Update on Sedation

Richard Telford
Exeter
Why use sedation?

Unpleasant diagnostic/therapeutic procedures

• Sympathetic management
• Sedation
• +/- Analgesia

• Increased patient tolerance / acceptance
• Increased technical success

Potential for:
• Cardiovascular depression
• Respiratory depression
<table>
<thead>
<tr>
<th>Date</th>
<th>Drug</th>
<th>Dose/units</th>
<th>Route</th>
<th>Time to be given</th>
<th>Name/Signature</th>
<th>Given by</th>
<th>Time given</th>
</tr>
</thead>
<tbody>
<tr>
<td>01.02.14</td>
<td>Fentanyl</td>
<td>200mg</td>
<td>IV</td>
<td>STAT</td>
<td>A.B</td>
<td>A.B</td>
<td>02:30</td>
</tr>
<tr>
<td>01.02.14</td>
<td>Midazolam</td>
<td>5mg</td>
<td>IV</td>
<td>STAT</td>
<td>A.B</td>
<td>A.B</td>
<td>02:42</td>
</tr>
<tr>
<td>01.02.14</td>
<td>Flumazenil</td>
<td>250mg</td>
<td>IV</td>
<td>STAT</td>
<td>A.B</td>
<td>A.B</td>
<td>03:51</td>
</tr>
</tbody>
</table>
Summary of talk

• Historical context
• Components of good sedation
• New developments
• Target controlled sedation
• Michael Jackson
Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing, and sedation methods

- 36 UK hospitals 14,149 gastroscopies
- 30 day morbidity & mortality
- morbidity 1:200
- mortality 1:2000
- ~ 1/3 deaths ascribed to use of sedation
- cardiopulmonary complications most prominent - in high risk patients

Quine et al. *Gut* 1995; **36**: 462-467
Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing, and sedation methods

• Pre-sedation assessment
• IV access < 50%
• Supplementary O₂ in 12.5% (15% in ASA 3-5)
• SaO₂ in 40%, lack of understanding
• Strong link between lack of monitoring, high benzodiazepine doses and adverse outcomes
• Elderly – excessive doses
• Drug combinations & synergism
• LA spray and aspiration pneumonia (p < 0.001)
• Minimal training, lack of supervision of inexperienced trainees
• Flumazenil usage (high doses and lack of recovery facilities)

Quine et al. Gut 1995; 36: 462-467
Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing, and sedation methods.

**TABLE I**  Mean dose of diazepam used against age

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Dose (mg)</th>
<th>+/- 1 SD (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>18.4</td>
<td>6.6</td>
</tr>
<tr>
<td>20-29</td>
<td>17.4</td>
<td>6.9</td>
</tr>
<tr>
<td>30-39</td>
<td>16.6</td>
<td>6.9</td>
</tr>
<tr>
<td>40-49</td>
<td>16.4</td>
<td>6.6</td>
</tr>
<tr>
<td>50-59</td>
<td>15.3</td>
<td>6.0</td>
</tr>
<tr>
<td>60-69</td>
<td>13.0</td>
<td>5.3</td>
</tr>
<tr>
<td>70-79</td>
<td>10.4</td>
<td>5.9</td>
</tr>
<tr>
<td>80-89</td>
<td>8.5</td>
<td>4.3</td>
</tr>
<tr>
<td>&gt;89</td>
<td>8.6</td>
<td>6.1</td>
</tr>
</tbody>
</table>

**TABLE II**  Mean dose of midazolam used against age

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Dose (mg)</th>
<th>+/- 1 SD (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>7.0</td>
<td>2.9</td>
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<tr>
<td>20-29</td>
<td>7.2</td>
<td>3.1</td>
</tr>
<tr>
<td>30-39</td>
<td>6.8</td>
<td>2.7</td>
</tr>
<tr>
<td>40-49</td>
<td>6.8</td>
<td>2.7</td>
</tr>
<tr>
<td>50-59</td>
<td>6.0</td>
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<tr>
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<td>1.8</td>
</tr>
<tr>
<td>&gt;89</td>
<td>3.1</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Reducing risk of overdose with midazolam injection in adults

- Nov 2004 – Nov 2008
  498 midazolam safety incidents - 3 deaths

- Lack of adequate training

- Failure to titrate drug dose to the patient

- Use high strength midazolam – often diluted leading to drug errors

- High usage of flumazenil to treat overdose
Reducing risk of overdose with midazolam injection in adults

The deadline date for ACTION COMPLETE is 9 June 2009

An executive director, nominated by the Chief Executive, working with the lead pharmacist and relevant medical/nursing staff should:

011/1 Ensure that the storage and use of high strength midazolam (5mg/ml in 2ml and 10 ml ampoules; or 2mg/ml in 5ml ampoules) is restricted to general anaesthesia, intensive care, palliative medicine and clinical areas/situations where its use has been formally risk assessed, for example, where syringe drivers are used.

