

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Presented as a Breakfast Symposium at the
44th ASHP Midyear Clinical Meeting and Exhibition

Monday, December 7, 2009
Las Vegas, Nevada

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Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

A G E N D A

- 6:15 a.m. – 6:45 a.m. **Buffet Breakfast**
- 6:45 a.m. – 6:50 a.m. **Welcome / Introductory Remarks**
Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP,
Program Chair
- 6:50 a.m. – 7:15 a.m. **Review of Pharmacoeconomic Considerations in the Intensive Care Unit (ICU)**
Sandra L. Kane-Gill, Pharm.D., M.S., FCCM, FCCP
- 7:15 a.m. – 7:40 a.m. **Applying Literature to Practice: The Pharmacist’s Role in Optimizing Cost-Effective Sedation in the ICU**
Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP
- 7:40 a.m. – 7:45 a.m. **Faculty Discussion and Audience Questions**
All Faculty

F A C U L T Y

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The faculty and planners report the following relationships:

Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP, Program Chair

Mr. Dasta declares that he has served as a consultant for Hospira and Baxter.

Sandra L. Kane-Gill, Pharm.D., M.S., FCCM, FCCP

Dr. Kane-Gill declares that she has served as a consultant for Codence and Hospira and has received a grant from Ortho McNeil.

Ron DeChant, M.S., B.S.Pharm.

Mr. DeChant declares that he has no relationships pertinent to this activity.

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

ACTIVITY OVERVIEW

It is commonly known that hospitalization costs for patients in the intensive care unit (ICU) are significantly higher than for patients on general patient care units. Drug costs are also higher for ICU patients than non-intensive care unit patients.

Pharmacoeconomic challenges continue to face health system pharmacists caring for patients especially in the ICU. In this symposium, highlights from the literature showcasing the importance of potential methods for analyzing drug therapy costs in ICU patients will be presented with a focus on sedation. Various factors that affect the optimization of therapy will be discussed as well as cost-effective strategies that pharmacists can utilize to manage ICU patients receiving intravenous sedation.

This educational activity will review best practices aimed at improving the management of intensive care patients receiving sedation treatment.

ACTIVITY OBJECTIVES

At the conclusion of this knowledge-based educational activity, participants should be able to

- Describe several methods of pharmacoeconomic analysis applicable to the intensive care unit (ICU).
- List at least three drivers of increased health care costs in the ICU.
- Summarize the existing pharmacoeconomic literature related to ICU sedation.
- Identify strategies that pharmacists can employ to optimize cost-effective therapy associated with ICU sedation.

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CONTINUING EDUCATION ACCREDITATION



The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1.0 hour (0.1 CEU) of continuing pharmacy education credit (ACPE activity #204-000-09-434-L01P).

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Available soon at <http://ashpmedia.org/symposia/sedation>

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Please note that individuals who claim CPE credit for the live symposium are ineligible to claim credit for the Web-based activity.

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Instructions for Processing CPE online at <http://ce.ashp.org>

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5. Enter the session code, which was announced during the activity, and select the number of hours equal to your participation in the activity. Pharmacists should only claim credit for the amount of time they participate in an activity.
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Date of Activity	Activity Code	Session Code (announced during the live activity)	CPE credit hours
Monday, December 7	09434		1

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Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Sandra L. Kane-Gill, Pharm.D., M.S., FCCM, FCCP

Associate Professor, Pharmacy and Therapeutics
University of Pittsburgh School of Pharmacy
Pittsburgh, Pennsylvania

Sandra L. Kane-Gill, Pharm.D., M.S., FCCM, FCCP received her baccalaureate pharmacy degree from Wayne State University in 1994. She completed an ASHP accredited pharmacy practice residency at West Virginia University Hospital. In 1998, she received her Doctorate of Pharmacy from the University of Toledo. Dr. Kane-Gill then pursued her Masters of Science in Pharmacy Administration with emphasis on Pharmacoeconomics and Health Outcomes at The Ohio State University, and she completed her Critical Care Fellowship at The Ohio State University. Upon completion of her training she joined the faculty of the University of Pittsburgh, School of Pharmacy, Department of Pharmacy and Therapeutics in the Center for Pharmacoinformatics and Outcomes Research in 2001. She was promoted to an Associate Professor in the School of Pharmacy in 2008. In addition, she is the Critical Care Patient Safety Officer at the University of Pittsburgh Medical Center, Department of Pharmacy.

Dr. Kane-Gill's research interests focus on economic, clinical, and humanistic evaluations for critically ill patients; specifically patient safety, quality of life in the critically ill, and developing models of cost for acute illness. She has served as Principal Investigator and Co-Investigator on several funded research grants in this area of study. Her work has been presented at several national and international professional meetings. She has published over 50 articles and book chapters.

Dr. Kane-Gill is committed to the education and training of future clinical pharmacists and researchers. She worked collaboratively to develop the first critical care elective at the University of Pittsburgh in the School of Pharmacy using human patient simulation. She has mentored several pharmacy residents in research projects. Dr. Kane-Gill is dedicated to the advancement of the profession of pharmacy through active membership in organizations such as the ACCP, SCCM, and the International Society for Pharmacoeconomics and Outcomes Research. Dr. Kane-Gill was recognized for her contributions to critical care medicine and pharmacy with her induction as a Fellow into the American College of Critical Care Medicine and as a Fellow in the American College of Clinical Pharmacy.

