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Practice guidelines for sedation and analgesia management of critically ill children: a pilot study evaluating guideline impact and feasibility in the PICU

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ABSTRACT

Aims: The aim of this study was to develop and implement guidelines for sedation and analgesia management in the paediatric intensive care unit (PICU) and evaluate the impact, feasibility and acceptability of these as part of a programme of research in this area and as a prelude to future trial work.

Method: This pilot study used a pre–post design using a historical control.

Setting: Two PICUs at different hospitals in an Australian metropolitan city.

Participants: Patients admitted to the PICU and ventilated for ≥24 h, aged more than 1 month and not admitted for seizure management or terminal care.

Intervention: Guidelines for sedation and analgesia management for critically ill children including algorithm and assessment tools.

Outcome variables: In addition to key outcome variables (ventilation time, medication dose and duration, length of stay), feasibility outcomes data (recruitment, data collection, safety) were evaluated. Guideline adherence was assessed through chart audit and staff were surveyed about merit and the use of guidelines.

Results: The guidelines were trialled for a total of 12 months on 63 patients and variables compared with the historical control group (n=75). Analysis revealed differences in median Morphine infusion duration between groups (pretest 3.63 days (87 h) vs post-test 2.83 days (68 h), p=0.05) and maximum doses (pretest 120 μg/kg/h vs post-test 97.5 μg/kg/h) with no apparent change to ventilation duration. Chart audit revealed varied use of tools, but staff were positive about the guidelines and their use in practice.

Conclusions: The sedation guidelines impacted on the duration and dosage of agents without any apparent impact on ventilation duration or length of stay. Furthermore, the guidelines appeared to be feasible and acceptable in clinical practice. The results of the study have laid the foundation for follow-up studies in withdrawal from sedation, point prevalence and longitudinal studies of sedation practices as well as drug trial work.

Strengths and limitations of this study

- Detailed outline of the guideline development process based on the consensus paper and available evidence.
- Original dual site feasibility (pilot) study testing the impact of guidelines on patient, quality and practice outcomes.
- Generation of clinical and trial process data to inform future trial work.
- No firm evidence or 'cause and effect' can be concluded due to the pre/post study design and small sample size.

INTRODUCTION

Sedation and analgesia are necessary components in the care of all critically ill patients, especially those requiring mechanical ventilation. The main indications for their use include: to reduce patient pain, anxiety and agitation, induce amnesia, facilitate mechanical ventilation, prevent the displacement of endotracheal tubes, and decrease cellular metabolism.[1–3] The detrimental impact of poor sedation practices intensive care units (ICUs) has increasingly become a focus for researcher and clinicians. The impetus for this stem from concerns about under-sedation and over-sedation.[4] Both under-sedation and oversedation have the potential to lead to agitated patients with compromised short-term safety issues and impact on duration of ventilation and length of stay (LOS).[5 6] The consequences of prolonged use of sedative and analgesic agents in the ICU patient include central nervous system activation, gastrointestinal disturbances and sympathetic hyperactivity. These signs and symptoms have been related to tolerance and withdrawal phenomena and also hold implications for the patient's physical and psychological well-

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being as well as healthcare costs.[7–9] These risks are potentially amplified in the critically ill child in the paediatric ICU (PICU) due to the developing brain.[10 11] The aim of this study was to develop and implement guidelines for sedation and analgesia management in the PICU and evaluate the impact, feasibility and acceptability of these as a part of programme of research in this area and as a prelude to future trial work.

BACKGROUND

The 2006 consensus guidelines on sedation and analgesia in critically ill children established a standard for clinical practice in PICUs.[12] The guidelines' key recommendations include advice on a loading dose and administration for analgesia and sedation medication, the use of validated pain and sedation assessment tools, withdrawal assessment, and the inclusion of non-pharmacological interventions. Surveys of sedation and analgesia management in PICUs have identified a lack of specific protocols for sedation and analgesia management.[13–15] This research has also highlighted wide variations in physician practice, nursing assessment, pharmacological agents, as well as administrative methods and doses. Limited use of assessment tools has also been reported, and there were no measurements or guidelines for withdrawal of drugs.

A number of studies have attempted to evaluate the impact of sedation and analgesia guidelines in PICU; however, the results have been varied.[16–20] Each of the studies successively added to our knowledge and understanding of sedation and analgesia management in critically ill children. However, differences in guideline specifics, models of care and study design may have contributed to the varied outcomes observed in the studies and limited their ability to inform best clinical practice. The aim of this study was to develop sedation and analgesia management guidelines based on the 2006 consensus recommendation and test their impact on patient outcomes as well as feasibility and acceptability in practice as a prelude to rigorous trial evaluation of guidelines in practice.

METHODS

Aims and objectives of study

The aim of this study was to develop and implement guidelines for sedation and analgesia management in the PICU and, following this, evaluate the impact, and acceptability and feasibility of their use in the clinical setting.

Study design

This dual site study used a pragmatic pretest and post-test design to examine the feasibility and impact of the guidelines on patient and practice outcomes. A chart audit was used to assess the implementation fidelity and a (nursing) staff survey was conducted to ascertain staff perceptions of guideline utility and acceptability in practice. The requirement for consent was waived.

Setting

The study units were two eight-bed, mixed medical–surgical (not cardiac surgery) PICUs located at tertiary referral children's hospitals admitting patients from 0 to 16 years of age. Postregistration qualifications in either paediatrics, ICU or PICU, were held by approximately 48% of the nursing staff.

Sample and participants

The target population was all patients ventilated for ≥24 h within the PICU, aged more than 1 month and not admitted for seizure management or terminal care. All eligible patients were consecutively enrolled into the study. As the main aim of the study was feasibility and acceptability of guidelines rather than hypothesis testing, the statistical power of the sample was of reduced importance at this stage. Charts of patients in the post-implementation phase were the focus of the audit. All nursing staff were invited to participate in the survey gauging staff perceptions and use of the guidelines in practice.

Guideline development

The sedation and analgesia guidelines for this study were developed around an algorithm for each of the identified phases of sedation (see online supplementary appendix 1). The key recommendations of the guidelines developed and tested in this study were based on the key recommendations in the 2006 consensus paper which are summarised in table 1.[12]

A range of non-pharmacological strategies to minimise patient stress and pain and optimise comfort are supported by varying levels of evidence ranging from case studies to Cochrane systematic reviews. These were not new strategies, but it was important to incorporate them into the guidelines to promote a holistic approach to pain and sedation management and reflect the recommendations of the consensus guidelines. Strategies recommended were aimed at moderating the PICU environment where possible (ie, minimising high-intensity light and noise, ensuring rest periods);[21 22] minimising discomfort of invasive devices; regular repositioning and limb support with pillows, pressure relieving devices or swaddling;[23 24] monitoring and optimising hydration, nutrition and essential cares (eg, oral and eye care); supporting parental visitation and reassurance as well as therapeutic (non-technical) touch.[25 26]