011/2 Ensure that in other clinical areas, storage and use of high strength midazolam, is replaced with low strength midazolam (1mg/ml in 2ml or 5ml ampoules).

011/3 Review therapeutic protocols to ensure that guidance on use of midazolam is clear and that the risks, particularly for the elderly or frail, are fully assessed.

011/4 Ensure that all healthcare practitioners involved directly or participating in sedation techniques have the necessary knowledge, skills and competences required.

011/5 Ensure that stocks of flumazenil are available where midazolam is used and that the use of flumazenil is regularly audited as a marker of excessive dosing of midazolam.

011/6 Ensure that sedation is covered by organisational policy and that overall responsibility is assigned to a senior clinician which, in most cases, will be an anaesthetist.
8. Mis-selection of high strength midazolam during conscious sedation

Mis-selection refers to when:

- a patient is given an overdose of midazolam due to the selection of a high strength preparation (5 mg/mL or 2 mg/mL) instead of the 1 mg/mL preparation, in a clinical area performing conscious sedation
- excludes clinical areas where the use of high strength midazolam is appropriate; these are generally only those performing general anaesthesia, intensive care, palliative care, or areas where its use has been formally risk-assessed in the organisation.

Setting: All settings providing NHS-funded care.

National safety requirement:

• All procedural sedation recorded in a 48 hour period in 6 acute hospitals in the SW
• 360 patients recruited
• Most sedation occurred in endoscopy (56%), theatre (30%) and cardiology (7%)
• Anaesthetists sedated patients exclusively in theatre
• Most frequent technique midazolam and fentanyl
• Propofol, Diazepam, Ketamine, Alfentanil, Morphine and Remifentanil also used!
Prospective cohort adult study – data collection over a 28 day period

- 2132 patients included
- Sedation provided exclusively by consultant anaesthetists and supervised trainees
- Significant adverse events in 23%
- 1.2% 30 day mortality
Significant adverse events defined as:

- Significant airway obstruction requiring the use of airway device(s)
- Significant hypoxia (SaO$_2$ < 90%) not responding to jaw thrust and/or increased O$_2$ flow
- Systolic BP < 90mmHg requiring iv fluids +/- vasopressor
- HR < 55 requiring chronotropic agent
- Abandoned procedure
- Unplanned tracheal intubation
- CPR
- Duration of post procedure admission > 2 hours
Safety of sedation for gastrointestinal endoscopy in a group of university-affiliated hospitals: a prospective cohort study


2,132 Patients

7 (0.3%) No sedation

2,100 (98.5%) Propofol

562 (26.8%) Propofol alone

133 (6.3%) Propofol + midazolam

681 (32.4%) Propofol + opioid

625 (29.8%) Propofol + midazolam + opioid

99 (4.7%) Other combinations with propofol

25 (1.2%) No propofol

5 (20%) Midazolam alone

7 (28%) Opoid alone

7 (28%) Midazolam + opioid

6 (24%) Other combinations without propofol
• NIBP and SaO$_2$ monitoring used in 100% of cases
• ECG and ET CO$_2$ monitoring in 63% of cases

• Median dose of propofol 200 mg i.e deep sedation likely to have been achieved given the high usage of “co-induction” drugs
LMA Gastro
Anaesthetists are in short supply...

This creates “turf wars”

- Endoscopy (USA, Australia, Europe)
  - anesthesiologists vs nurse anaesthetists
  - anaesthesiologist vs endoscopists
- Emergency department (USA, Australia, UK)
- Dental clinics
  - sedation vs GA (Poswillo report)
Meet Maisie….

• She is 80, pretty fit and lives in the elegant Georgian seaside town of Sidmouth
• She has had two hip replacements
• This morning she leant forward, there was a sharp pain in her hip and she fell to the floor
• She was brought to hospital by ambulance and the nice doctors in ED have told her the hip is dislocated
• Fortunately they can give her a drug called propofol and sort her hip out
Maisie wants a “Quality Service”

- **Timely** - reducing waits and harmful delays for both those who receive and those who give care
- **Safe** - avoiding harm (to patients and staff)
- **Effective** - care based on scientific knowledge to all who could benefit and refraining from actions to those not likely to benefit
- **Efficient** - avoiding waste of equipment, supplies, ideas, and energy
- **Equitable** - care that does not vary in quality because of personal characteristics (gender, ethnicity, geographic location, and socio-economic status)
- **Patient Centered** - care respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions

*Crossing the Quality Chasm: A New Health System for the 21st Century, The Institute of Medicine, 2001*
If you had “insider knowledge” who would you want to “sedate” Maisie to relocate her hip??