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Sandra L. Kane-Gill, Pharm.D., M.S., FCCM, FCCP

P R E S E N T A T I O N

A Review of Pharmacoeconomic Considerations in the Intensive Care Unit (ICU)

O V E R V I E W

Clinical, economic and humanistic outcomes are all important components to consider in the optimization of patient care. Assessing health care economic evaluations in the literature that pertain to agitation treatment options requires familiarity with types of evaluations. These include: cost minimization analyses; cost-effectiveness analyses; and cost-utility analyses. Further, an appreciation for the cost components considered in economic evaluations is important. Ideally, a detailed economic evaluation (i.e. micro-costing) is desirable, but in reality this information is not always available. Alternative approaches have been used to capture all relevant costs such as hypothetical cohorts and total cost of the ICU stay. The goal to optimal patient care is thinking beyond drug acquisition cost.

L E A R N I N G O B J E C T I V E S

At the conclusion of this knowledge-based educational activity, participants should be able to

- Describe the pharmacoeconomic analyses most often used that are applicable to the intensive care unit (ICU).
- List at least three drivers of increased health care costs in the ICU.
- Explain the utility of pharmacoeconomic data for sedatives in making patient care decisions.

A Review of Pharmacoeconomic Considerations in the ICU

Sandra Kane-Gill, Pharm.D., M.S.
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Objectives

- Describe the methods of pharmacoeconomic (PE) analysis applicable to the intensive care unit (ICU)
- List at least three drivers of increased health care costs in the ICU
- Explain the utility of PE data in making patient care decisions

How many audience members have a responsibility to perform some type of cost analysis as part of your job?

What is a Cost Effectiveness Analysis (CEA)?

- Compares cost and outcomes of two interventions
- All costs are related to a single, common effect
- Outcome is worth its corresponding costs
- Not designed to cut costs, but how to use health care resources better!

Why we need CEA/CUA*

- When outcomes are difficult to interpret...

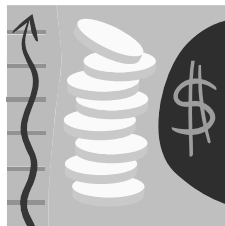
<u>Drug A</u>	<u>Drug B</u>
20 deaths	10 deaths
25 strokes	50 strokes
\$120,000	\$200,000

- Which drug is better?

*CUA = cost utility analysis CEA = cost effectiveness analysis

Consider ALL Relevant Cost Drivers of Drug Therapy

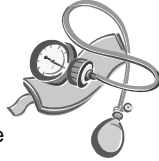
1. Acquisition cost
2. Waste cost
3. Preparation cost
4. Distribution cost
5. Administration cost
6. Toxicity cost
7. Monitoring cost



All relevant costs = Total cost of care

CEA Outcomes

- Intermediate Effectiveness Outcomes- surrogate endpoints
 - mmHg blood pressure reduction
 - % serum cholesterol reduction
 - Duration at a target sedation score
- Final Effectiveness Outcomes
 - Mortality, years of life gained, presence of disease, length of stay
 - Preferred but not easily measured



What is a Cost Utility Analysis (CUA)?

- Type of cost-effectiveness analysis
- Outcome - the number of life years saved adjusted to account for loss of quality from morbidity
- Utility is a measure of preference for a particular health state
- “Quality-adjusted life year” (QALY) – a health utility measure which combines quality with quantity of life

When should CUA be used?

- Quality of life is the important outcome
 - Primary purpose is palliative rather than curative
- Quality of life is an important outcome
 - Drug somewhat effective but also fairly toxic
- Intervention affects both morbidity and mortality
- Comparing interventions that have a wide range of different outcomes

MacKeigan LD et al. *AJHP* 1992;49:2236-2245.

Cost Minimization Analysis (CMA) - Definition

- Compares two or more treatments with assumed or demonstrated equivalency in efficacy
- Cost is measured in dollars
- Since efficacy is assumed to be equivalent, it is not measured
- Focus – determine the *least costly* treatment alternative

When to Use CMA?

When comparing...

- Different dosage forms/ dosing strategies of the same drug
- Generic versus branded drugs
- Drugs with a “class effect”

Template for an Ideal PE study

- Multidisciplinary panel of experts to determine treatment pathway
- Discuss all possible therapies (e.g., sedatives) for inclusion plus their dispensing, prescribing, administering, and monitoring costs
- Adverse drug events would be considered
- Perform multi-institutional, prospective, randomized controlled trial in a homogenous population with an adequate sample

Dasta JF, Kane-Gill SL. *Crit Care Clin* 2009;25:571-583.

Have you seen an ideal pharmacoeconomics study?

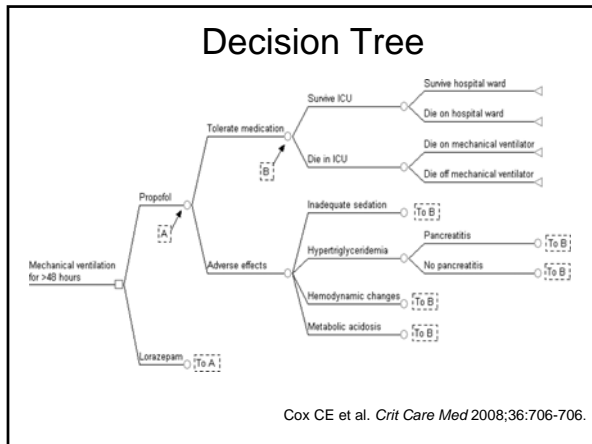
A more realistic approach?



