



Cost effectiveness of a benzodiazepine vs a nonbenzodiazepine-based sedation regimen for mechanically ventilated, critically ill adults ☆☆☆★



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ABSTRACT

Purpose: Nonbenzodiazepine sedation (eg, dexmedetomidine or propofol) may be more cost effective than benzodiazepine (BZ) sedation despite its higher acquisition cost.

Materials and methods: A cost effectiveness (CE) analysis of noncardiac surgery, critically ill adults requiring at least 1 day of mechanical ventilation (MV) and administered either BZ or non-BZ sedation, that cycled health states and costs daily using a Markov model accounting for daily MV use until intensive care unit (ICU) discharge, was conducted from a third-party perspective. Transition probabilities were obtained from a published meta-analysis, and costs were estimated from best evidence. Sensitivity analyses were run for all extubation and discharge probabilities, for different cost estimates and for the specific non-BZ administered. **Results:** When non-BZ rather than BZ sedation was used, the incremental cost-effectiveness ratio to avert 1 ICU day while MV or while either MV or non-MV was \$3406 and \$3136, respectively. The base-case analysis revealed that non-BZ sedation (vs BZ sedation) resulted in higher drug costs (\$1327 vs \$65) but lower total ICU costs (percent accounted for MV need): \$35 380 (71.0%) vs \$45 394 (70.6%). Sensitivity analysis revealed that BZ sedation would only be less costly if the daily rate of extubation was at least 16%, and the daily rate of ICU discharge without MV was at least 77%. The incremental CE ratio to avert 1 ICU day while MV or non-MV was similar between the dexmedetomidine and propofol non-BZ options.

Conclusions: Among MV adults, non-BZ sedation has a more favorable CE ratio than BZ sedation over most cost estimates.

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Sedation is routinely administered to maintain patient comfort and facilitate mechanical ventilation (MV) in critically ill adults [1]. The 2013 American College of Critical Care Medicine's Pain, Agitation, and Delirium Clinical Practice Guidelines provides a weak recommendation to use a nonbenzodiazepine (ie, propofol or dexmedetomidine) rather than benzodiazepine (BZ) (ie, midazolam or lorazepam) sedative in this population [2]. This recommendation is based on controlled trials that suggest that this strategy may shorten the duration of MV, reduce length of intensive care unit (ICU) stay, and possibly lower delirium prevalence [3–8].

Despite the potential advantages of non-BZ sedative regimens, BZ use in the ICU remains common. [9] Benzodiazepines have a rapid onset of action, will induce deep sedation when it is required, and

have a low acquisition cost. [10] Excessive levels of sedation during BZ therapy can be mitigated using daily sedation interruption or an intermittent dosing strategy [11,12], and recent reports suggest the risk for delirium with BZ use may be lower than originally thought [13–15]. Thus, controversy exists, from both a clinical and economic perspective, of whether a non-BZ or non-BZ-based sedative should be the first-line sedative strategy in the ICU [2,16–18].

Published ICU cost analyses demonstrate that use of either propofol or dexmedetomidine is associated with lower health care expenditures than BZ therapy despite their greater acquisition cost. [19–22] However, these pharmacoeconomic analyses suffer from important potential methodological limitations including being based on clinical data from only one single trial, a failure to evaluate all clinically relevant outcomes that may influence cost, and a failure to evaluate the actual cost effectiveness of the comparison sedative agents [23].

A recent meta-analysis of randomized controlled studies that compared non-BZ with BZ sedation regimens in critically ill adults who were not undergoing cardiac surgery found that use of non-BZ sedation resulted in shorter lengths of MV and ICU stay [24]. This

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systematic review included a careful quality assessment of each trial, incorporated sensitivity analyses, and evaluated those outcomes most likely to drive ICU cost (ie, duration of MV and length of ICU stay). The aim of this study was to determine, from a third-party payer and hospital administrator perspective, whether a non-BZ sedation strategy is cost effective compared with a BZ sedation approach in critically ill, mechanically ventilated adults not undergoing cardiac surgery.

1. Methods

1.1. Study design

This cost-effectiveness analysis was designed so that it met consolidated health economic evaluation reporting standards [25]. A stochastic, probabilistic Markov model was constructed using TreeAge Pro 2013 R1.1 (TreeAge, Williamston, MA) to estimate the outcomes and associated costs of critically ill, mechanically ventilated adults managed with either a BZ or non-BZ sedation strategy (Fig. 1). A Markov model allows one to model the costs of patients on a 24-hour cycle as they move from one health state to another (eg, from being intubated to being extubated or from being admitted to the ICU to being discharged from the ICU).