- After all the procedure is simple and
- Surely the person administering the anaesthetic is excellent – after all they are a Doctor

Does it really matter?

- Obviously the adverse consequences are negligible – it's just a quick whiff!
What about the 4 hour trolley wait?
• 100 patients
• Mean age 73 (range 37 – 93)
• ASA fasting guidelines “used as a guide and not a rule”
• Bolus 1 mg /kg propofol after 3 minutes pre O₂
• Hip relocation attempted after 1 minute
• 96% success rate. “All recovered uneventfully”
• 8% desaturated (SaO₂ < 92%)
• 4% needed bag mask ventilation
• 4% vasopressor use

“The chances of dying in hospital as a result of a clinical error is 33,000 times more likely than dying in a plane crash” 1

“You’ll be fine!

“If healthcare was an airline, only dedicated risk takers, thrill seekers and those tired of living would fly on it” 2

1. Sir Liam Donaldson, Chief Medical Officer 2006
• The principal responsibility of the RCOA is to ensure the quality of patient care through the maintenance of standards in anaesthesia, pain management and intensive care
Letter to Governance Committee.....

• Applauded attempts to manage these patients expeditiously
• Not sedation but a GA in a remote site
• Loose adherence to the Trust’s fasting policy
• Lack of availability of skilled assistance
• 95% CI for a respiratory complication 2.6 – 13.4
• The complication rate appeared greater than other published studies
• Pointed out that a sample size of 1000’s was needed to convince him of the safety of this technique
Safe Sedation Practice for Healthcare Procedures

Standards and Guidance

July 2013
Practical components of good sedation

• The Target State
• Pre-assessment
  Inadequate pre-assessment is a recurring factor in sedation-related adverse events and poor outcomes for all specialties
• Consent
• Fasting
  Not required for single agent conscious sedation
  Fasting as for GA otherwise
• Choice of Technique
  For non-painful procedures sedation alone is sufficient
  Painful procedures usually require sedative + opioid
Practical components of good sedation

• The use of checklists to improve safety & quality
• The understanding of titration to effect
• Implications of the use of multiple drugs & infusions
• The elderly, frail or at-risk patient
• Monitoring, supplementary oxygen, capnography
• The Team and the Role of the Operator-Sedationist
Practical components of good sedation

• Educational and Training Standards
• Use defined methods of sedation following formal training to optimise safety
• Benefits of a sedation service/sedation committee within an institution - analogous to the Pain Management Team - main role education
• Audit and critical incident reporting
• Continuous quality improvement
• Sedation courses and the role of simulation
Adverse event reporting tool to standardize the reporting and tracking of adverse events during procedural sedation: a consensus document from the World SIVA International Sedation Task Force

K. P. Mason¹*, S. M. Green², Q. Picevooli³ and the International Sedation Task Force†

**Editor's key points**

- Sedation techniques vary and adverse events (AEs) are relatively rare.
- Absence of standardized definitions and terminology for sedation-AEs, impedes monitoring and comparison of outcomes.
- An International Sedation Task Force has addressed these problems.
- An event-reporting tool for sedation related AEs is presented for widespread adoption.
A standardized data collection tool to record the outcome of procedural sedation
## Tracking and Reporting Outcomes of Procedural Sedation (TROOPS)

A standardized quality improvement tool from the International Committee for the Advancement of Procedural Sedation

www.TROOPS-sedation.com

### No adverse events during sedation or recovery: (form completed)

- Positive pressure ventilation
- Naloxone or flumazenil
- Oral airway

### Sentinel

- Tracheal intubation
- Neumuscular blockade
- Pulmonary aspiration

### Suspected Etiology

- Apnea
- Respiratory depression
- Upper airway obstruction
- Laryngospasm
- Hypotension
- Bradycardia
- Cardiac arrest
- Seizure or seizure-like movements
- Patient active resistance or need for restraint
- Sedation complication
- Paradoxical response
- Unpleasant recovery reaction/ agitation
- Unpleasant recall

### Intermediate

- Bolus IV fluids
- Chest compressions
- Vasoactive drug administration
- Death
- Neurological deficit

### Intermediate

- Anticonvulsant administration
- Sedation insufficient
- Escalation of care or hospitalization
- Provider dissatisfied
- Patient/family dissatisfied

### Presenting with INTERMEDIATE items can endanger patients if not promptly managed, or reflect suboptimal sedation quality or patient experience and warrant timely reporting with peer scrutiny.