But this is what we have...

- Hypothetical cohort studies
- Compare the expected costs of short, intermediate and long-term sedation with propofol, lorazepam and midazolam
 - Preparation, administration, adverse drug reactions (ADRs), therapeutic failures
- Compare propofol vs intermittent lorazepam and propofol vs midazolam
 - Acquisition costs, ICU and hospital costs, ADRs, professional costs

MacLaren R et al. *Pharmacotherapy* 2005; 1319-1328.
Cox CE et al. *Crit Care Med* 2008;36:706-706.



Enlarged version on page 18

- ### We also have....
- Evaluation of total hospital costs¹
 - Retrospective analysis of cardiac surgery patients in 250 hospitals
 - Midazolam plus propofol (n= 9996) and midazolam plus propofol plus dexmedetomidine (n=356)
 - Randomized controlled trial (RCT) with an economic component²
 - Dexmedetomidine and lorazepam
 - Not a formal economic analysis; costs accrued before randomization
- ¹ Dasta JF et al. *Pharmacotherapy* 2006;26:798-805.
² Phanharipande PP et al. *JAMA* 2007;298:2644-253.
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- ### And....
- Piggyback economic trial on RCT¹
 - Dexmedetomidine and midazolam
 - Considered: ICU costs, mechanical ventilation, ADRs, drugs
 - Pharmacoeconomic trials²
 - Midazolam and propofol
 - Considered: MD visits, RN time, diagnostic tests, drugs
- ¹ Dasta JF et al. *Crit Care Med* (epub ahead of print).
² Anis AH et al. *Anesthesiology* 2002;96:196-201.
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Lessons Learned

- Costs described in most studies have limitations
- Higher drug acquisition costs may not translate into increases in total hospital costs
 - Phanharipande PP et al. *JAMA* 2007;298:2644-253.
- More expensive therapies can have overall economic benefit to the institution
 - Muellejans B et al. *Crit Care* 2006;10:R91.
 - Dasta et al. *Pharmacotherapy* 2006;26:798-805.
- Selecting the least costly treatment may not be as easy as selecting one agent
 - MacLaren R et al. *Pharmacotherapy* 2005;25:1319-1328.

Dasta JF, Kane-Gill SL. *Crit Care Clin* 2009;25:571-583.

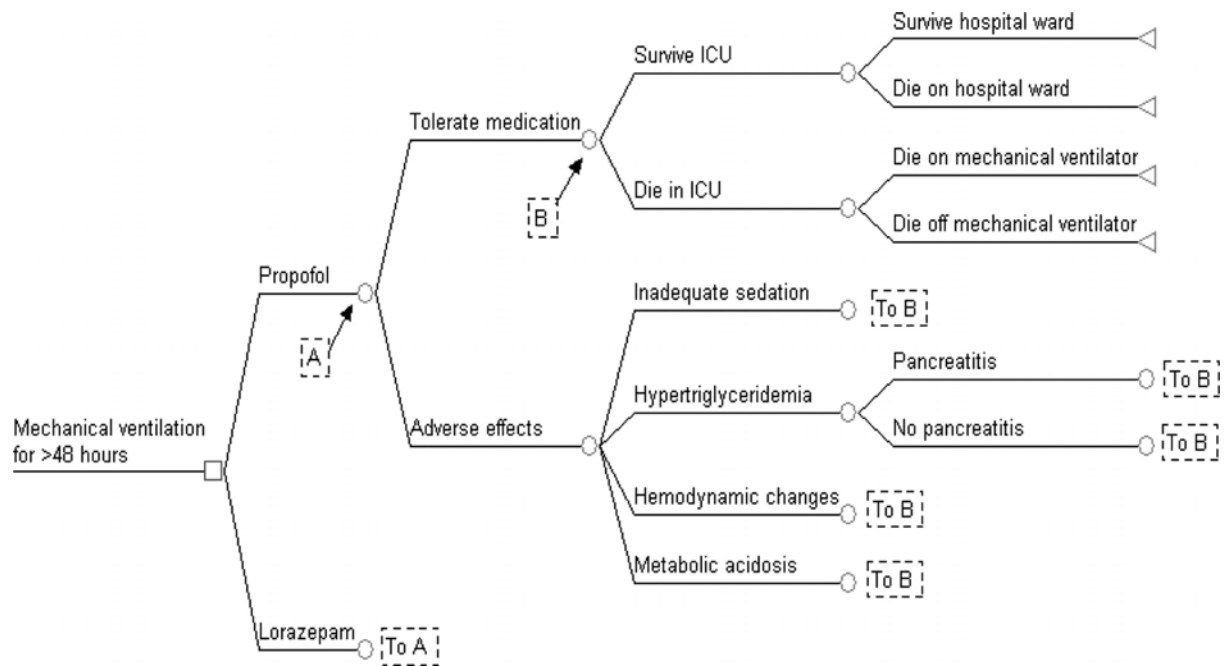
Patient Care Decisions

- Utility of PE Data = Economic outcomes of interest to your institution
 - Total cost of care
 - Length of stay
 - Duration of mechanical ventilation
 - Adverse drug reactions
 - Time spent at treatment endpoint
 - Cost of drug therapy (dispensing to administration)
 - Acquisition cost of the drug
- How do we balance clinical outcomes?
 - Mortality and time spent at goal therapy

Summary

- Understand the type of PE study being conducted & the limitations for applicability at your institution
- Ideal PE studies may not be realistic to perform so carefully evaluate the positives and negatives of what we have
- Determine cost drivers of interest to your institution for patient care utility
- Our goal should be total cost of care evaluations

Decision Tree



Cox CE et al. *Crit Care Med* 2008;36:706-706.