New assessment scales for behavioural state, pain and withdrawal assessment were integral to the guidelines. These included the State Behaviour Scale (SBS),[27 28] the Multidisciplinary Assessment of Pain Scale (MAPS)[29–32] and the Opioid Benzodiazepine Withdrawal Assessment Scale (WAS).[33 34]

The three phases of sedation (acute, plateau and weaning) management were derived from patterns

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Table 1 Summary of 2006 consensus paper recommendations for sedation management of critically ill children

1. Non-pharmacological interventions	i. Any correctable environmental and physical factors causing discomfort should be addressed alongside the introduction of pharmacological agents
	ii. A normal pattern of sleep should be encouraged. Attention should be paid to lighting, environmental noise and temporal orientation of patients
2. Pain assessment and analgesic management	i. All critically ill children have the right to adequate relief of their pain. Local and regional anaesthetic techniques should be considered. A patient controlled analgesia (PCA) device may be useful in older children
	ii. Pain assessment should be performed regularly by using a scale appropriate to the age of the patient and routinely documented. The level of pain reported by the patient must be considered the current standard of analgesia. Patients who cannot communicate should be assessed for the presence of pain-related behaviours and physiological indicators of pain. A therapeutic plan for analgesia should be established for each patient and regularly reviewed
	iii. Recommended pharmacological agents for analgesia include opioids (eg, morphine, fentanyl) for the relief of severe pain, non-steroidal anti-inflammatory drugs (NSAIDs) for moderately severe pain, and paracetamol for mild to moderate pain
3. Sedation assessment and recommended or commonly used sedative agents	i. Adequate analgesia should be provided to all critically ill children regardless of the need for sedation. The use of clinical guidelines for sedation is recommended
	ii. The level of sedation should be regularly assessed and documented using a validated and age-appropriate sedation assessment scale. The desired level of sedation should be identified for each patient and regularly reassessed. Doses of sedative agents should be titrated to produce the desired level of sedation
	iii. Recommended pharmacological agents for sedation include midazolam or clonidine. Early use of enteral sedative agents (eg, chloral hydrate, promethazine) is recommended. Propofol should not be used to provide continuous sedation in critically ill children
4. Withdrawal syndrome assessment, prevention and management	i. The potential for opioid and benzodiazepine withdrawal syndrome should be considered after 7 days of continuous therapy
	ii. When subsequently discontinued, the doses of these agents may need to be routinely tapered

observed in a retrospective audit conducted earlier by the research team[35 36] and from the literature.[9 12 37–39] The guidelines reflect the dynamic nature of a PICU patient's admission and allow for movement between and within phases according to the patient's need, response and condition.

As the main aim of the guidelines was to improve consistency in medication practices, it was vital to get a consensus on prescribing practices within the study units. Even the authors of the consensus guidelines noted that there was limited evidence to draw on and the recommendations were based on knowledge of drug pharmacokinetics, case study reports, expert opinion and also the understanding of pain management, drug tolerance and withdrawal medicine. Morphine and midazolam are the most common analgesic and sedative agents used in PICUs[3 14 35 40] and the drugs of choice in the study units. They are typically used in combination as together they have a synergistic effect that often allows for use of lower doses. Midazolam doses can be reduced as much as 30–50% when combined with an opioid.[41] Nonetheless, prolonged and/or heavy sedation persists in critical care units, and as a result tolerance and withdrawal syndrome complicate recovery.

In the acute phase, the guidelines proposed a significant loading dose to achieve the desired analgesia and sedation goals, followed by regular patient assessment and incremental medication changes to achieve and maintain these goals. If the maximum dose allowed was reached (ie, 300 µg/kg/h for the past 4 h), then use of adjunct or alternative drugs was recommended (ie, clonidine, fentanyl). 'Drug cycling' has been reported to be helpful in the UK, where 25% of PICUs surveyed reported rotation of sedatives to minimise tolerance.[3] In another paper, consultant intensivists conducted biweekly chart reviews of each patient in the ICU and regularly changed their sedation regimens.[42] Although these authors imply success with drug tolerance, no numerical data was offered in support.

Once in the plateau phase, the key change in practice was the recommended conversion from intravenous to long-acting enteral agents. This approach is based on the principles of narcotic withdrawal where withdrawal syndrome is managed by conversion to an orally active drug with a longer half-life (such as methadone or diazepam) that has a more steady state serum concentration, more readily facilitating a slow tapering of the drug and minimising the severity of withdrawal symptoms or

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even development of the withdrawal syndrome.[43–46] The advantages of methadone are an oral bioavailability of 75–80%, allowing for oral administration, and a prolonged half-life of 12–24 h, allowing twice daily administration (*ibid*). There is a general reluctance to use diazepam for critically ill patients because of its long elimination and concerns about excessive and prolonged sedation. However, similar to methadone, diazepam's long-acting active metabolites theoretically should result in small changes in serum drug concentrations and may decrease fluctuations in sedation state and therefore be a more appropriate agent for long-term sedated patients.[39]

The formal acknowledgement of a sedation weaning phase with a dedicated assessment tool and tapering regime was new practice for the study units. No validated opioid or benzodiazepine weaning schedule was found; however, a consensus of opinion across the literature supports a daily reduction of 5–10% or an initial reduction of 20–40%, followed by a 10% reduction once or twice daily, depending on the patient response.[39 47] The protocol for sedation weaning incorporated into these guidelines approximated these recommendations.

Guideline implementation

The guidelines encompassed many changes in practice: new assessment scales, standardisation of practice, conversion to oral agents, algorithms and a discreet weaning pathway. In the interest of maximising staff understanding and uptake of the tools, a phased implementation process was adopted with the gradual introduction of each tool into the units, followed by orientation and implementation of the algorithm phases and medication administration. Staff in-services introducing the study and guidelines were held over an initial fortnight with phased introduction and implementation of each assessment tool over the following months. These were further supported by bedside education on tool use and supplemented by information and teaching aids on the units' computer system.

In practice, the PICU team set sedation and analgesia goals as part of the daily patient review and staff at the bedside (usually nurses) used the guidelines to achieve the set goals.

Outcome variables

Data were collected from all eligible patients over 24 months (12 months historical control and 12 months post-implementation), plus a break to allow for the implementation period. In addition to the main study outcomes, the pilot study collected outcomes to establish feasibility of the protocol and processes. The main study outcomes measured included total ventilation time (TVT), sedation doses and duration, LOS in the PICU, plus quality indicators, such as accidental extubation and readmission rates. It was important to establish that the outcomes were not adversely affected by the guidelines before considering larger and more extensive trial work. Feasibility data outcomes included the success of screening and recruitment strategies; data collection and entry processes; confirmation of Research Nurse time and cost, and produced further estimates of ventilation times and medication dosing, which can be used to finalise sample size requirements for the larger trial, and inform funding applications for same. Potentially confounding variables collected included patient age, gender, diagnosis and the Paediatric Index of Mortality (PIM2) as a measure of acuity. Nurses in the study setting routinely collect and record standard demographic and biophysiological patient measurements on the local computerised information system. The revised PIM2 is a simple model of mortality in PICU based on admission data and uses 10 explanatory variables.[48] Post-implementation compliance/fidelity was assessed by chart review using an audit tool based on the 19 key components of the guidelines. Adherence to 75% of the key components overall and then within each phase was nominally chosen as the minimum acceptable value for fidelity at this stage. However, the results whatever they were would inform any future implementation processes and trial work. Nursing staff perceptions of the guidelines were ascertained through administration of a researcher-developed survey with questions on ease of use, impact on practice, perceived benefit, facilitation of team management and promotion of nurse autonomy at the bedside. Staff members were also given the opportunity to comment on strengths and limitations of the guidelines.