### Sentinel

- Patient active resistance or need for restraint
- Sedation complication
- Paradoxical response
- Unpleasant recovery reaction/ agitation
- Unpleasant recall

### Sentinel Items are life-threatening and warrant immediate reporting and the highest level of peer scrutiny.

### Footnotes/Definitions

- The goal of the Tracking and Reporting Outcomes Of Procedural Sedation (TROOPS) form is to provide a standardized and practical tool intended for daily use to record procedural sedation adverse events, interventions, and outcomes relevant to the continuous assessment of patient safety and quality of care. This tool is intended for use by all types of sedation providers in all locations and for patients of all ages. It was developed by multidisciplinary consensus from the International Committee for the Advancement of Procedural Sedation (www.ProceduralSedation.com). Its elements can readily be incorporated into electronic medical records.

- TROOPS intentionally excludes time event durations and specific thresholds (e.g., vital signs, oxygen desaturation, capnography) in favor of interventions and outcomes, which are more objective, clinically relevant, and more reliably recorded.

- Positive pressure ventilation (PPV) includes bag-mask ventilation (BMV), bilevel positive airway pressure (BiPAP), continuous positive airway pressure (CPAP) and laryngeal mask airway (LMA).

- Pulmonary aspiration is inhalation of oropharyngeal or gastric contents into the trachea during sedation or recovery and the appearance of new respiratory signs and symptoms.

- Apnea is cessation of ventilatory effort.

- Respiratory depression is decrease in ventilatory effort.

- Upper airway obstruction is partial or complete obstruction of the upper airway responsive to airway positioning or oral/nasal airway placement.

- Laryngospasm is partial or complete closure of the vocal cords that is not responsive to airway repositioning or oral/nasal airway placement.

- Escalation of care includes significant prolongation of clinical care (including delayed discharge) or hospitalization due to sedation factors, including transfer to a higher level of care.

- Need for restraint is more than minor physical restraint on more than one, brief occasion.

- Paradoxical response is an unanticipated restlessness or agitation in response to sedatives.

- Unpleasant recovery reaction/agitation is abnormal behaviors during the recovery stage of sedation (e.g., agitation, delirium, hallucinations) which are distressing to the patient or providers.
How can we make sedation safer?

- Patient selection
- Patient assessment
- Suitable facilities
- Suitably trained personnel
Patient selection

- Able to understand and cooperate
- Extremes of age
- Patient information
- Informed consent
Patient assessment

Rigorous as for GA

• Medical and social history
• Examination
• Investigations
• The airway
Facilities

Suitable treatment and recovery areas

- Oxygen
- Suction
- Tipping trolleys
- Resuscitation equipment
- Resuscitation and reversal drugs
Personnel

• At least two trained and experienced members of staff

• Dedicated sedationist if multiple drugs or continuous i.v. infusion
Recovery

• Suitable facilities

• Trained staff

• Explicit discharge criteria

• Clear aftercare instructions
<table>
<thead>
<tr>
<th>Minimal Sedation Anxiolysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Responsiveness</strong></td>
<td>Normal response to verbal stimulation</td>
</tr>
<tr>
<td><strong>Airway</strong></td>
<td>Unaffected</td>
</tr>
<tr>
<td><strong>Spontaneous Ventilation</strong></td>
<td>Unaffected</td>
</tr>
<tr>
<td><strong>Cardiovascular Function</strong></td>
<td>Unaffected</td>
</tr>
<tr>
<td>Responsiveness</td>
<td>Moderate Sedation/Analgesia (&quot;Conscious Sedation&quot;)</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Purposeful** response to verbal or tactile stimulation</td>
</tr>
</tbody>
</table>

| Airway               | No intervention required                        |

| Spontaneous Ventilation | Adequate                                         |

<p>| Cardiovascular Function | Usually maintained                               |</p>
<table>
<thead>
<tr>
<th>Responsiveness</th>
<th>Deep Sedation/Analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Purposeful** response following repeated or painful stimulation</td>
</tr>
<tr>
<td>Airway</td>
<td>Intervention may be required</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>May be inadequate</td>
</tr>
<tr>
<td>Ventilation</td>
<td>Usually maintained</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Function</td>
</tr>
<tr>
<td>Responsiveness</td>
<td>General Anesthesia</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------</td>
</tr>
<tr>
<td></td>
<td>Unarousable even</td>
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<tr>
<td></td>
<td>with painful</td>
</tr>
<tr>
<td></td>
<td>stimulus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Airway</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>often required</td>
</tr>
</tbody>
</table>

| Spontaneous    | Frequently        |
| Spontaneous    | inadequate        |
| Ventilation    |                   |

| Cardiovascular | May be            |
| Function       | impaired          |
Defining the competencies for safe practice

.....practitioners intending to produce a given level of sedation should be able to rescue patients whose level of sedation becomes deeper than initially intended. Individuals administering moderate sedation/analgesia (“conscious sedation”) should be able to rescue patients who enter a state of deep sedation/analgesia, while those administering deep sedation/analgesia should be able to rescue patients who enter a state of general anesthesia.

