DREAMY

Peter Odor, ST6 Anaesthetics
Chair of PLAN, Chief Investigator of DREAMY

Direct REporting of Awareness in MaternitY patients

A multi-centre observational study of accidental awareness under general anaesthesia in obstetric surgery patients
A Pan-London Trainee Network for Research and Quality Improvement

• Established 2014

• Represented by all schools in London
AAGA – 1:19,000

AAGA – 1:670

AAGA in obstetric anaesthesia

Diagram showing the exponential decay in induction agent and rise in volatile concentration.
Aims

1. To describe, using direct questioning with a Brice questionnaire, the proportion of women who report AAGA following general anaesthesia for obstetric indication surgery in the UK

2. Describe experience and psychological implications of AAGA in obstetric patients

3. 12 month outcome reporting, using structured interview schedule follow up – Post-Traumatic Stress Disorder Checklist (PCL-5)

4. Review of the surgical, anaesthetic and patient factors that make obstetric patients more likely to report AAGA than the non-obstetric population
Study design

Rare event = multiple centres, long term recruitment

• Prospective, observational, multi-centre cohort study, with recruitment planned for 12 months
• Written consent
• Sponsored by St. George’s University of London
• Sample size = approx. 2000 patients
• >40 sites
1. Screen all eligible individuals with a standardised tool (i.e. “Thrice Brice”)
2. Rigorously assess each potential report with further investigation
3. Reaching a consensus classification of the event against pre-established definitions of AAGA
x2, in hospital

after 30 days (and potentially up to 12 months)
Study design

**Obstetric surgery + GA**
- e.g. LSCS, EUA, MROP

**0-24h after surgery**
- Screening
- Participant information sheet
- Written consent

**24-48h after surgery**

**In-hospital follow-up**

**30 day follow up**

Conditional follow up (structured interviews), if suspected awareness

**1 year outcomes**
Collaborators

Dr. Nuala Lucas, OAA committee
NAP 5 core review panel

Prof. Jaideep Pandit
NAP 5 lead
University of Oxford

Prof. Jackie Andrade
Professor Psychology,
University of Plymouth
NAP 5 core review panel

Dr. Ramani Moonesinghe
SNAP-1 Consultant Lead

Dr. Maurizio Cecconi
St. George's
South London CRN
DREAMY Consent
Basic principles

• Written consent
• Must take place before any study activity / 1st Brice questionnaire
• Consent documented with signed, dated consent form
• Willingness to continue in the study should be confirmed every time you have contact with the participant
• Don’t need to give reason for withdrawing; if volunteered then document in the notes
• GCP training via NIHR / local R&D
Check meets eligibility criteria

• Inclusion/exclusion criteria
• Found in Protocol Section 7 or on Departmental Summary Poster
• Adult, capacity, ≥24/40 gestation, GA, surgery within 48 post-partum
Single consent form

- Check form version
- Single consent for all activities
- Copy for patient, copy for ISF, original for patient notes

“Opt out” of 30 d follow up by not providing contact details on Brice questionnaire
Key points to discuss

• **PIS contains approved descriptions**
• Observation study: only activity = completing short series of questionnaires / phone calls
• “If we identify that you may have memories of events under general anaesthesia then we will invite you to receive a series of telephone calls”
• Personal data for follow up
Where? When?

- Post-natal ward / obstetric HDU
- Provide PIS
- Describe study
- “Rapid”
- Within 24h of GA = OK
Suggested process

• Work into usual post-natal follow up routine (but must be <24h following surgery)
  
• Identify potentially eligible patients (i.e. received GA)
• Hand out PIS at start of follow up round
• Return to discuss study – explain aim, methods, benefits/hazards

• Written consent form
Completing the consent form

- Initial each item (common mistake to tick, but initials used to demonstrate that completed by participant and not another person)
- Name, date, sign by participant
- Name, date, sign by person taking consent
- Copies, as directed – original in notes, copy in ISF, copy to patient
- File in ISF and patient notes
Troubleshooting

• If felt to be a conflict of interests (e.g. a patient that suffered complications or suspected high risk of AAGA) → recommend that consent is taken by someone independent and NOT the anaesthetist responsible for intra-operative care

• Use same assessments as per clinical requirements to determine need for translator services, and therefore eligibility for inclusion

• If in doubt about capacity or English language skills → exclude

• If unable to recruit <24h post op → can still recruit >24h → still complete x2 Brice questionnaires and note variance on screening log
Troubleshooting