Statistical analysis

Data were analysed using PASW V.18.0 (SPSS Inc.). Descriptive statistics were used for demographic data. Continuous values reported were medians and ranges due to the large spread of the data. Categorical variables were reported as counts and percentages. Non-parametric Mann-Whitney or Cross tabulation and Pearson's χ^2 were performed to compare groups. The probability of remaining ventilated between groups was analysed using survival analysis. Adherence to guidelines was reported in counts and percentages. The influence of diagnostic group on guideline adherence was analysed using Pearson's correlation and comparison of means using Student t test. Survey responses were reported in counts and percentages as well as significant themes derived from qualitative data.

RESULTS

During the two study periods (12 months each), 173 and 235 patients were ventilated in the respective preguideline and postguideline implementation periods. After screening for eligibility, 75 and 70 patients were enrolled into the pre and post groups. Seven patients were lost to the study in the post-test group because of deviation from research protocol (n=5), one group of parents did not consent to use the drugs, and one was transferred to

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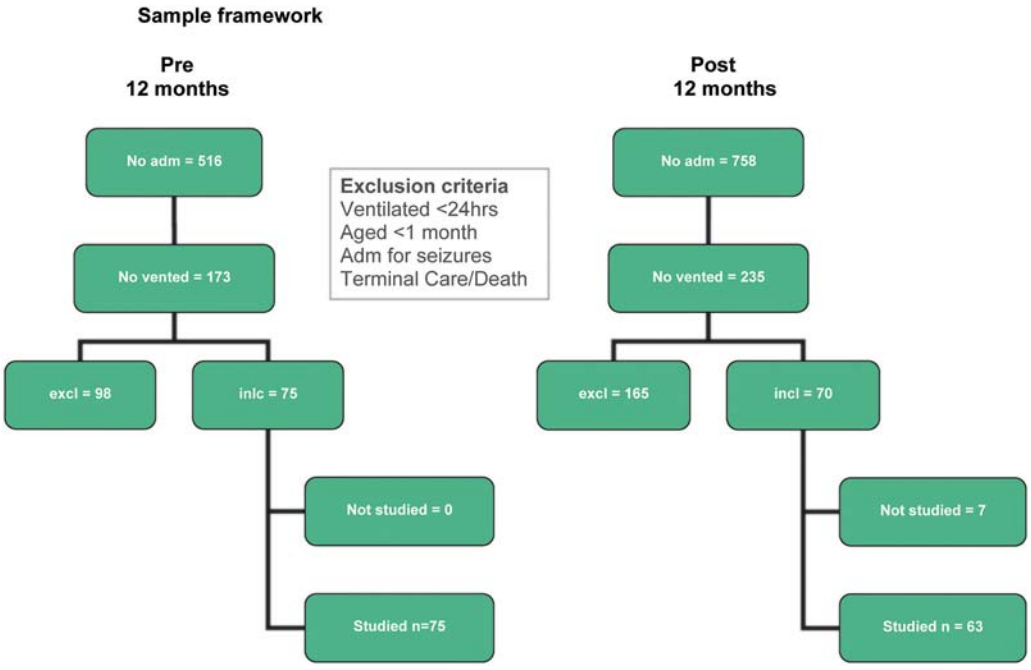

Figure 1 Sample framework (adm, admission; excl, exclusion; incl, inclusion).

another hospital. Ultimately, there were 75 in the control group and 63 in the post-implementation group. Data were analysed on a *per-protocol* basis. Figure 1 demonstrates the sampling framework and exclusion criteria.

Table 2 shows the main characteristics measured for each sample. Both groups were comparable with no significant differences between age, weight, sex or reason for admission. There were also no differences identified between the TVT and LOS for each group. There were no incidents of accidental extubation or readmission within 48 h for participants in either group for the study.

Table 3 shows the different drug characteristics between groups, demonstrating a greater variance in drug usage. The decrease of 19 h in the median infusion time of morphine between groups approached significance (87 vs 68 h, p=0.059). There were changes in the median minimum and maximum morphine doses, though not significantly. A reduction of 11 h was identified with median infusion of midazolam between groups; however, this difference was not significant. Significant changes in the median minimum and maximum doses of midazolam were observed (minimum 10 vs 17 µg/kg/h, p<0.001 and maximum 120 vs 180 µg/kg/h, p<0.001).

Applying the Kaplan-Meier curve of risk to the probability of remaining ventilated to each group demonstrated that the post-test group did not have an increased risk of remaining ventilated (see figure 2).

Table 2 Baseline characteristics in the study groups

	Pre, n=75	Post, n=63	Statistic
Age (years), median (IQR)	2.08 (5.6)	1.75 (4.5)	NS Mann-Whitney
Weight (kg), median (IQR)	11.5 (15.62)	12 (11)	NS Mann-Whitney
Sex, N (%)	Male, 45 (60%)	Male, 38 (60%)	NS χ^2
Primary diagnosis, N (%)	Resp, 29 (39%)	Resp, 21 (33%)	NS χ^2
PIM, median (IQR)	5.00 (9)	5.20 (5.3)	NS Mann-Whitney
TVT (days), median (IQR)	4.02 (5.36)	3.12 (7.68)	NS Mann-Whitney
LOS (days), median (IQR)	6.3 (6.76)	5.8 (7.90)	NS Mann-Whitney

NS=not statistically significant, that is, p≥0.05.
LOS, length of stay; PIM, Paediatric Index of Mortality; TVT, total ventilation time.

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Table 3 Outcome variable comparison between study groups

	Pre, n=75 Median (IQR)	Post, n=63 Median (IQR)	Difference and statistic
Morphine			
Infusion duration (h)	87 (136.5)	68 (78)	−19 h p=0.059
Minimum dose (μg/kg/h)	10 (11)	17 (10)	+7 μg /kg/h NS
Maximum dose (μg/kg/h)	120 (102.25)	97.5 (52.75)	−22.5 μg /kg/h NS
Midazolam			
Infusion duration (h)	71 (154)	60 (90)	−11 h NS
Minimum dose (μg /kg/h)	10 (12)	24 (20)	+14 μg/kg/h p<0.001
Maximum dose (μg/kg/h)	120 (101.75)	180 (143.25)	+60 μg/kg/h p<0.001

NS=not statistically significant, that is, p≥0.05.