Rescue of a patient from a deeper level of sedation than intended is an intervention by a practitioner proficient in airway management and Advanced Life Support..........
AIMS:

- To set standards for the training of non-anesthesiologists, physicians and nurses, who are going to administer sedation during GI endoscopy procedures
- To expand the specific knowledge, competence, and skills necessary for endoscopists and nursing staff for endoscopy sedation, and management of its complications, to ensure patient comfort and safety
- To support individual endoscopy departments, national societies, and official bodies in developing local or national recommendations and curricula
### Safe Sedation in the Emergency Department

<table>
<thead>
<tr>
<th>Depth of sedation</th>
<th>Minimum staffing levels</th>
<th>Competencies of sedating practitioner</th>
<th>Location and Facilities</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal sedation with Entonox</td>
<td>One Physician or Emergency Nurse Practitioner (ENP)</td>
<td>Current Immediate Life Support (ILS) or Advanced Life Support (ALS) certification or equivalent agreed locally</td>
<td>Anywhere within the Emergency Department (ED)</td>
<td>Pulse oximetry</td>
</tr>
<tr>
<td>Moderate sedation/analgesia (‘conscious’ sedation) using intravenous agents, typically benzodiazepines</td>
<td>One physician as sedationist and one Physician or ENP as operator and one Nurse</td>
<td>Current ILS or ALS certification and Local sign off for Level 1 sedation training*</td>
<td>Resuscitation room facilities****</td>
<td>ECG, NIBP, Pulse oximetry, The use of capnography is recommended</td>
</tr>
<tr>
<td>Deep sedation/analgesia</td>
<td>As above</td>
<td>Royal College of Anaesthetists initial assessment of competence and Local sign off for Level 2 sedation training**</td>
<td>Resuscitation room facilities****</td>
<td>Standards conforming to AABGI guidelines for general anaesthesia* and The use of capnography is mandatory</td>
</tr>
</tbody>
</table>

Propofol for adult procedural sedation in a UK emergency department: safety profile in 1008 cases


Summary of propofol sedation guideline

Perform an airway assessment
Fasting assessment
Consider the risk/benefit for at risk patients
Monitor oxygen saturation, electrocardiogram, respiratory rate, noninvasive blood pressure
Equipment check
Patient consent
Pre-oxygenation with $F_{1O_2}$ of 1.0 for 3 min
1 mg kg$^{-1}$ i.v. propofol bolus
Incremental top ups of 0.25 mg kg$^{-1}$ propofol as required
# Checklist for nurses and doctors performing procedures under IV anaesthesia

## PRE-PROCEDURE
- Consider propofol anaesthesia for joint relocation or cardioversion
- Perform an airway assessment (are you confident of being able to ventilate this patient if necessary)
- Consider risk/benefit of anaesthesia for at risk patients: the elderly, the morbidly obese and those with concomitant medical disease including: cerebrovascular disease, heart disease, lung disease, renal disease, liver disease and jaundice, bleeding disorders, full stomach.
- Obtain informed consent for the procedure
- Estimate patient weight (ideally weigh the patient)
- Move patient to the resuscitation room: monitor sats, ECG, RR and NIBP (the latter set for rpt every 5 mins)
- Cannulate patient
- Preparation of drugs; have atropine and metaraminol available. Check and record observations prior to procedure
- Equipment check: suction, pillow available, airway equipment

## FASTING
Record the patient’s fasting state in the boxes above. Comply with the RCoA guidelines: 2 hours for clear non-particulate and non-carbonated fluid; 6 hours for solid food.