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2. Cox CE, Reed SD, Govert JA et al. Economic evaluation of propofol and lorazepam for critically ill patients undergoing mechanical ventilation. *Crit Care Med* 2008; 36(3):706-714.
3. Dasta JF, Kane-Gill SL. Pharmacoeconomics of sedation in the ICU. *Crit Care Clin* 2009; 25:571-583.
4. Dasta JF, Jacobi J, Sesti A et al. Addition of dexmedetomidine to standard sedation regimens after cardiac surgery: An outcomes analysis. *Pharmacother* 2006; 26(6):798-805.
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6. MacKeigan LD, Pathak DS. Overview of health-related quality-of-life measures. *Am J Hosp Pharm* 1992; 49:2236-2245.
7. MacLaren R, Sullivan PW. Pharmacoeconomic modeling of lorazepam, midazolam, and propofol for continuous sedation in critically ill patients. *Pharmacotherapy* 2005; 25(10):1319-1328.
8. Muellejans B, Matthey T, Scholpp J et al. Sedation in the intensive care unit with remifentanyl/propofol versus midazolam/fentanyl: a randomized, open-label pharmacoeconomic trial. *Crit Care Med* 2006; 10(R91):1-9.
9. Pandharipande PP, Pun BT, Herr D et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients. *JAMA* 2007; 298(22):2644-2653.

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SELF-ASSESSMENT QUESTIONS

1. If treatment options have comparable efficacy, which type of economic evaluation is appropriate to apply?
 - a. Cost minimization analysis.
 - b. Cost effectiveness analysis.
 - c. Cost utility analysis.
 - d. Cost outcome analysis.

2. Which economic evaluation requires a common effect of measurement?
 - a. Cost minimization analysis.
 - b. Cost effectiveness analysis.
 - c. Cost utility analysis.
 - d. Cost outcome analysis.

3. What cost component(s) should be considered in the evaluation of treatment alternatives?
 - a. Drug acquisition cost.
 - b. Drug acquisition and drug monitoring costs.
 - c. Drug acquisition and drug administration costs.
 - d. Drug acquisition, drug monitoring and drug administration costs.

Answers

1. a
2. b
3. d

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP, *Program Chair*

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University of Texas College of Pharmacy

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Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP is Professor Emeritus, The Ohio State University College of Pharmacy and Adjunct Professor, University of Texas College of Pharmacy in Austin, Texas. He retired from The Ohio State University (OSU) in 2007 after 31 years, and he currently resides in Austin. He serves as a health care consultant to pharmaceutical and device companies, and provides ICU pharmacy consulting services to Seton Medical Center Williamson County. Mr. Dasta has provided evaluation and insight into investigational and marketed drugs and devices, formulary evaluations, protocol development, and pharmacoeconomic perspectives.

Mr. Dasta was one of the first pharmacist members of the Society of Critical Care Medicine (SCCM) and helped establish the role of the pharmacist in this multidisciplinary society. SCCM honored him by creating the Joseph F. Dasta Critical Care Pharmacy Outcomes Research Grant in 2000. He was recently elected to a three-year term on council. He is a Fellow of the American College of Clinical Pharmacy and the American College of Critical Care Medicine. He serves on the editorial board of Critical Care Medicine and Annals of Pharmacotherapy, and he has more than 200 peer-reviewed publications, abstracts, brief communications, and book chapters. He has given over 250 lectures on various topics related to critical care and health outcomes. His research has focused on health economics and patient safety of acute care pharmaceuticals. Specific areas of interest include acute pain, sedation, sepsis, acute renal failure, acute heart failure, and hypertensive emergencies.

Mr. Dasta received his Bachelor of Science in pharmacy in 1974 from West Virginia University School of Pharmacy and M.S. and residency in hospital pharmacy from OSU in 1976. He was the 2008 recipient of the Jack L. Beal Post-baccalaureate Alumni Award from OSU. He began his academic career in 1976 at OSU and developed one of the first practice sites and post-doctoral training programs in critical care pharmacy. He has trained 11 residents and nine fellows who have become prominent practitioners, researchers, and leaders in the profession and in the pharmaceutical industry.

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Joseph F. Dasta, M.S., B.S.Pharm., FCCM, FCCP, *Program Chair*

P R E S E N T A T I O N

Applying Literature to Practice: The Pharmacist's Role in Optimizing Cost-Effective Sedation in the ICU

O V E R V I E W

While the ICU is an expensive location to deliver patient care, it is important to optimize therapy for the agitated, mechanically-ventilated patient. Optimal sedation can be achieved by administering the most appropriate sedative to achieve the target sedation goal. Acquisition costs of drugs are only one factor associated with the selection of the best drug for the patient. There are costs associated with suboptimal care in the agitated ICU patient. For example under-sedated patients may pull out tubes and lines. One study reported the 1997 cost of device removal was \$181 per event. These patients may also develop tachycardia and increase myocardial oxygen requirements resulting in an acute myocardial infarction. In contrast, over-sedation may be the cause of prolonged time on the ventilator and of delays in diagnosis for a neurologic disorder.