• Patient still eligible for recruitment after “brief” period in intensive care (dedicated section on Suspected AAGA questionnaire). Limit to patients sedated/ventilated for <24h with rapid return of capacity post-extubation

• Check protocol for answers to queries

• Contact Chief Investigator
Basic principles

• Good quality source data is the foundation upon which research outcomes are based

• If in doubt and cannot locate reliable source data for entry → leave CRF field empty (*there are no mandatory data fields on the DREAMY data server*)

• Participant can “opt out” of telephone follow up by not including contact details on the Brice questionnaire CRF

• Willingness to continue in the study should be confirmed every time you have contact with the participant
Brice questionnaire (1st)

• After written informed consent
• <24h after GA

• Or at earliest opportunity (e.g. for patient unwell on HDU)
Modified Brice questionnaire

Patient name: **Anne Other**
Date of birth: **01/01/1985**

Date and time of GA: **22/05/2017 hh: 12 mm 30**
Today's date and time: **23/05/2017 hh: 09 mm 30**

Brice questionnaire repetition: 1 [✓] 2 [ ] 3 [ ]

Co-investigator's name: **Peter Odor**
Hospital: **SGH**

For telephone follow up purposes (occurs approximately 30 days after your anaesthetic) please provide the following:
Mobile telephone: **0772 345678** Email address: **anne.other@example.com**

Full name and DoB

Investigator to complete; use time of extubation

Brice 1 & 2 in hospital; 3rd for telephone follow up

Investigator to complete with own name

Use full name of DREAMY hospital code (in ISF)

Participant can omit if wish to opt out of further follow up. Only need to be entered once
Categorical or free text response. Provide additional paper for free text response, if required

<table>
<thead>
<tr>
<th>1. What is the last thing you remember before going to sleep?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being in the pre-op area</td>
</tr>
<tr>
<td>Being with family</td>
</tr>
<tr>
<td>Feeling mask on face</td>
</tr>
<tr>
<td>Burning or stinging in the IV line</td>
</tr>
<tr>
<td>Other (Free Text):</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. What is the first thing you remember after waking up?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing voices</td>
</tr>
<tr>
<td>Feeling mask on face</td>
</tr>
<tr>
<td>Seeing the operating room</td>
</tr>
<tr>
<td>Being with family</td>
</tr>
<tr>
<td>Nothing</td>
</tr>
<tr>
<td>Other (Free Text):</td>
</tr>
</tbody>
</table>
Brice positive response?

If in doubt then follow DREAMY Suspected AAGA Protocol (9.3, ~ offer a suspected AAGA questionnaire)

3. Do you remember anything between going to sleep and waking up?

No:
Yes: Hearing voices
Unable to move or breathe
Feeling pain
Feeling surgery without pain
Hearing events of the surgery
Anxiety/stress
Sensation of breathing tube

Other (Free Text): 

4. Did you dream during your procedure?

No:
Yes:
What about (Free Text): Dreamt about flowers

_______________________________

_______________________________

_______________________________

_______________________________

_______________________________

_______________________________
5. Were your dreams disturbing to you?
   - No: \(\checkmark\)
   - Yes: \(\square\)

6. What was the worst thing about your operation?
   - Anxiety: \(\square\)
   - Pain: \(\square\)
   - Recovery process: \(\square\)
   - Functional limitations: \(\square\)
   - Awareness*: \(\square\)

* Awareness means becoming conscious when the anaesthetist intended you to be unconscious during your general anaesthetic. Please refer to the DREAMY Participant Information Sheet for more information about awareness under general anaesthesia. If you are unsure whether you may have experienced an awareness episode then please record your thoughts on this questionnaire then ask to speak to an anaesthetist.