## THE PROCEDURE
- Pre-oxygenate the patient with an FiO₂ of 1.0 for 3 minutes prior to anaesthesia. Alternatively get the patient to perform five vital capacity breaths
- Give 1mg/kg IV of propofol as a bolus (though less for DC cardioversion procedures)
- Continue allowing the patient breath on FiO₂ of 1.0
- Perform the procedure when patient unconscious i.e.not responding to command
- Give incremental top ups of 0.25mg/kg of propofol prn
- Gently ventilate if the patient remains apnoeic and O₂ sats fall <94% until saturation reads > 94%

## HIGHER RISK PATIENTS
- For the elderly or patients with cardiovascular or cerebrovascular disease or pre-standing hypotension:
  - Consider whether the sedation is safe
  - The patient should be preloaded with 500ml of saline solution via a large bore cannula and a blood giving set
  - Consider an initial bolus of 0.5 rather than 1mg/kg
  - Metaraminol should be drawn up by diluting 10mg in 20ml sodium chloride 0.9%, aiming to give boluses of 0.5mg for resistant hypotension
World SIVA adverse sedation event-reporting tool


<table>
<thead>
<tr>
<th>World SIVA adverse sedation event recording tool configured for a webpage or paper form. Completion of this tool requires execution of all five steps. Responses to each step will often occupy different columns.</th>
</tr>
</thead>
</table>

**Step 1:** Was there one or more adverse events associated with this sedation encounter?
- No, this form is now complete.
- Yes, fill out remainder of form below.

**Step 2:** Please **DESCRIBE** the adverse events(s). Check all that apply.

### Minimal risk descriptors
- Vomiting / Retching
- Subclinical respiratory depression
- Muscle rigidity, myoclonus
- Hypersalivation
- Paradoxical response
- Recovery agitation
- Prolonged recovery

### Minor risk descriptors
- Oxygen desaturation (75–90%) for <60 s
- Apnoea, not prolonged
- Airway obstruction
- Failed sedation
- Allergic reaction without anaphylaxis
- Bradycardia
- Tachycardia
- Hypotension
- Hypertension
- Seizure

### Sentinel risk descriptors
- Oxygen desaturation, severe (<75% at any time) or prolonged (<90% for >60 s)
- Apnoea, prolonged (>60 s)
- Cardiovascular collapse/shock
- Cardiac arrest/absent pulse

**Step 3:** Please note the **INTERVENTIONS** performed to treat the adverse events(s). Check all that apply.

### Minimal risk
- No intervention performed
- Administration of:
  - Additional sedative(s)

### Minor risk
- Airway repositioning
- Tactile stimulation or the administration of:
  - Supplemental

### Moderate risk
- Bag valve mask-assisted ventilation
- Laryngeal mask airway
- Oral/nasal airway

### Sentinel intervention
- Chest compressions
- Tracheal intubation or the administration of:
  - Neuromuscular block

- Other, specify below
Indications for ED propofol sedation.

- Sentinel adverse event rate of 1.1% (95% CI 0.5–1.7), with no adverse outcomes
  - 5 hypoxia
  - 6 hypotension requiring vasopressors
New agents - Dexmedetomidine

- Available in the UK from October 2011 - licence - Sedation in ICU
- Full agonist $\alpha_{2b}$-adrenoceptor subtype
  Produces analgesia and sedation without respiratory depression or paradoxical confusion
- Produces “arousable sedation”
  *Sedated patients appear asleep, but are rousable and co-operative to verbal command – and then go back to sleep*
- MAC - sparing (25% - 70%)
- Causes more bradycardia and less hypotension than clonidine
- Reduction in dosage of volatile anaesthetic and opioid drugs
- Significant decreases in the incidence of:
  *delirium and agitation (and possibly cognitive impairment)*
  *opioid requirements (and opioid-induced hyperalgesia)*
  *nausea and vomiting*
Dexmedetomidine - pharmacokinetics

- Slow onset time and variable offset. Offset is strongly context sensitive
- Not a drug that is easy to use if you are in a hurry, or during an operating list that requires a rapid turnover
- Time to achieve a peak effect is at least 10 minutes after the attainment of adequate plasma levels of the drug
- Thus very easy to overshoot when titrating dosage to clinical effect

Sleigh J. *Anaesthesia* 2012, 67, 1189–1201
One suggested sedation recipe – 70 kg man

- Dilute dexmedetomidine to a concentration of 4 µg/ml (one 200 µg ampoule in a 50-ml syringe)
- Start loading infusion at 50 ml/hr (200 µg/hr) for about 15 min, until the target sedation level is reached (typically requires ¼–½ the syringe (50–100 µg), and corresponds to effect-site levels of 0.7–1.0 ng.ml
- Slow the infusion to about 12.5 ml.hr (50 µg.hr) and adjust according to the sedation level required

For frail patients, or if used as part of a general anaesthetic technique:

*Halve the above regimen*

Sleigh J. *Anaesthesia* 2012, 67, 1189–1201
Target controlled sedation
Sedation for oocyte retrieval using target controlled infusion of propofol and incremental alfentanil delivered by non-anaesthetists