The probability of remaining ventilated was reduced in the post-test group (by just less than a day at 21 h); however, this was not statistically significant.

Other observed changes in practice were the greater use of adjunctive and alternative medication, in particular methadone. Results showed that, prior to the guideline implementation, there was limited use of alternative medications (1–2 alternative medications or even none). Post-guideline implementation the numbers of alternative medications used increased. A more detailed analysis revealed a significant difference with the use of methadone pre 3%—post 33%, p<0.001; diazepam pre 5%—post 25%, p=0.001; chloral hydrate pre 32%—post 58%, p=0.002; propofol pre 60%—post 20%, p<0.001; and neuromuscular blockade agents pre 60%—post 47.6%, not significant.

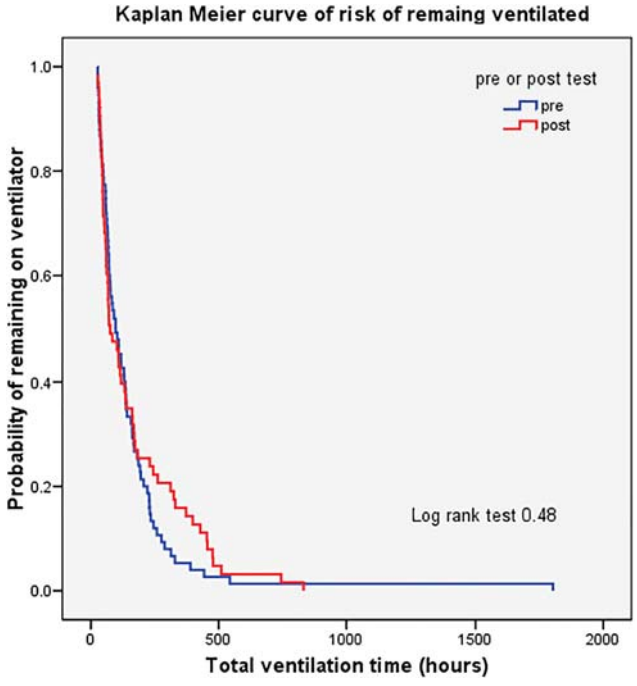

Figure 2 Kaplan-Meier curve of risk of remaining ventilated between groups.

Implementation fidelity (chart audit)

Sixty-three charts from the post-implementation period were reviewed to identify the level of staff adherence to the 19 key components of the guidelines and quantify the level of assessment and scoring. Overall adoption was achieved in 23 (36%) of the charts audited. Separate analysis within each of the phases demonstrated that adoption was achieved in 30 (47.6%) in the acute phase, 23 (36.5%) in the plateau phase and 25 (39.7%) in the weaning phase. Pain and sedation scores were assessed and documented in 95% (n=60) of charts in the acute and plateau phases, and in 85% (n=54) of charts in the weaning phase. The withdrawal score was assessed and documented appropriately in 75% (n=47) of charts.

Staff survey

The response rate was 49% (n=54). Participants' responses were divided into four categories: awareness/use, strengths, limitations and suggestions for improvement. Fifty-two (96%) respondents stated they regularly referred to the guideline to assist with decision-making and to provide prompts and cues. There appeared to be some confusion as to who was primarily responsible for the initiation of the guidelines, with 12 (23%) suggesting that it is was the consultant's responsibility and 32 (60%) stating that it was the responsibility of the bedside nurse. Table 4 outlines further responses.

The perceived strengths of the tool included the structured nature of the guidelines, promotion of consistency in practice and the resulting increased awareness regarding sedation management. Conversely, the perceived limitations included the perceived complexity of algorithm, confusion with delineation and movement between phases, and the lack of accommodation of increased drug tolerance with long-term patients. Staff suggested simplifying the algorithm and using larger print, incorporating recommendations for short-term patients and providing clinical example as guides. Box 1 provides a sample of staff comments on the perceived strengths and weaknesses of the guidelines. Overall, four major themes were expressed by study participants (see box 1): (1) a knowledge deficit about some aspects of the

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Table 4 Staff perceptions of sedation guidelines in practice

Questions	Yes response n=54 (%)
The sedation guidelines and flow chart are easy to follow	58.5
The flow chart facilitates the sedation management process	87
Patients benefit from having a constructive escalation programme	96.3
Patients benefit from having a constructive titration programme	94.3
Patients benefit from having a constructive weaning programme	96.2
A multidisciplinary approach enhances sedation management	96.3
The guidelines give me more autonomy in managing sedation	68.5
The guidelines improve overall sedation management	88.5

guidelines, (2) high value placed on individualised patient care, (3) perceived ineffectiveness of the guidelines for some patients and (4) disagreement between doctors and nurses on responsibilities.

Box 1 Staff perceptions of strengths and limitations of sedation guidelines

Strengths
- The bedside nurse 'knows' the patient and their requirements, can initiate changes, use objective data on the screen, see changes and ask for a review if needed
- It is a clinical tool to justify an increase or decrease in sedation. Allows for uniform/consistent decision-making
- Empowers and rationalises nursing changes in sedation
- Everyone using the same guide should translate to more consistent care. There is more autonomy for nurses, particularly with less experienced registrars. It potentially irons out variations in individual consultant preferences
- It has increased the awareness among staff and prompts discussion
- It places importance on sedation and assists nurses to provide better sedation. Patients more comfortable equals parents more comfortable

Limitations
- Can be complicated because of the amount of detail
- Needs definitions and differential diagnoses for each of the phases
- Not all patients fit the guidelines or respond as predicted
- Requires full concentration with attention to detail and practice to become familiar
- Lack of medical leadership/ownership shared
- Difficult to continue in ward, particularly with weaning
- Have trouble with some long-term patients following the guidelines and keeping them comfortable

DISCUSSION

This pragmatic pilot study demonstrated the use of guideline-directed sedation and analgesia management was not associated with increased ventilation times or PICU LOS. The results of the study also showed that the guidelines were generally feasible and acceptable in clinical practice with predominantly positive feedback from nursing staff using them. Full adoption of all aspects of guidelines was not realised, but results demonstrated improved levels of patient assessment and increased use of enteral agents (in line with guideline recommendations).

The observed increases in median minimum and maximum doses of morphine and midazolam do not appear to be associated with an increase in patient TVT or LOS, and in fact the duration of each infusion was reduced. Similar changes in medication administration have been observed in other PICU guideline studies.[16–20]

The results of the Kaplan-Meier Risk analysis indicate that there was potentially a reduced risk of remaining ventilated in the post-test group (though this was not statistically significant). However, a median difference of 21 h between groups may be viewed as 'clinically significant' as this time difference in the clinical setting could translate to earlier extubation and/or discharge. Larger randomised trial studies are warranted to allow firm conclusions to be made.

Only a small proportion of participants were ultimately eligible for the study (43% and 31%, respectively), which has implications for the projected timeline, research assistant time and costs and data collection for a larger multisite trial. The results also revealed the huge spread of the clinical data and the challenge this posed for researchers. Follow-on studies would possibly need to consider subcategories of patients, that is, short-term, medium-term and long-term ventilated, and analyse them within these categories.