Other (Free Text):

- Too many people making me nervous
- Not expecting a C-section

Ensure that corrections are crossed through and still legible
Reminder to follow Suspected AAGA Protocol

Note to local investigator team

If the participant reports memories of the period between "going to sleep" and "waking up then follow the DREAMY Suspected AAGA Protocol.
Brice questionnaire (2nd)

• Ideally 24-48h after GA

• Capture memories that may not have been present at the time of the first Brice questionnaire completion

• Or if recruited participant recruitment >24h following GA then perform 1\textsuperscript{st} Brice at earliest opportunity and 2\textsuperscript{nd} Brice 24h afterwards. Note variance in screening log. Durations between GA and Brice questionnaires automatically calculated by DREAMY REDCap web data entry portal
Interpreting Brice responses

• Anything that might be a memory occurring between time of anaesthetic induction and extubation = potentially “+ve Brice”

• May include responses to any of Q3-6 (memories, dreams, worst event)

• May include explicit +ve categorical responses to Q3 (“Do you remember anything between going to sleep and waking up?”) e.g. hearing events of surgery

• May include +ve response to “awareness” in Q6 (“What was the worst thing about your operation?”)
Interpreting Brice responses

• If in doubt then contact Chief Investigator and offer Suspected AAGA questionnaire

• Suspected AAGA questionnaire can be paper form or telephone interview (or facilities available for face-to-face interview, if requested)

• Brice responses will be formally assessed separately and alongside Suspected AAGA questionnaires by the DREAMY Research team, and categorised using the Michigan Awareness Classification Instrument
• Figure 4, page 19 of DREAMY protocol 1.0. Suspected AAGA follow up flowchart
Anaesthesia Episode CRF

• Retrospective data capture from anaesthetic chart and patient notes
• Can be entered directly onto DREAMY REDCap data entry web portal (using, smartphone) or via completion of paper CRF then transcription of data
• Aim is to capture overview of obstetric general anaesthetic activity and variables potentially associated with awareness
**Anaesthesia Episode**

**Patient name:** Anne Other

**Date of birth:** 01/01/1985

**Name of investigator completing form:** Peter Odor

**Age:** 32 years

**Parity:** G_ P_ 1 1

**Procedure:** LSCS

**Urgency of surgery/LSCS:** Emergency/Cat. 1

**ASA:** 1 _ 2 _ 3 _ 4 _ 5 _

**Booking BMI (kg/m\(^2\):**
- <18.5 _
- 18.5-24.9 _
- 25-29.9 _
- >35 _

**Anaesthesia times:**
- Start: 11 hh: 30 mm
- Finish: 12 hh: 30 mm
<table>
<thead>
<tr>
<th>Drug/dose for induction only; complete all that apply</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction agents:</strong></td>
</tr>
<tr>
<td>Thiopentone</td>
</tr>
<tr>
<td>Propofol</td>
</tr>
<tr>
<td>Fentanyl</td>
</tr>
<tr>
<td>Alfentanil</td>
</tr>
<tr>
<td>Other (e.g. Ketamine, Reminfentanil):</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Dose:</td>
</tr>
<tr>
<td>400</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Planned GA or conversion; indication</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>De novo or conversion to GA:</strong></td>
</tr>
<tr>
<td>De novo</td>
</tr>
<tr>
<td>Conversion</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Indication for GA:</strong></td>
</tr>
<tr>
<td>Clinical urgency</td>
</tr>
<tr>
<td>Maternal preference</td>
</tr>
<tr>
<td>Regional block contraindicated</td>
</tr>
<tr>
<td>Other:</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Rapid sequence induction:</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Maintenance agent(s): tick all that apply</strong></td>
</tr>
<tr>
<td>Sevoflurane</td>
</tr>
<tr>
<td>Isoflurane</td>
</tr>
<tr>
<td>Desflurane</td>
</tr>
<tr>
<td>Nitrous oxide</td>
</tr>
<tr>
<td>Propofol (TIVA)</td>
</tr>
<tr>
<td>Remifentanil (TIVA)</td>
</tr>
</tbody>
</table>
Gain impression of MAC dosing. Submit lowest, highest and estimated median during time between KTS and closure (as can be best obtained from documentation)

Overall MAC (incl. co agents)

MAC:  
- Lowest: 0.6
- Highest: 1.4
- Estimated median: 1.1

Primary airway device:
- Cuffed ETT
- LMA Supreme

If a supraglottic airway device used, was this because of difficult intubation?:
- Yes
- No

Grade of laryngoscopy:
- 1
- 2a
- 2b

Difficult intubation:
- Yes
- No

Used GEM for 2nd attempt and successful. No use of alternate laryngoscope.

If no MAC recording, then document End Tidal anaesthetic agent. Document if known whether additive MAC (e.g. with nitrous oxide).