As a patient remains in the ICU, the average daily cost ranges from \$3000-4000 and incremental costs of mechanical ventilation averages \$1500 per day. Although there is an abundance of clinical literature on ICU sedation, there are only a few pharmacoeconomic studies in this area. There have been several studies evaluating the effect of sedative protocols on outcomes but few describe costs. One study reported a reduced length of ICU stay and a decrease in acquisition costs with implementation of a protocol on sedation, analgesia, and neuromuscular blockade. Pharmacists can be a driving force behind these ICU protocols by coordinating the ICU team to develop, implement, and update the protocol based on newly available data.

Two formal pharmacoeconomic evaluations of published clinical trials should be highlighted. In the first study, a decision analytic model was used to determine cost-effectiveness of sedatives from a trial of mechanically-ventilated patients randomized to receive intermittent lorazepam or propofol infusion. The most cost-effective regimen was propofol, resulting in lower hospitalization costs averaging \$6300, and nearly four more ventilator-free days. Propofol dominance was seen in 91% of the simulations. Finally, a cost-minimization analysis of a randomized clinical trial of mechanically-ventilated patients receiving either midazolam or dexmedetomidine for long-term infusion was conducted. Patients randomized to dexmedetomidine had total ICU costs that were \$9679 lower than patients receiving midazolam. This cost reduction was driven primarily from lower ICU and mechanical ventilation costs, despite the fact that median acquisition cost of dexmedetomidine was considerably higher than midazolam, which has been off patent for many years. ICU pharmacists can play a vital role in optimizing ICU sedation care by developing sedation guidelines and recommending the most cost-effective sedation strategy.

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LEARNING OBJECTIVES

At the conclusion of this knowledge-based educational activity, participants should be able to

- Compare and contrast cost-related factors associated with over and under-sedation.
- Describe the role pharmacists can play in ICU protocols at their institution.
- Describe cost-effectiveness of propofol vs. intermittent lorazepam.
- Evaluate total ICU costs associated with midazolam vs. dexmedetomidine in mechanically ventilated patients.

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

Applying Literature to Practice: The Pharmacist's Role in Optimizing Cost-Effective Sedation in the ICU

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Learning Objectives

- Compare and contrast cost-related factors associated with over- and under-sedation
- Describe role of the pharmacist in ICU sedation protocol development
- Describe cost-effectiveness of propofol vs. intermittent lorazepam
- Evaluate total ICU cost reductions of dexmedetomidine vs. midazolam

True or False?

If a patient is on a mechanical ventilator, then over-sedation is not a problem since the ventilator will "breathe" for the patient.

Causes and Costs of Over-sedation

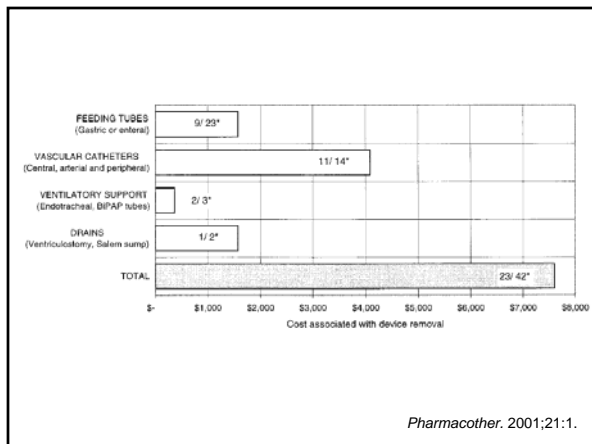
- Excessive and prolonged dosing of opioids and benzodiazepines
- Inexpensive treatment: reduce dosage
- Adverse drug events (ADE) with naloxone or flumazenil
- May require CT scan/neurology consult
- Expensive consequence: \$1500/day incremental cost of mechanical ventilation

Crit Care Clin. 2009;25:571.

Causes and Costs of Under-sedation

- Tachycardia, increased mixed venous oxygen saturation (MVO₂)
- Worsening myocardial ischemia
- Short and long-term psychological effects
- Cost of device removal
 - 10 patients removed 42 devices (GI/vascular)
 - 74% were “significantly agitated” 2 hr before
 - Total \$7606 or \$181/event (1997 costs)
 - Did not include 6 more ICU days (11.4 vs. 4.7)

Crit Care Clin. 2009;25:571, Pharmacother. 2001;21:1.



Pharmacother. 2001;21:1.

Enlarged version on page 33

How many of you have implemented protocols at your institution?

- Pneumonia/sepsis protocols
- Sedation protocols
- DVT (deep vein thrombosis) prophylaxis
- 14 published studies on economic benefit of sedation protocols
- Reduction of sedation costs with no prolongation of ICU stay

Expert Opin Pharmacother 2006;7:2047.

Pharmacist-enforced sedation protocol: duration of ventilation

- Before-after study in 2 medical ICU (MICU)
- Guidelines existed in both groups
- "After" group - had active pharmacist input
- 3 months evaluation per group in 156 pts
- Well-matched in age and APACHE II score
- Mechanical ventilator (MV) duration (8.9 vs. 5.3 days)
- ICU length of stay (LOS) (10.6 vs. 7.0 days)
- Hospital LOS (19.8 vs. 11.8 days)

Crit Care Med. 2008;36:427.

Pharmacist Interventions

Laboratory monitoring	6%
Added home psyche Rx	4%
Stop sedative agent	20%
Add sedative agent	32%
Add bolus dosing	11%
Decrease infusion rate	18%
Add PRN agents	9%

Crit Care Med. 2008;36:427.