Edwards JA et al. *Anaesthesia* 2010;65:453-461

- Target controlled infusions require less interventions than intermittent bolus techniques
- Starting target concentration 1.4 μg/ml
  - Propofol concentration increased by 0.2 μg/ml increments to maximum of 2 μg/ml
- Analgesia with 250 μg increments of alfentanil to maximum of 1500 μg
- 4232 cases
  - No desaturation
  - 1 airway event (jaw thrust)
  - 1 transient apnoea
  - Equates to airway incident rate of 0.5 / 1000 cases (95% CI 0.1 – 1.6 / 1000 cases)
- 99% of patients would have the same method again
TCI sedation

Three Compartment Model

**Bolus Elimination Transfer (BET) algorithm**

- **B**olus injection
- **E**limination - Exponentially decreasing infusion rate
- **T**ransfer – Fixed rate infusion
Three Compartment Model plus an “Effect Site”

\[ I \quad V_2 \quad k_{12} \quad k_{21} \quad V_1 \quad k_{13} \quad k_{31} \quad V_3 \]

*V_2*  
Rapidly Equilibrating Compartment

*V_1*  
Central Compartment

*V_3*  
Slowly Equilibrating Compartment

Drug Administration

*Ve*  
Effect Site

\[ k_{10} \quad k_{1e} \quad k_{e0} \]

Hysteresis
Remifentanil/Propofol Synergism

(N = 49 Patients)

S = success (no response to skin incision)  F = failure (response to skin incision)

Fragen et al, data on file with Glaxo Pharmaceuticals
Remifentanil infusion rates for sedation

Note it takes 5 half lives (25 minutes) to reach a steady state with a fixed rate infusion.
Remifentanil infusion rates for sedation

- 0.2 μg/kg/min
  - Apnea likely
- 0.1 μg/kg/min
  - Respiratory depression
- 0.05 μg/kg/min
  - Little likelihood of respiratory depression
- 0.025 μg/kg/min
  - Few problems expected
  - Modestly analgesic
TCI remifentanil settings

- 0.5 – 1 ng/ml target concentration - analgesia
- 2 - 2.5 ng/ml target concentration - respiratory depression
- 5 – 6 ng/ml target concentration – apnoea likely
- 2ng/ml remifentanil blood concentration provides an analgesic effect equivalent to 66 – 70% nitrous oxide
Remifentanil sedation guidelines

• *Don’t titrate remifentanil to sedation.*
• Administer supplemental oxygen.
• Monitor carefully for ventilatory depression
• Treat ventilatory depression by turning off infusion.
  • Reversal of remifentanil with naloxone should almost never be necessary
• Decrease doses in elderly by around 50%
The Future? - SedaSys

Investigational sedation delivery system. The system is an investigational product limited by U.S. law to investigational use only.
One thousand ASA class I to III adults undergoing routine colonoscopy or OGD

RESULTS: 496 SED & 504 CSC. Area under the curve of oxygen desaturation was significantly lower for SED (23.6 s·%) than for CSC (88.0 s·%; P = .028). Patients were predominately minimally to moderately sedated in both groups. SED patients were significantly more satisfied than CSC patients (P = .007). Clinician satisfaction was greater with SED than with CSC (P < .001). SED patients recovered faster than CSC patients (P < .001). The incidence of adverse events was 5.8% in the SED group and 8.7% in the CSC group.
SEDASYS® Computer-Assisted Personalized Sedation System - P080009

New machine could one day replace anesthesiologists

Sedasys costs $150 – 200 per procedure compared to $2,000 for an anesthesiologist!

Non anesthesiologist delivered sedation with 1% propofol for upper and lower GI endoscopy
Quicker recovery leading to increased efficiency with decreased costs
Johnson & Johnson “pulled the plug “on Sedasys because of poor sales
Bedroom based anaesthesia!
Conrad Murray drops claim Jackson swallowed propofol

Lawyers for Dr Conrad Murray have stepped back from claims that Michael Jackson swallowed a fatal dose of propofol when he was out of sight.

The claim had been a key argument in Dr Murray's defence at the trial over the superstar's death. They may still argue he injected the dose himself.

The change came a day after the doctor who performed Jackson's autopsy said he could not have self-administered it.

Dr Murray has pleaded not guilty to involuntary manslaughter.
Conrad Murray 'responsible' for Michael Jackson's death

Michael Jackson's doctor made 17 flagrant violations when administering propofol to the star, an expert on the potent anaesthetic has told the court.

Dr Steven Shafer said the drug should never be used to treat insomnia and Dr Conrad Murray's negligence was directly responsible for Jackson's death.

The expert called Dr Murray "clueless" about the drug that contributed to the 50-year-old singer's June 2009 death.