Space available for additional notes on the web data entry portal
If known from anaesthetic chart, otherwise omit

Not necessarily immediate post-op (i.e. recovery) but post-op ward

Document any additional descriptions (e.g. suspected drug error) and include on the web data entry portal

<table>
<thead>
<tr>
<th>Neuromuscular blockade:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Suxamethonium</td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td></td>
</tr>
<tr>
<td>Rocuronium</td>
<td>✓</td>
</tr>
<tr>
<td>Other ____________________</td>
<td></td>
</tr>
<tr>
<td>Other ____________________</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Nerve stimulator use:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes ✓</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Reversal use:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Neostigmine/glycopyrolate</td>
<td></td>
</tr>
<tr>
<td>Sugammadex ✓</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Depth of anaesthesia monitor use:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BIS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Most senior anaesthetist present:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ST3-4</td>
<td>✓</td>
</tr>
<tr>
<td>ST5-7</td>
<td></td>
</tr>
<tr>
<td>Staff grade</td>
<td></td>
</tr>
<tr>
<td>CT1-2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location of extubation:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Theatre</td>
<td>✓</td>
</tr>
<tr>
<td>Critical care (Level 2 or 3)</td>
<td></td>
</tr>
<tr>
<td>Recovery</td>
<td></td>
</tr>
<tr>
<td>Other: ________________</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post operative destination:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery suite/post natal ward</td>
<td>✓</td>
</tr>
<tr>
<td>Delivery suite HDU (midwifery-led)</td>
<td></td>
</tr>
<tr>
<td>Critical care (Level 2 or 3)</td>
<td></td>
</tr>
<tr>
<td>Other: ________________</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Estimated blood loss:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-499ml</td>
<td></td>
</tr>
<tr>
<td>500-999ml</td>
<td>✓</td>
</tr>
<tr>
<td>1000-1999ml</td>
<td></td>
</tr>
<tr>
<td>&gt;2000ml</td>
<td></td>
</tr>
</tbody>
</table>
Suspected AAGA questionnaire

- Follow Suspected AAGA follow up protocol
- Section 9.3 of DREAMY Protocol
Troubleshooting

• Contact Chief Investigator, but do not share any patient identifiable data by email
• If in doubt and cannot locate reliable source data for entry → leave CRF field empty (*there are no mandatory data fields on the DREAMY data server, except the Local Study ID*)
• Free text boxes on the DREAMY REDCap web data entry portal for additional descriptions
• If patient transferred intubated to ICU post-operatively, then document time of transfer from theatre as finish time for anaesthesia and post-operative destination as Critical Care on the CRF. Location of extubation can be completed as Critical Care.
Basic principles

• Web portal for data entry
• [https://dreamy.sgul.ac.uk](https://dreamy.sgul.ac.uk)
• 256 bit AES encryption for data transfer and storage
• Meets all NHS Digital Information Governance Toolkit standards, Data Protection Act compliance etc.
• Logging of activity
• User accounts for data upload to PI at each site
DREAMY REDCap Web Data Entry Portal

• Please upload data within 21 days of GA

• See dedicated training guide on DREAMY website: http://www.uk-plan.net/DREAMY
DREAMY
ISF & Site Management
Basic principles

• Investigator Site File template for DREAMY available
• Repository for all study documents
• Confirm validity of research, conduct and integrity of data collecting
• Kept in a secure locked room
• Need to be available for auditing and monitoring purposes
• Local investigator team to ensure contents appropriately filed and kept up to date
• Archived in accordance of sponsor requirements
Training

• Good Clinical Practice training (https://learn.nihr.ac.uk)
• DREAMY “how to” guides
• Ask local R&D department for support
<table>
<thead>
<tr>
<th>Screening Number</th>
<th>Subject Initials</th>
<th>Date of Birth (dd/mm/yyyy)</th>
<th>Date Consent Signed (dd/mm/yyyy)</th>
<th>Date Screened (dd/mm/yyyy)</th>
<th>Is subject eligible to participate in study?</th>
<th>Study ID</th>
<th>Comments</th>
<th>Data uploaded</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A.O.</td>
<td>01/01/1985</td>
<td>22/05/2017</td>
<td>22/05/2017</td>
<td>Yes, Provide Study ID</td>
<td>SGH001</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>N.O.</td>
<td>02/02/1982</td>
<td>22/05/2017</td>
<td>22/05/2017</td>
<td>Yes, Provide Study ID, No, Provide comment</td>
<td></td>
<td>Not English speaker</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>B.B.</td>
<td>03/03/1983</td>
<td>25/05/2017</td>
<td>25/05/2017</td>
<td>Yes, Provide Study ID</td>
<td>SGH002</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Consecutive number for local screening