Cost-effectiveness:
propofol vs. lorazepam

- Lorazepam used for long-term sedation
- This study is a decision analysis model of a clinical trial
- Randomized controlled trial (RCT) of intermittent lorazepam vs. propofol in patients > 48 hours of ventilation
- Direct costs were incorporated in the model and adjusted to 2007 dollars
- ICU costs based on other published data

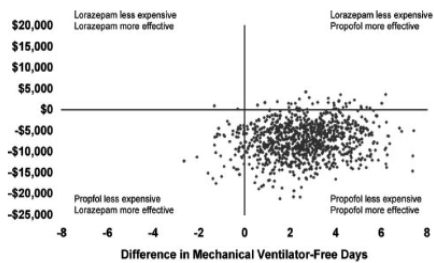
Crit Care Med. 2008;36:706, Crit Care Med. 2005;33:1266.

Cost-effectiveness:
propofol vs. lorazepam

- Propofol group had lower costs (\$45,631 vs. \$52,009)
- Three more ventilator-free days
- Propofol was less costly or more efficacious in 94% and 90% of the 1000 simulations, respectively

Crit Care Med. 2008;36:706.

Scatterplot: Probabilistic analysis comparing incremental costs and effects



Crit Care Med. 2008;36:706.

Enlarged version on page 34

“Interestingly, our analysis suggests that even newer, more expensive sedatives such as dexmedetomidine (average cost, \$300-500/day) are likely to have favorable value in comparison with other sedatives if their primary or adjunctive use is associated with a comparative reduction in either ICU or hospital length of stay by as little as 1 day”

Crit Care Med. 2008;36:706.

Dexmedetomidine vs. midazolam: A cost minimization analysis of a clinical trial (SEDCOM)*

- Recent publication
- Pharmacoeconomic analysis of a randomized clinical trial
- One of only a few studies evaluating cost of care vs. evaluating drug cost alone

*SEDCOM = Safety and Efficacy of Dexmedetomidine Compared to Midazolam

Dasta JF, Kane-Gill SL, Pencina M et al. *Crit Care Med.* 2010 (in press).

Rationale for this cost study

- Recently published prospective RCT of mechanically-ventilated ICU patients requiring > 24 hours of sedation and ventilation
 - 224 patients randomized to dexmedetomidine (DEX), 122 randomized to midazolam (MID)
 - Differences in clinical effects and resources were documented but costs were not determined

JAMA. 2009;301:489-499.

Major Clinical Findings

- Equal sedative efficacy - each group was at their target sedation goal 75% of the time
- In comparison to MID patients, DEX patients demonstrated
 - Higher incidence of bradycardia and hyperglycemia
 - Lower rate of tachycardia and hypertension requiring treatment
 - 25% lower prevalence and approximately 1 day shorter duration of delirium
 - 50% fewer infections
 - Shorter time to extubation (median 2 days), $p=0.01$
 - ICU stay (median 1.5 days) not statistically different compared to MID, $p=0.24$

JAMA. 2009;301:489-499.

Economic Analysis

- Equal sedation efficacy permitted a cost minimization analysis
- Compare costs of care between groups and select the therapy generating the lowest cost
- Investigators blinded to treatment group for all cost analysis
- Economic analysis performed post-hoc and from the institutional perspective
- Costs were estimated by multiplying actual resource used by U.S. representative cost using Medicare schedules, peer-reviewed literature, and IMS drug prices

Crit Care Med. 2005;33:1266.

Total ICU costs post-randomization

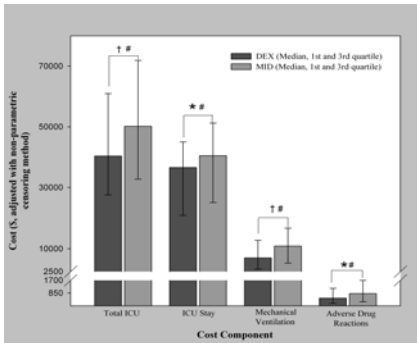
- Components of total ICU costs
 - Cost of ICU stay
 - Cost of mechanical ventilation
 - Cost associated with adverse drug reactions probably or possibly related to study drug
 - Acquisition cost of study drugs
- For censored patients two strategies used
 - No imputation
 - Non-parametric imputation method (adjusted)
- Median regression approach was used

Median Regression Model of Primary Outcome^a – Adjusted Total ICU Cost

Variable	Regression coefficient	95% confidence interval	p
Dexmedetomidine	-9679.10	-17044.70, -2313.51	0.010
Age	258.43	19.76, 497.11	0.034
Sex	-1758.30	-8694.36, 5177.76	0.618
APACHE II Score	504.59	-28.92, 1038.10	0.064

^a Model controlling for patient race, hospital type, size, geographical location and teaching status. APACHE, Acute Physiology and Chronic Health Evaluation.

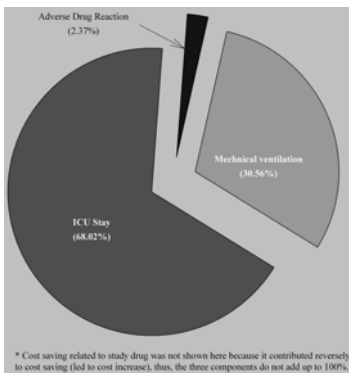
Crit Care Med. 2010 (in press).