The guidelines and implementation process in this study also appear to have increased the awareness and usage of alternative medications to complement or replace morphine/midazolam. This was particularly evident with the use of methadone and diazepam. Use of methadone rose from 3% pretest to 33% post-test. Use of diazepam rose from 5% pretest to 25% post-test. One of the key recommendations to emerge from the literature, and therefore included in the guidelines, was the transition from continuous intravenous analgesia and sedation to regular oral agents. Prolonged administration of opioids and benzodiazepines may result in the development of drug tolerance and then withdrawal syndrome if these agents are abruptly discontinued.[9 38 49 50] Research has shown that this can be prevented by slowly tapering the intravenous administration of the drug or switching from intravenous morphine and midazolam to orally active drugs with a longer half-life, such as methadone and diazepam.[44 46] In general, the increased use of adjunct medication was evidence of the clinician's use of guideline recommendations.

Sedation, Pain and Withdrawal scores were all captured but difficult to summarise meaningfully as a

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research variable. We recommended that a useful variable for follow-up in studies would be to calculate the percentage of time each patient spent in a designated 'zone' and determining the appropriateness and success/failure of management accordingly.

The audit of implementation fidelity demonstrated that the assessment and documentation of patient's pain and sedation was well recorded, reflecting sound staff understanding and uptake of the new assessment tools. The adoption score for the withdrawal phase was the lowest of the three phases, which may have resulted from less familiarity and knowledge with the tool and phase. This is consistent with findings found in a review of similar studies.[51] Suggested reasons for non-adherence included complexity of the guideline or algorithm, staff not valuing or understanding the goal of the guideline and perceived redundancy of the guideline if the staff were already competent practitioners in this area (*ibid*). Potential solutions to these issues included ongoing staff education and timely feedback related to the guideline to continuously reinforce importance, ease of use and troubleshoot issues.[52] In addition to surveying staff opinion, it is also important to conduct periodic chart audits to quantify guideline fidelity. This will help minimise self-report bias as was reflected somewhat in this study.[53] Staff perceptions of guideline principles and use were positive, although the level of adherence was variable. So the full impact of the guidelines was not realised.

In conjunction with the audit, a survey of nursing staff perceptions and attitudes was undertaken to establish if these influenced adoption of the guidelines. In line with other similar studies, nurses were largely positive and constructive in their feedback.[18 16 54] All feedback has been utilised to improve the guidelines. Involving staff and providing feedback during the process of procedural change is a vital step in optimising follow trial success and ultimately translation to practice. Follow-on trials should also build in mechanisms to capture multidisciplinary staff experience and feedback.

The importance of the findings of this study is that they indicate that collaborative guidelines can be used to manage the PICU patient's comfort and pain without compromising quality of care (TVT, LOS, quality indicators). The results are similar to those in the adult population where guideline or protocol-driven sedation has been linked to a reduction in duration of continuous intravenous sedation, ventilation time and associated healthcare costs.[55–59] Evaluation of feasibility outcomes has aided in the development of a realistic plan regarding participant recruitment, staff education to optimise guideline fidelity, safety of guidelines in clinical practice and collection of key outcome variables.

IMPLICATIONS AND RECOMMENDATIONS

No definitive causal effect can be attributed to the guidelines on outcomes due to the pre–post study design and small sample size. Full adoption of all phases and tools in the guidelines was not realised and this has implications for ongoing implementation and larger trial work. Additionally, the small response rate and selective population for the survey may introduce some bias in the current understanding of staff acceptance of the guidelines. A more inclusive (medical and nursing) survey population is recommended for follow-up research. Conducting the study in two units assists with the generalisability of the study and its results. Some specifics of the guidelines and algorithm, however, might need modification to reflect local practice, for example, use of different drugs (fentanyl instead of morphine) and different patient populations (post cardiothoracic surgery).

The study results are most useful in informing the structure and outcome measures for a follow-on clinical trial in this area.

Results from the study, audit and survey have informed changes and modifications to optimise staff understanding and use of sedation guidelines in practice. Weaning from sedation agents and the concept of withdrawal appear to be areas of practice that need more attention. The researchers went on to trial and evaluate a revised withdrawal assessment tool and a study comparing the outcomes of dexmedetomidine versus midazolam is about to start. The study units plan to continue to use the guidelines and tools in their modified form pending the results of a larger trial work recently completed in the USA. The modern ICU is an important focus for quality improvement efforts. Guidelines cannot automatically guarantee improved quality of care; however, they do direct the clinician in the pursuit of this objective, particularly when supported by high-level evidence.

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Data sharing statement A copy of the guidelines is supplied as an appendix or can be made available by emailing Debbie.Long2@health.qld.gov.au.

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GUIDELINES FOR THE ADMINISTRATION OF SEDATION AND ANALGESIA IN MECHANICALLY VENTILATED CHILDREN

PURPOSE:
To outline the management of sedation and analgesia in critically ill children receiving mechanical ventilation.

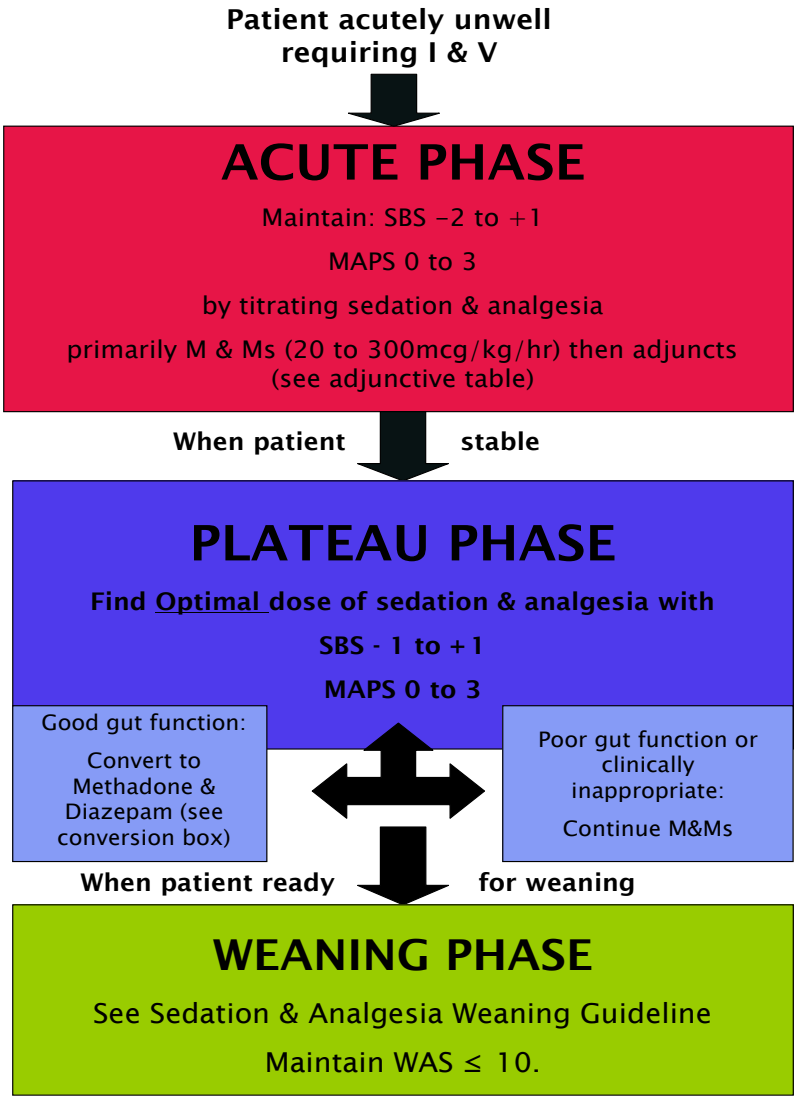
BACKGROUND / SUPPORTIVE DATA:
Sedation and analgesia are necessary components of the care of all critically ill children, especially those requiring mechanical ventilation. The main indications for the use of sedation and analgesia include: to reduce pain and discomfort, to reduce anxiety and agitation, to induce amnesia, to facilitate mechanical ventilation, to prevent the displacement of endotracheal tubes, and to decrease cellular metabolism. The consequences of prolonged use of sedative and analgesic agents in the PICU patient include central nervous system activation, gastrointestinal disturbances, and sympathetic hyperactivity. These signs and symptoms have been related to tolerance and withdrawal phenomena and hold implications for the patient's physical and psychological well being as well as health care costs.

