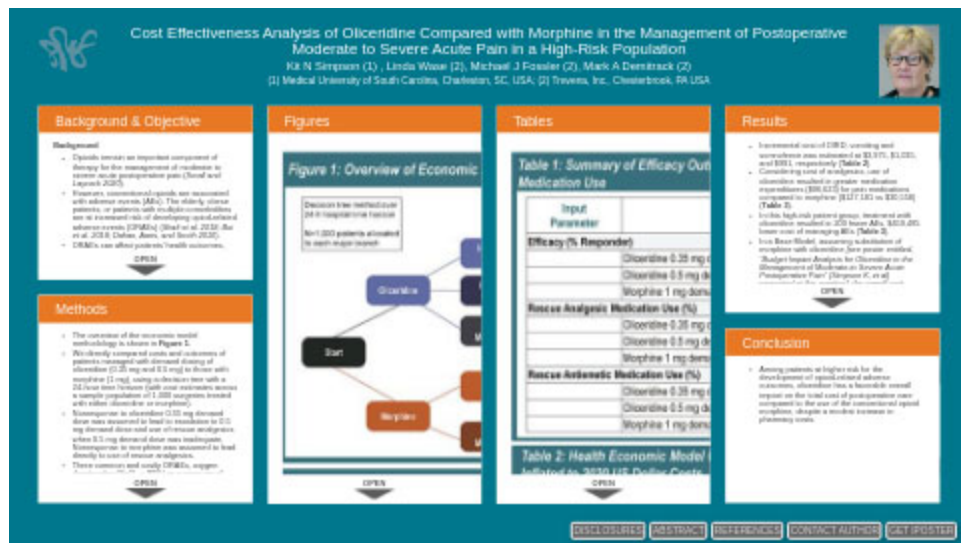


Cost Effectiveness Analysis of Oliceridine Compared with Morphine in the Management of Postoperative Moderate to Severe Acute Pain in a High-Risk Population



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PRESENTED AT:



BACKGROUND & OBJECTIVE

Background

- Opioids remain an important component of therapy for the management of moderate to severe acute postoperative pain (*Small and Laycock 2020*).
- However, conventional opioids are associated with adverse events (AEs). The elderly, obese patients, or patients with multiple comorbidities are at increased risk of developing opioid-related adverse events (ORAEs) (*Shafi et al. 2018; Bui et al. 2018; Dahan, Aarts, and Smith 2010*).
- ORAEs can affect patients' health outcomes, compromising optimal postoperative recovery (*Small and Laycock 2020; Shafi et al. 2018*).
- Oliceridine, a new class of IV opioid analgesic acting at μ -opioid receptors, is selective for G-protein signaling (achieving analgesia) with limited recruitment of β -arrestin (associated with ORAEs).

Objective

- To estimate cost-effectiveness of oliceridine compared to morphine for postoperative pain in high-risk patients.

METHODS

- The overview of the economic model methodology is shown in **Figure 1**.
- We directly compared costs and outcomes of patients managed with demand dosing of oliceridine (0.35 mg and 0.5 mg) to those with morphine (1 mg), using a decision tree with a 24-hour time horizon (with cost estimates across a sample population of 1,000 surgeries treated with either oliceridine or morphine).
- Nonresponse to oliceridine 0.35 mg demand dose was assumed to lead to escalation to 0.5 mg demand dose and use of rescue analgesics when 0.5 mg demand dose was inadequate. Nonresponse to morphine was assumed to lead directly to use of rescue analgesics.
- Three common and costly ORAEs, oxygen desaturation ($\text{SpO}_2 < 90\%$) as a measure of opioid-induced respiratory depression (OIRD), vomiting, and somnolence were utilized.
- Risk ratios were based on AE rates observed in the two pivotal controlled Phase 3 studies (*Viscusi et al. 2019; Singla et al. 2019*). The pivotal studies used in the model were the basis of FDA approval for oliceridine.
- Risk ratios were then applied to AE rates observed in the elderly (≥ 65 years) and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) patients from the open-label Phase 3 safety study of oliceridine (*Bergese et al. 2019*).
- Costs of analgesics (including rescue) and antiemetics were tabulated based on rates observed in Phase 3 studies. Standard cost weights from National discharge data and literature sources were used to estimate hospital budget impact & costs for each AE.
- Average daily price was set to \$100 for oliceridine and \$15 for morphine.
- Costs were enumerated as differences in cost of analgesics and differences in resources utilized to manage these AEs in the first 24 hours post-surgery.
- The Analytic Framework of the model is provided in **Figure 2**.
- A summary of the data input related to efficacy outcomes and rescue analgesic and rescue antiemetic medication use is provided in **Table 1**.