1.2. Perspective

It was assumed that BZ and non-BZ sedative regimens have a comparable efficacy in maintaining patients at the targeted level of sedation [2–8] but that use of a non-BZ regimen may result in less time intubated and fewer days spent in the ICU [14]. Other cost analyses have found that differences in the costs associated with the use of these sedatives are largely determined by a composite cost associated with the time spent intubated and the time spent in the ICU [19–22]. The third-party perspective of this analysis took into account the efficacy of each sedation strategy as well as associated outcomes and costs of care. Key stakeholders in our analysis included third-party insurance payers, the government (eg, Centers for Medicare and Medicaid Services), and the patients themselves.

1.3. Clinical inputs, study population, and comparators

All clinical data for our analysis were derived from a recent meta-analysis that included randomized control trials published in English comparing either a midazolam or lorazepam sedation regimen with either dexmedetomidine or propofol in mechanically ventilated, critically ill medical or surgical adults not undergoing cardiac surgery (Electronic Figs. 1 and 2) [24]. The outcomes evaluated in this systematic review included ICU length of stay, duration of MV, delirium prevalence, and short-term mortality. Given that neither delirium prevalence nor short-term mortality differed between the BZ and non-BZ groups, these outcomes were not included in our analysis. Daily transition probabilities for each outcome (ie, intubated, extubated but remaining in the ICU, and extubated but discharged from the ICU) were estimated from the weighted means for all studies that were included in the meta-analysis for each particular outcome. Although 6 studies included in the meta-analysis evaluated length of ICU stay [3–8], only 4 evaluated duration of MV [4–6,8].

1.4. Outcomes measured

The primary outcome of the analysis was the incremental cost-effectiveness ratios (ICERs) of averting a day in the ICU and averting a day of MV when using a non-BZ (vs a BZ sedative) to maintain patient comfort. The secondary outcomes included cost of medication and average cost of care.

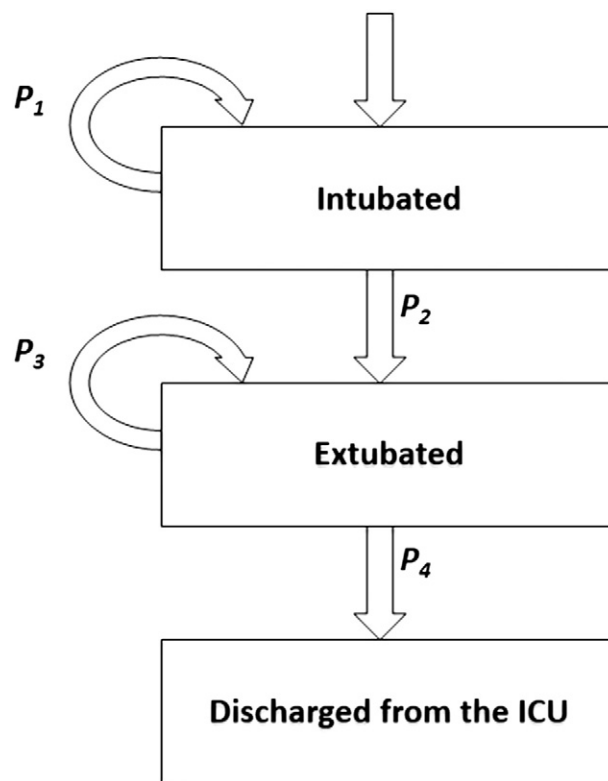


Fig. 1. Graphic overview of the Markov model. All critically ill adults enter the model mechanically ventilated. P_1 is the probability of remaining intubated in the ICU. P_2 is the probability of being extubated and remaining in the ICU. P_3 is the probability of remaining in the ICU after being extubated. P_4 is the probability of being discharged from the ICU.

1.5. Cost of ICU stay

Values for the daily cost of an ICU stay, with and without MV, were obtained from a previously published analysis based on data from the National Drug Code Health Hospital Patient Level Database, where data were derived from Uniform Bill-92 (UB-92) (Table 1) [26]. In this analysis, cost data were collected between October to December 2002 from 253 hospitals, most of which were US hospitals containing less than or equal to 200 beds. Patients were at least 18 years old and were required to have a UB-92 revenue code of 200 (general ICU), 201 (surgical ICU), 202 (medical ICU), or 208 (trauma ICU). Pediatric patients and UB-92 codes 204 (psychiatric ICU) and 207 (burn ICU) were excluded. The patient cohort was then separated by intubation status. Costs were found to be greatest on day 1 of ICU admission, decreasing, and then eventually plateauing by day 3.

Although nearly 25% of the patients across the 6 trials included in the meta-analysis were surgical, only medical ICU costs were used in our analysis because specific outcomes (eg, intubation status)

Table 1
Cost of medical ICU stay

	Day in ICU		
	Day 1	Day 2	Day 3
Cost when intubated			
2002 ^a	\$5366	\$4306	\$3759
2012 ^b	\$6848	\$5495	\$4797
Cost when extubated			
2002 ^a	\$3531	\$3153	\$2809
2012 ^b	\$4506	\$4024	\$3585

^a Based on [26].

^b Costs adjusted for inflation using Bureau of Labor Statistics Consumer Price Index calculator.

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