Tolerance is one of the major reported adverse effects associated with continuous benzodiazepine infusions. Tolerance may be defined as a decrease in the effectiveness of a drug after prolonged use or as the requirement of larger doses to achieve the same effect. This phenomenon is due to an adaptation of neuronal cells and not a change of metabolism of the drug. One method of addressing this adverse effect, drug tolerance, is to recognise its occurrence and introduce alternative sedation agents titrated to an accepted sedation level.

A second adverse effect of the prolonged use of analgesic and sedation agents is withdrawal or abstinence syndrome. In paediatric patients, withdrawal syndrome is due to the development of tolerance to sedation and analgesic drugs not dependence or addiction. Studies have shown a strong positive correlation between large total doses of midazolam and the occurrence of withdrawal symptoms. Local, national and international audits have all shown that drug tapering is conducted in very few patients and that most patients have their sedation and analgesic agents abruptly discontinued. Thus, the incidence of withdrawal symptoms may be related to the infrequent tapering of sedation and analgesic agents.

There exists a plethora of literature discussing the adverse effects of sedation and analgesia in the critical care environment, particularly its prolonged use. There appears to be a consensus about the need and benefits of a systematic and coordinated approach to sedation administration, tapering and titration in the PICU.

SUMMARY OF SEDATION ALGORITHM:



EVIDENTIARY TABLE:

Strategy	Evidence
Use of protocol	The use of protocol directed sedation can reduce the duration of mechanical ventilation, ICU and hospital stay and can result in safe, cost-effective improvements.[1-5]
SBS – Sedation Scale	Reliable and valid scale for use in paediatric critical care.[6-8]
PICU MAPS – Pain Scale	Reliable and valid scale for use in paediatric critical care, particularly pre-verbal children.[9-12]
Withdrawal Assessment Scale	Combination of validated tool and Great Ormond Street Hospital protocol[13-18]
Accumulative dose	Up to 300 mcg/kg/hr for Midazolam
Weaning timeframes	[13, 19]
Mandatory review	[20]
Conversion to oral drugs	Diazepam, Methadone [24-26]

SUGGESTED PHARMACOLOGICAL TREATMENT OF PROCEDURAL PAIN AND DISCOMFORT:

Drug Group	Drug	Indications	Evidence
Topical Local Anaesthetic	Angel Cream EMLA	PIV/IAL insertion Venepuncture Arterial Stab Portacath access Lumbar puncture* CVL/ICC insertion*	[1-5]
	Lignocaine 2% & Chlorhexidine 0.05%	IDC insertion	[6, 7]
	Lignocaine 4%	Bronchoscopy*	[8, 9]
Sub-cutaneous injection	Lignocaine 1%	ICC/CVL insertion*	[2]
Disassociative Agent	Ketamine	CVL/ICC insertion Gastroenterology procedure Bronchoscopy Bone marrow aspiration Wound management procedure	[10, 11]
Short acting anaesthetic agent	Propofol	CVL/ICC insertion Gastroenterology procedure Bronchoscopy Bone marrow aspiration	[10, 12]
Short acting sedative & analgesic agent	Morphine & Midazolam	ETT Suctioning Movement/Position change	[30]

* used in conjunction with other drugs

SUGGESTED NON-PHARMACOLOGICAL MEASURES FOR OPTIMISING PATIENT COMFORT

Treatment	Evidence
Positioning & body support	[13-16]
Reassurance by staff and/or parents	[14]
Minimise discomfort of invasive devices (e.g. ETT, CVLs, and drainage tubes).	[14]
Optimise hydration, nutrition, essential cares (e.g. mouth, eye).	[17-19]
Massage, or rocking	[20, 21]
Swaddling	[22-24]
Non-nutritive sucking	[25-27]
Decrease external stimuli (noise, light, movement or handling)	[15, 28, 29]
Music therapy	[20]

SUGGESTED ADJUNCTIVE PHARMACOLOGICAL THERAPIES FOR MAXIMISING PATIENT COMFORT

Drug	Approach	Evidence
Propofol	2.5-3.5mg/kg stat then 7.5-15mg/kg/hr[30] ; 4-6mg/kg/hr[31]	[30-34]
Morphine	20mcg/kg prn	[30]
Midazolam	20mcg/kg prn	[30]
Ketamine	1mg/kg/hr	[30, 32, 33, 35]
Chloral Hydrate	25mg/kg q6h[36] maximum 5g	[35, 36]
Fentanyl	If allergic or renal failure 5-10mcg/kg/hrl	[30, 34, 35]
Promethazine	Oral 0.5mg/kg q6h Maximum 1mg/kg	[37]
Chlorpromazine	0.25-1mg/kg/q6-8h	
Clonidine	3-5mcg/kg q8h	[30, 35, 36, 38]
Haloperidol	0.1mg/kg- 0.1mg/kg q12h	[39]
Phenobarb	5mg/kg/day	[36]
Paracetamol	90mg/kg/24hrs- accumulation in hepatotoxic in pts with impaired LF-	[30]
Codeine	Max 1mg/kg/dose	[30]
Ibuprofen	10mg/kg q6h Precautions- asthma, renal impairment, under 6mths	[30]