- AE incidence risk-ratio computation from pooled Phase 3 controlled studies and estimations derived from ATHENA study in high-risk patients is shown in **Figure 3**.

FIGURES

Figure 1: Overview of Economic Model Methodology

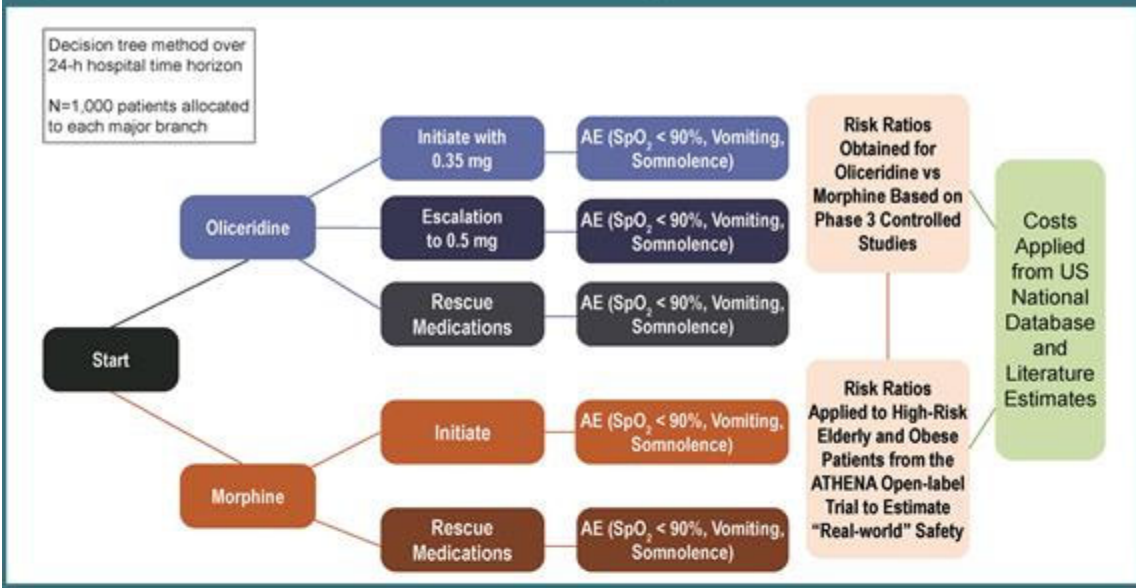


Figure 2: Health Economic Model: Analytic Framework

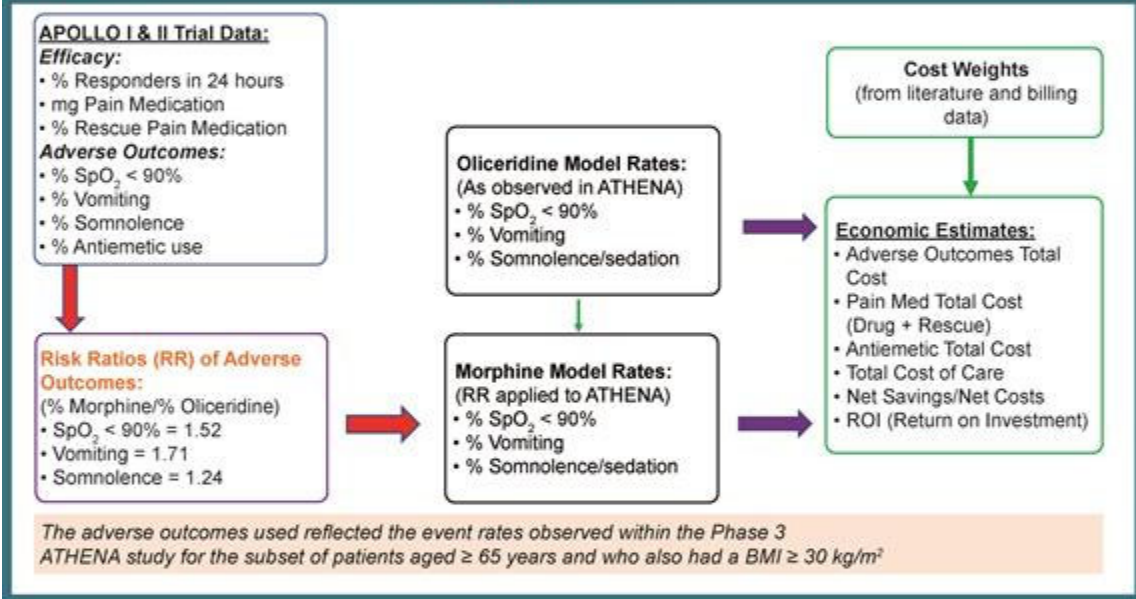
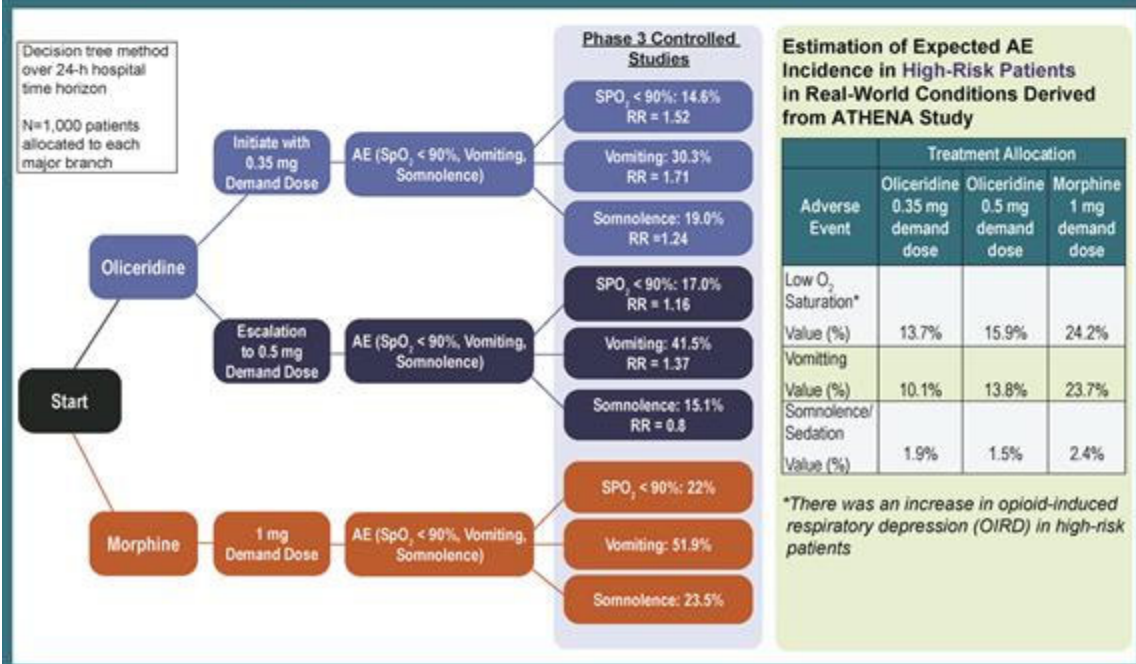


Figure 3: AE Incidence Risk-Ratio Computation from Pooled Phase 3 Controlled Studies and Estimations Derived from ATHENA Study in High-Risk Patients



TABLES

Table 1: Summary of Efficacy Outcomes, Rescue Analgesic, and Rescue Antiemetic Medication Use

Input Parameter	Treatment Allocation	Value
Efficacy (% Responder)		
	Oliceridine 0.35 mg demand dose initial responders	66.1%
	Oliceridine 0.5 mg demand dose incremental proportion of responders	19.4%
	Morphine 1 mg demand dose	73.6%
Rescue Analgesic Medication Use (%)		
	Oliceridine 0.35 mg demand dose	17.0%
	Oliceridine 0.5 mg demand dose	14.5%
	Morphine 1 mg demand dose	12.0%
Rescue Antiemetic Medication Use (%)		
	Oliceridine 0.35 mg demand dose	45.3%
	Oliceridine 0.5 mg demand dose	51.1%
	Morphine 1 mg demand dose	62.9%

Table 2: Health Economic Model Cost Weights for OIRD, Vomiting, and Somnolence Inflated to 2020 US Dollar Costs

Event Type	2020 Cost Weights Used for Base Model*	± 20% Range for Sensitivity Analysis	Cost in 2017 US Dollars (Low- High)
Respiratory depression (Low O ₂ saturation)	\$ 3,975	\$3,180 - \$4,770	\$4,589 (\$3,625 - \$5,552)
Vomiting	\$ 1,035	\$828 - \$1,242	\$1,344 (\$972 - \$1,716)
Somnolence	\$ 991	\$793 - \$1,189	\$1,250 (\$904 - \$6,353)

*2020 costs reflect the inflated cost from the low range of the 2017 cost.