Dr Shafer said Dr Murray's delay in calling an ambulance had been "completely and utterly inexcusable".
Why did MJ die?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Heart Blood</th>
<th>Hospital Blood</th>
<th>Femoral Blood</th>
<th>Vitreous</th>
<th>Liver</th>
<th>Gastric Contents</th>
<th>Urine</th>
<th>Urine Scene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol</td>
<td>3.2</td>
<td>4.1</td>
<td>2.6</td>
<td>&lt;0.40</td>
<td>6.2</td>
<td>0.13 mg</td>
<td>0.15</td>
<td>&lt;0.10</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>0.68</td>
<td>0.51</td>
<td>0.84</td>
<td>&lt;0.40</td>
<td>0.45</td>
<td>1.6 mg</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Diazepam</td>
<td>&lt;0.10</td>
<td>Present</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Norbifenfynol</td>
<td>&lt;0.05</td>
<td>---</td>
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<td>---</td>
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<td>---</td>
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<td>---</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.162</td>
<td>---</td>
<td>0.169</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.0046</td>
<td>---</td>
<td>---</td>
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<td>---</td>
<td>0.0066</td>
<td>0.025</td>
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<tr>
<td>Ephedrine</td>
<td>ND</td>
<td>---</td>
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<td>---</td>
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<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

D. Anderson
Supervising Criminalist II
7/15/09
Why did MJ die?

- Weighed 61.7 kg

- Propofol concentrations:
  Heart 3.2 mcg/ml, femoral vein 2.6 mcg/ml

- Lorazepam concentrations:
  Heart 0.162 mcg/ml, femoral vein 0.169 mcg/ml

- Midazolam concentration:
  Heart 0.0046 mcg/ml
Blood concentrations of lorazepam (in ICU)

Lorazepam concentrations:
   Heart 0.162 mcg/ml, femoral vein 0.169mcg/ml

In ICU patients the lorazepam EC$_{50}$ for:

- Ramsay sedation score 5 (Asleep responds to firm facial tap) = 0.152mcg/ml
- Ramsay sedation score 6 (Asleep and unresponsive to both firm facial tap and loud verbal stimulus) = 0.188mcg/ml
- Midazolam: 0.0046mcg/ml

0.152 mcg/ml = Ramsay 5
0.188 mcg/ml = Ramsey 6

Barr J et al. Anesthesiology  2001;95:286-298
A clinical dilemma.....

• A 51 year old patient is scheduled to receive sedation at a standalone private plastic surgery facility for a minor cosmetic procedure.

• She informs the nurses she plans to return to alone her home 25 miles away via taxi and has made no arrangements for any one to look after her that evening.

• What would you do?
Lorazepam is approximately twice as potent as midazolam

PROPOFOL AND MIDAZOLAM ACT SYNERGISTICALLY IN COMBINATION

T. G. SHORT AND P. T. CHUI
Why are anaesthetists in demand in all these areas?

Because we are the experts in the management of:

- The airway
- The breathing
- The circulation
Eat normally on the day of your appointment and avoid alcoholic drinks.

Take your routine medication as normal unless advised not to by the treating team.

A responsible adult escort must accompany you to your appointment, stay within the department during the procedure and escort you home after your treatment under sedation. Please expect to be in the hospital for approximately 2 hours.

It is essential that your escort gives attention to you and therefore should not be responsible for children, elderly and/or dependent relatives.

Arrangements must be made to ensure that you are supervised for 24 hours.

Your escort should be able to take you home in a private taxi or car. If either you or your escort appears to be unwilling or unable to comply with these requirements the sedation will not be administered.

Sensible clothing is advised, avoiding tight sleeves and high-heeled shoes. Please make sure your finger nails are clear of varnish or acrylic nails.

For the next 24 hours, you must not:
- return to work;
- drive any vehicle or ride a bicycle;
- consume alcohol;
- operate machinery (including kitchen equipment);
- climb heights (e.g. ladders, scaffolding);
- be in charge of other people;
- make important decisions (e.g. signing legal documents).

Patients who are trying to conceive, are pregnant or are breast-feeding must inform their surgeon in advance of their appointment.
Isobologram

Line of additivity

Inhibition

Synergism

Less

More
Dexmedetomididine in the ED

- 13 patients with acute behavioural disturbance in whom at least 2 attempts at sedation with other drugs had failed

- Effective in 2/5 - given loading dose only
  - 1 hypotensive

- Effective in 3/8 with infusion
  - 5 hypotensive, 1 bradycardia, 1 AF, 2 intubated!

Study was ceased for safety reasons because of the frequency and severity of adverse effects...