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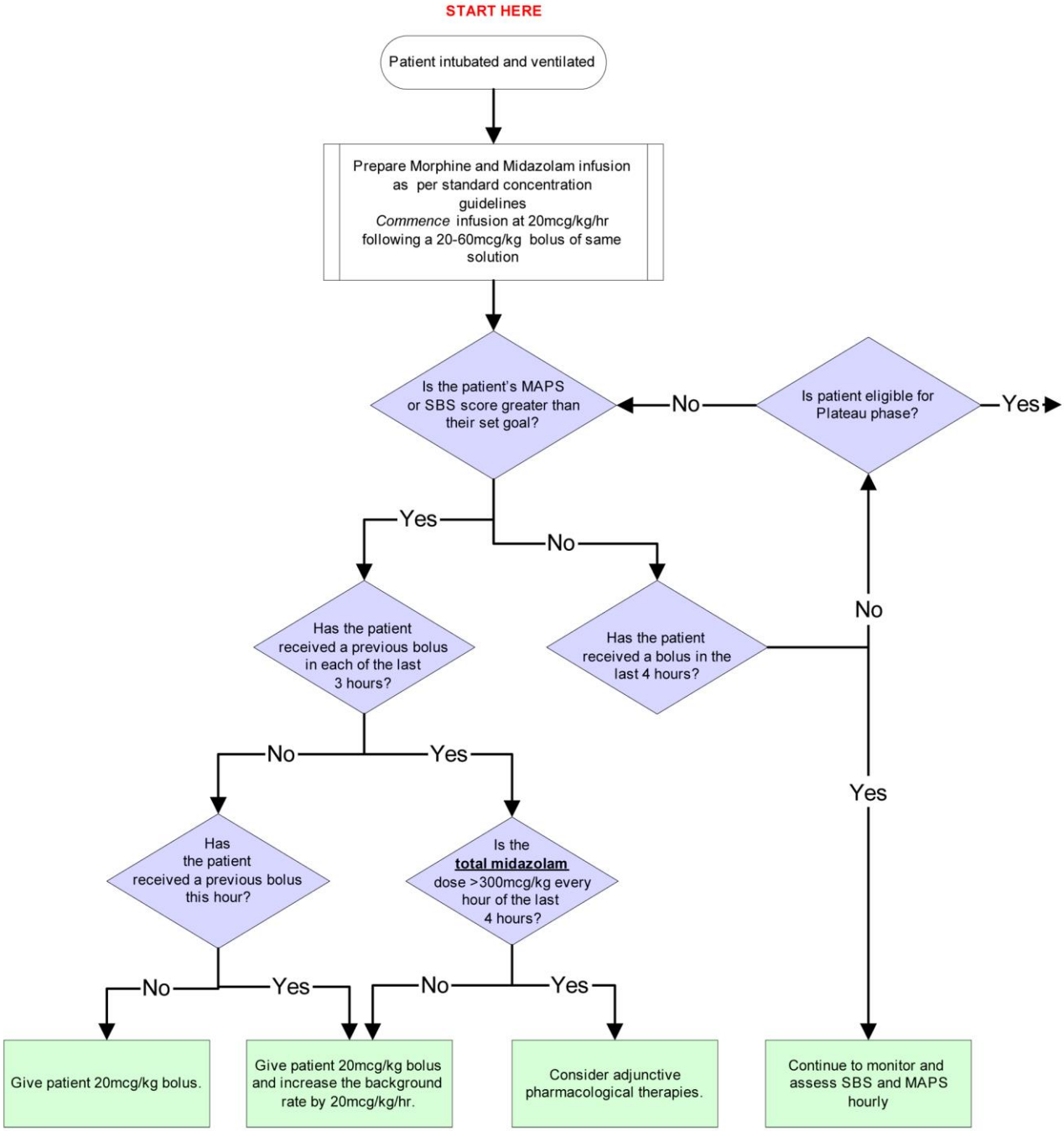
Acute Phase

DEFINITION:
Acutely unwell, new admission, expectation that illness/ injury will worsen, potentially unstable where poor levels of sedation would be detrimental to patient.
Eg. Raised ICP, onset of oscillation, return from OT.

GOALS:
Sedation: SBS -2 to -1
Pain: MAPS 0 to 3

DO NOT USE GUIDELINE IF PATIENT IS:
- Admitted for management of seizure activity
- < 1 year of age,
- has underlying renal impairment
- has a metabolic condition

