggesting that 5% of reports may have an intrinsic basis.

Ireland

The incidence of AAGA in Ireland was notably similar to, but slightly more uncommon than, our estimated for the UK incidence of AAGA (Table 3). The smaller number of general anaesthetics in the public sector in Ireland, coupled with the paucity of AAGA cases, makes numerical analysis limited, but several similar themes are evident as in the UK. We believe the similarities in Ireland, with different arrangements for healthcare to the UK, serve to validate our findings of NAP5 in the UK.

Conclusions

The full text of the NAP5 Report (http://www.nationalauditprojects.org.uk/NAP5_home) provides considerably more details for the various sections than is provided earlier, and also makes numerous specific recommendations. These have implications for individual anaesthetists and surgical teams, the relevant speciality organizations, and NHS organizations including hospitals, Trusts, and Boards. Anaesthetists are advised to reflect on several areas of their practice, notably in their use of NBDs, the preparation and administration of these and other drugs, particularly during patient transfer, and communication, both with the patient before anaesthesia and, if AAGA is suspected, within the team. Speciality organizations are encouraged to consider more detailed guidance in respect of minimal standards of monitoring, especially in relation to monitoring NMB, training in i.v. anaesthesia and the adoption of an anaesthesia-specific checklist as part of the WHO surgical checklist (Fig. 4). NHS organizations are advised to accept that rational planning of theatre lists and less

cumbersome management of drug storage both contribute tangibly to patient safety. All parties are encouraged to work together—and with industry—to agree on safer standards of drug presentation and identification to prevent error.

Authors' contributions

All authors designed the methods and data collection instruments. J.J.P. handled the data collection and analysed the data. All authors commented on presentation of data and requirements for further analysis. J.J.P. and T.M.C. wrote the manuscript and all authors offered comment and made amendments.

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Declaration of interest

All conflicts of the NAP5 team have been registered at the NAP5 website http://www.nationalauditprojects.org.uk/NAP5_home. Specific to this paper: J.J.P. is the Scientific Officer of the Difficult Airway Society and an editor of *Anaesthesia*. T.M.C. and E.P.O'S. serve on the Editorial Board of the *British Journal of Anaesthesia*. M.W. has received honoraria and travel expenses from Abbvie and Abbott pharmaceutical companies.

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