† p ≤ 0.01, * 0.01 < p < 0.05 (based on median regression model for each cost component, comparing DEX to MID, controlling for patient race, hospital type, size, geographical location and teaching status)
p < 0.05 when equivalent analysis was done on unadjusted cost.

Crit Care Med. 2010 (in press).

Enlarged version on page 35



* Cost saving related to study drug was not shown here because it contributed reversely to cost saving (led to cost increase), thus, the three components do not add up to 100%.

Median acquisition costs: DEX \$1,166 vs. MID \$60

Crit Care Med. 2010 (in press).

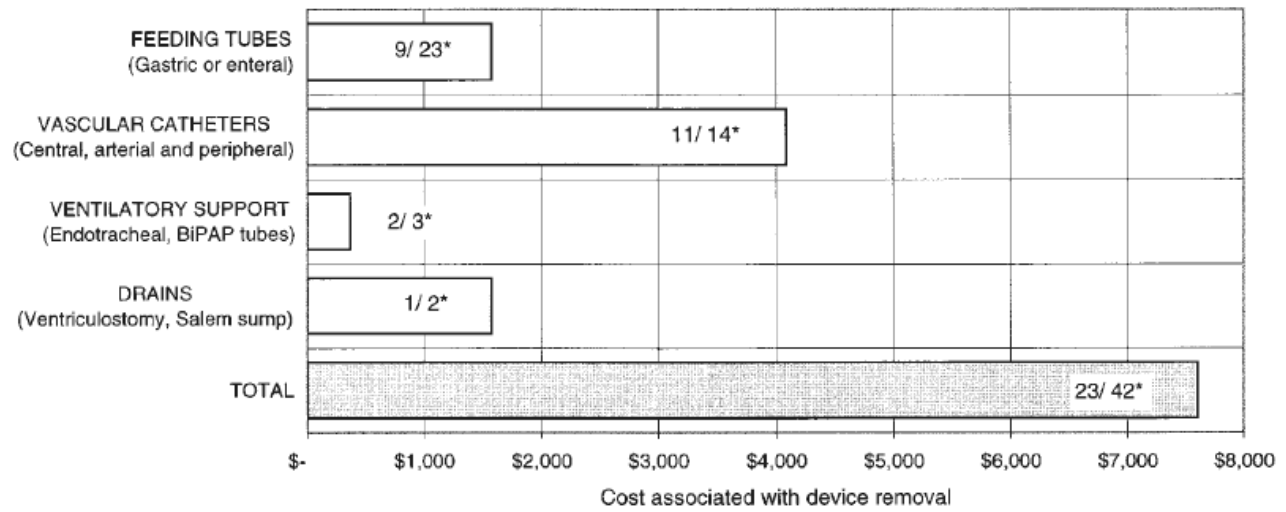
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Conclusion

- Despite higher acquisition costs, DEX patients have significantly lower total ICU costs compared to MID for ICU sedation
- Cost savings mainly due to
 - Decreased lengths of ICU stay
 - Time on mechanical ventilator in patients receiving DEX

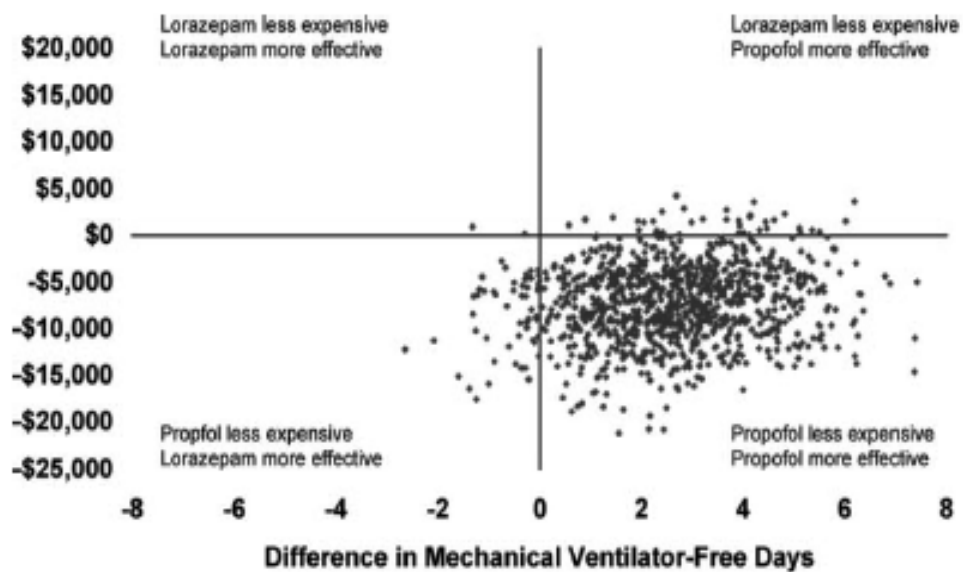
Overall Summary

- Costs of over- and under-sedation should be considered
- ICU sedation protocols provide components for optimal care and the pharmacist is key in this process
- Cost studies should account for beneficial effects and adverse drug events
- Evolving role of DEX in optimal ICU care