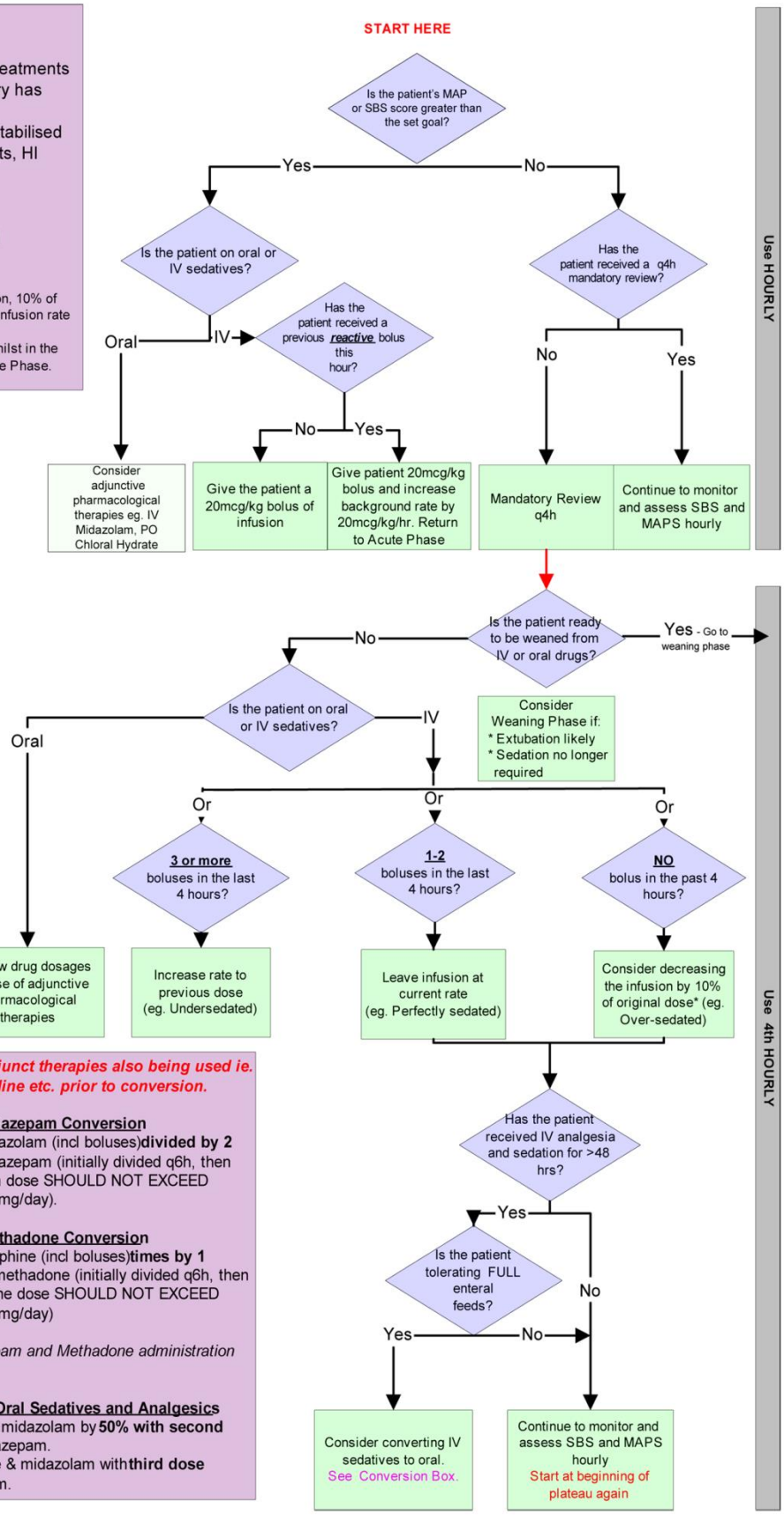


Plateau Phase

DEFINITION:
Patient stable, acute treatments completed, illness/injury has reached it's peak.
Eg. Sepsis resolving, stabilised ventilatory requirements, HI being rewarmed.

GOALS:
Sedation: SBS -1 to +1
Pain: MAPS 0 to 3

* When titrating the IV infusion, 10% of original dose means 10% of infusion rate when first reduction made.
If patient returns to theatre whilst in the plateau phase, return to Acute Phase.



Consider amount of adjunct therapies also being used ie. Chloral Hydrate, Clonidine etc. prior to conversion.

IV Midazolam to Oral Diazepam Conversion
Total mg/24hrs of IV midazolam (incl boluses)**divided by 2** = Total mg/24hr of PO diazepam (initially divided q6h, then b.d.) Maximum diazepam dose SHOULD NOT EXCEED 0.1mg/kg/dose (total =40mg/day).

IV Morphine to Oral Methadone Conversion
Total mg/24hrs of IV morphine (incl boluses)**times by 1** = Total mg/24hrs of PO methadone (initially divided q6h, then b.d.) Maximum methadone dose SHOULD NOT EXCEED 0.2mg/kg/dose (total =80mg/day)

Alternate/stagger Diazepam and Methadone administration times.

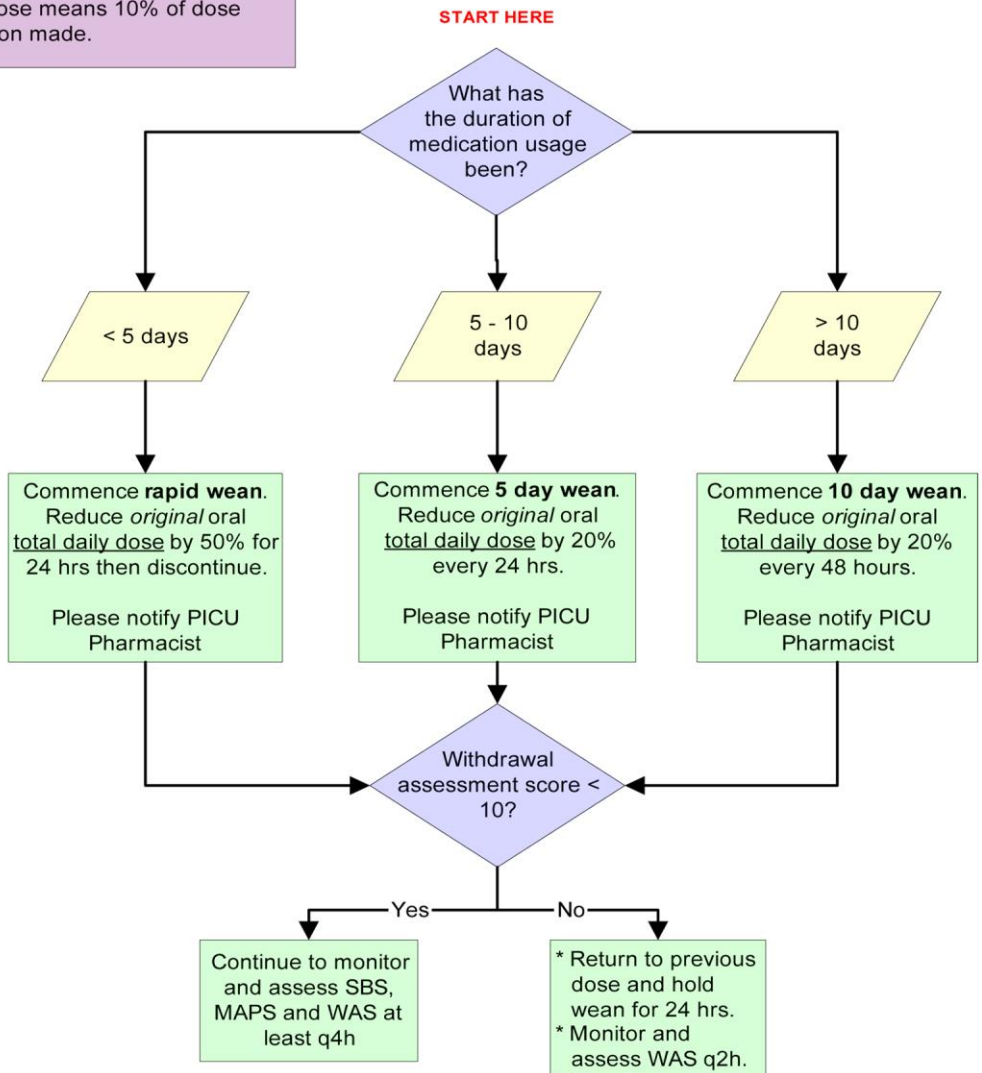
Conversion from IV to Oral Sedatives and Analgesics
Decrease IV morphine & midazolam by **50% with second dose** of methadone & diazepam.
Discontinue IV morphine & midazolam with **third dose** of methadone & diazepam.

Weaning Phase

DEFINITION:
When weaning from sedative and analgesic agents is required.
Eg. Imminent PICU discharge, no longer ventilated.

GOALS:
Sedation: SBS 0 to +3
Pain: MAPS 0 to 3
Withdrawal: <10

10% of original dose means 10% of dose when first reduction made.



Weaning Tips

- The above strategies offer approximate timeframes for weaning.
- A total daily dose can be reduced by changing the dose AND/ OR the frequency
- The minimum dose of Methadone at any time SHOULD NOT be below 0.5mg (0.1mls)

Example of 5 day wean: (TDD = Total daily dose)
Day 1: TDD 50mg - 12.5mg q6h
Day 2: TDD 40mg - 10mg q6h
Day 3: TDD 30mg - 15mg b.d.
Day 4: TDD 20mg - 10mg b.d.
Day 5: TDD 10mg - 5mg bd OR 10mg daily