Consecutive number for local recruitment

Principal Investigator Signature: P. M. Odor
Date (dd/mm/yyyy): 22/5/2017
Screening process

• Local publicity – emails, posters, clinical governance meetings...
• “Normalise” process of patient consent and recruitment
• Robust system for each local site to capture and screen potentially eligible participants
• Study team communications e.g. Whatsapp (no patient data)
• Identify GA patients at handover times
• Managing weekends, locum cover, delayed consent etc.
Patient identifiable information

• Collected and entered to the secure REDCap data entry web portal only

• Do not send any patient identifiable information by email to the research team e.g. name, address, date of birth. Use only the DREAMY Study ID to identify a participant
Protocol deviations / Safety reporting

- Incident log included in ISF for local record keeping (section 3.4 of ISF)
- No Adverse Events / Adverse Reactions / SAE / SAR etc. that meet requirements for notification to sponsor

- AR / Related Events can be documented in patient notes
Troubleshooting

• Site initiation phone call ahead of study launch – book your slot
• Regular review of recruitment
• Notification of recruitment targets per site
• Keep ISF documentation up to date and available
• Obstetric / midwifery +/- psychologist leads for site
Basic principles

http://nap5.org.uk/For-Patients#pt
Three stages

**Meeting**
- Face-to-face meeting with patient
- Listen carefully to patient’s story to detail and understand their experience
- Accept the patient’s story as their genuine experience
- Express regret that the event has happened (this does not constitute an admission of liability)
- Consult with local clinical psychologist

**Analysis**
- Seek cause of awareness using NAPS process
- Check details of patient’s story with monitoring details and with staff
- Seek independent opinion of analysis

**Support**
- To detect impact early, in first 24 hours check for 4 cardinal signs of impact: (1) flashbacks; (2) nightmares; (3) new anxiety state; (4) depression
- Active follow-up at 2 weeks
- If impact persists, formal referral to psychiatric/psychological services
Stage 1

• **Face to face meeting with patient**
  • Ideally this should include the anaesthetist who provided the anaesthesia care. Where this is a trainee, a suitably senior colleague should attend

• **Listen to and accept the patient story and experience**
  • Take a careful note of all details provided by the patient (type of experience e.g. auditory sensations or pain and/or paralysis).
  • Make an attempt to classify the patient’s situation according to the modified NPSA score

• **Express regret**
  • This is not an admission of error or medicolegal culpability

• **Consult with local clinical psychologist.** Early involvement may be of value where there is evidence of distress or severe trauma responses
Stage 2 Analysis

• Check details of patient’s story
  • As NAP5 (and others have shown), patients may be mistaken in several ways.
  • Patient may have experienced an unpleasant dream not involving specific surgical events. Events during the immediate post-operative or pre-operative period may be incorrectly attributed as intra-operative

• Seek cause of awareness using NAP5 process.
  • Some cases have no apparent cause and may be due to insensitivity to anaesthesia
Stage 2 – cause identification

<table>
<thead>
<tr>
<th>Contributory factors</th>
<th>Contributory</th>
<th>Causal</th>
<th>Mitigating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication (includes verbal, written and non-verbal: between individuals, teams and/or organisations)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education and Training (e.g. availability of training)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Equipment/resource factors (e.g. clear machine displays, poor working order, size, placement, ease of use)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Medication (where one or more drugs directly contributed to the incident)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organisation and strategic (e.g. organisational structure, contractor/agency use, culture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient (e.g. clinical condition, social/physical/psychological factors, relationships)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task (includes work guidelines/procedures/policies, availability of decision making aids)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Work and environment (e.g. poor/excess administration, physical environment, work load and hours of work, time pressures)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Stage 3 - Support

• (Detect impact early)
  • If there are flashbacks, nightmares, any new anxiety state or symptoms of depression. If early symptoms are concerning early referral to an appropriate psychologist or psychiatrist is advised.

• Two week review. The same follow up should be conducted at 2 weeks. Even where true AAGA is unlikely, NAP5 has shown that the patient interpretation is of such importance that the impact of peri-operative unpleasant experiences may be severe and psychological support is still needed.

• Support for impact. If impact persists, a formal psychological review is needed.