Table 3: Estimates for the Comparative Cost of Care for 1,000 High-Risk Surgical Patients Treated On-Demand with Either Oliceridine or Morphine

	Oliceridine [0.35 mg with escalation to 0.5 mg for nonresponse] (N=1,000)	Morphine 1 mg (N=1,000)	Difference (Oliceridine - Morphine)
Cost of pain medication for 24 hours/patient	\$ 108.14	\$ 15.00	(\$ 93.14)
Response rate %	66.1%	73.6%	(7.5%)
% Escalated to 0.5 mg	19.4%	N/A	N/A
Total number of AEs:	309	509	(200)
Respiratory depression (Low O ₂ saturation)	157	242	(85)
Vomiting	128	237	(109)
Somnolence	24	30	(6)
Cost of pain medication	\$ 127,181	\$ 30,558	\$ 96,623
Cost of managing AEs	\$ 778,764	\$ 1,238,259	(\$ 459,495)
TOTAL COST	\$ 907,115	\$ 1,271,059	(\$ 363,944)

The model results shown were based on an assumed average daily cost of oliceridine of \$100/day for the 0.35 mg dose and \$124/day for the 0.5 mg dose, resulting in \$108.14 as the weighted cost for day 1.

The total cost also includes the cost of antiemetics: \$1,170 in the oliceridine arm and \$2,242 in the morphine arm.

RESULTS

- Incremental cost of OIRD, vomiting and somnolence was estimated at \$3,975, \$1,035, and \$991, respectively (**Table 2**).
- Considering cost of analgesics, use of oliceridine resulted in greater medication expenditures (\$96,623) for pain medications compared to morphine (\$127,181 vs \$30,558) (**Table 3**).
- In this high-risk patient group, treatment with oliceridine resulted in 200 fewer AEs, \$459,495 lower cost of managing AEs (**Table 3**).
- In a Base Model, assuming substitution of morphine with oliceridine [*see poster entitled, "Budget Impact Analysis for Oliceridine in the Management of Moderate-to Severe Acute Postoperative Pain" (Simpson K, et al) presented at this meeting*], the overall cost savings were \$228,454 for 1,000 surgeries.
- Use of oliceridine for patients at higher risk for the emergence of ORAEs provides additional overall cost savings of \$135,490.

CONCLUSION

- Among patients at higher risk for the development of opioid-related adverse outcomes, oliceridine has a favorable overall impact on the total cost of postoperative care compared to the use of the conventional opioid morphine, despite a modest increase in pharmacy costs.

ABSTRACT

OBJECTIVES:

Use of conventional opioids for postoperative pain is associated with increased adverse events (ORAEs) in high-risk patients such as the elderly (≥ 65 years) or obese ($\text{BMI} \geq 30\text{kg/m}^2$) affecting outcomes and compromising analgesia. Oliceridine, a new class of μ -opioid receptor IV agonist, is selective for G-protein signaling (achieving analgesia) with limited recruitment of β -arrestin (associated with ORAEs). We estimated the cost effectiveness of oliceridine vs morphine for postoperative pain in high-risk patients.

METHODS:

We compared costs & outcomes of patients managed with demand dosing (DD) of oliceridine (0.35mg and 0.5mg) to those with morphine (1mg), using a decision tree with a 24-hour time horizon and sample population of 1,000 surgeries for each arm. Three common and costly ORAEs; respiratory depression ($\text{SpO}_2 < 90\%$, RD), vomiting, and somnolence. Costs were enumerated as differences in cost of analgesics and resources utilized to manage these AEs within 24 hours post-surgery. Risk ratios (RR) were based on AE rates observed in two pivotal controlled Phase-3 studies. The RRs were then applied to AE rates observed in the elderly (≥ 65 years) and obese ($\text{BMI} \geq 30\text{kg/m}^2$) patients from an open-label Phase-3 observational study of oliceridine. Costs of all analgesics and antiemetics were tabulated based on rates observed in Phase-3 studies. Standard cost weights from national discharge data and literature-sources were used to estimate hospital costs & costs per AE. Average price for oliceridine was set to \$100/day and morphine, \$15/day.

RESULTS:

In the high-risk patient group, use of oliceridine resulted in 200 fewer AEs (vs morphine), and \$459,495 lower cost of AEs. The overall savings on cost of care were estimated at \$363,944 (\$907,115 for oliceridine vs \$1,271,059 for morphine) for each treated population of 1000 patients.

CONCLUSION :

Use of oliceridine in high-risk surgical patients provides a favorable health economic outcome compared to morphine.

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