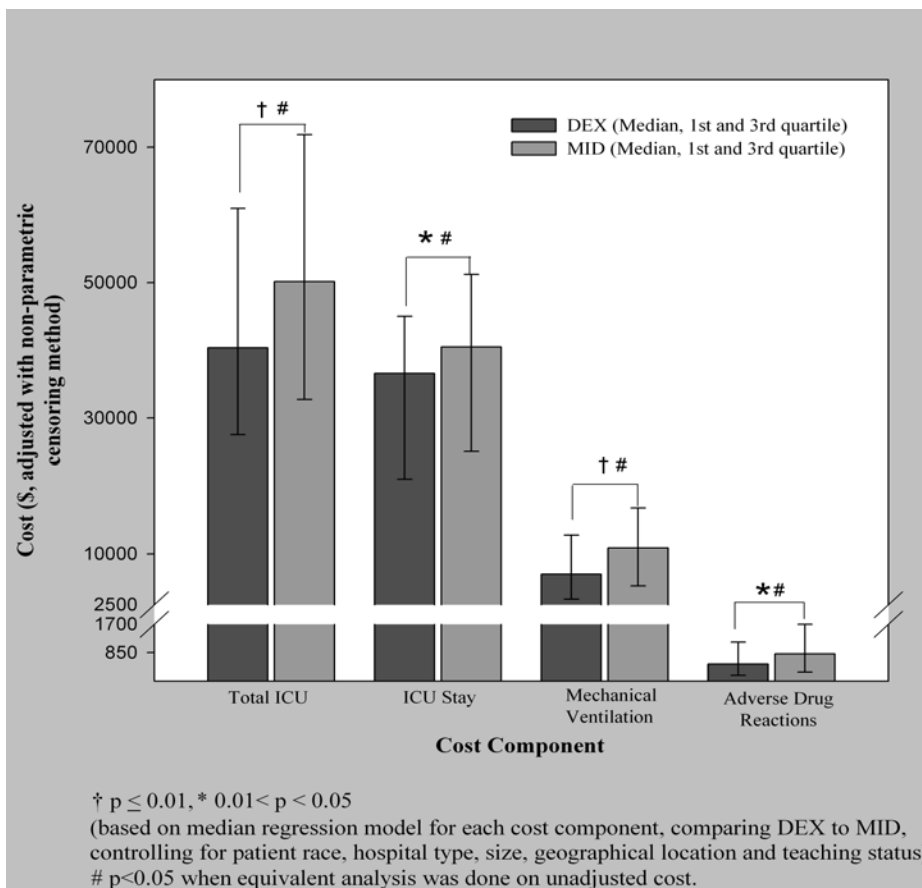


Pharmacother. 2001;21:1.

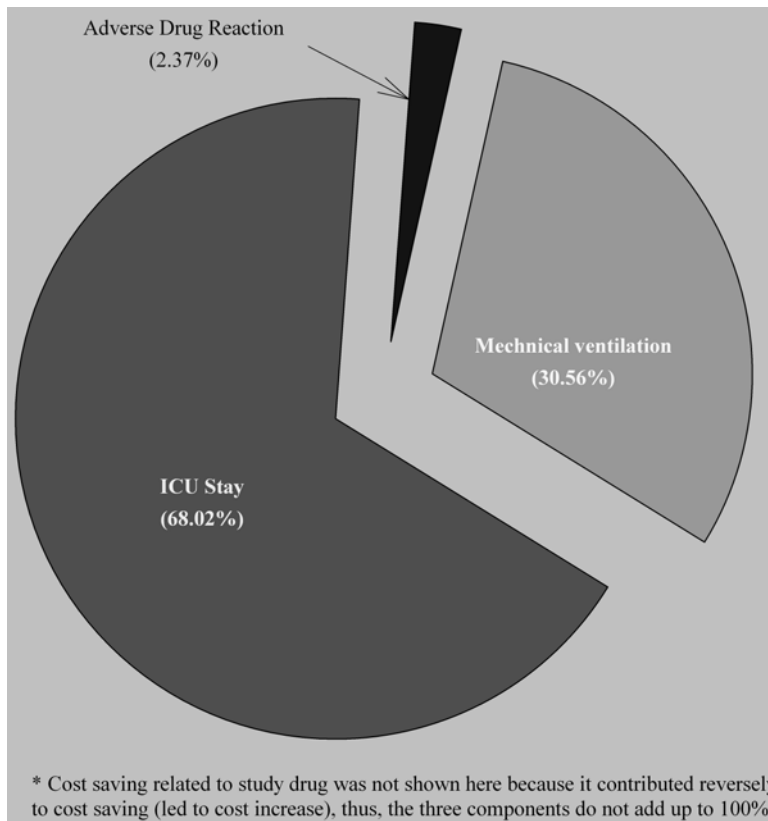
Scatterplot: Probabilistic analysis comparing incremental costs and effects



Crit Care Med. 2008;36:706.



Crit Care Med. 2010 (in press).



Median acquisition costs: DEX \$1,166 vs. MID \$60

Crit Care Med. 2010 (in press).

Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

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Intravenous Sedation in the Intensive Care Unit: Applying Pharmacoeconomic Principles

SELF-ASSESSMENT QUESTIONS

1. The 1997 cost per event associated with patient removal of devices in the ICU was:
 - a. \$80.
 - b. \$180.
 - c. \$280.
 - d. \$580.

2. Over-sedation with drugs that decrease respiratory drive can prolong the time on mechanical ventilation. Each day a patient is on the ventilator, the incremental cost is approximately how much?
 - a. \$150.
 - b. \$1500.
 - c. \$15000.
 - d. \$45000.

3. Most studies evaluating the effect of ICU sedation protocols on outcomes have used a before-after design.
 - a. True.
 - b. False.

Answers

1. b
2. b
3. a