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ORIGINAL RESEARCH

# A Cost-Effectiveness Study Comparing Ready-to-Administer and Traditional Vial-and-Syringe Method for Opioids

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## ABSTRACT

***Objective***: The purpose of this study was to develop a cost-effectiveness model for manufacturer-prepared prefilled ready-to-administer (RTA) syringe products versus the traditional vial-and-syringe administration of intravenous (IV) opioids.

***Methods***: Cost parameters included cost of manufacturer-prepared prefilled RTA syringe product, traditional vial and syringe, drug preparation, drug administration, drug waste, and severity of error. Effectiveness endpoint included number of preparation and administration errors in each comparator arm. Simple decision tree was used, and incremental cost-effectiveness ratio (ICER) was calculated as the reduction in the incremental errors per observation with RTA compared with traditional vial-and-syringe method. One-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) were conducted to test the robustness of the model. TreeAge Pro software was used to create and analyze the decision model. All the cost parameters were converted to USD 2021.

***Results***: Base-case analysis showed that the cost of the RTA arm was lower by $182.61 and the number of errors in the RTA arm was lower by 94%, compared with the traditional vial-and-syringe arm. The manufacturer-prepared prefilled RTA syringe product was found to be cost-effective with an incremental savings of $22,554 per additional error avoided. Sensitivity analysis showed that ICER value was most sensitive to the probability of errors; however, the results were robust in showing that RTA is the preferred cost-effective option, when both the costs and effectiveness parameters were varied substantially.

***Conclusion***: This economic evaluation analyzed costs of using manufacturer-prepared prefilled RTA syringe product IV opioids and incremental benefits in terms of reduced errors, adverse events, and their associated costs. Manufacturer-prepared prefilled RTA syringe product was found to be cost-effective, demonstrating cost savings by reduction in the error rates. Integrating and adopting RTA syringe products within a health system could play an

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important role in improving care, building efficiency, increasing patient safety, and saving money.

**Keywords:** Ready-to-administer; Prefilled syringe; Cost-effectiveness analysis; Medication errors; Opioids

**Key Summary Points**

Manufacturer-prepared prefilled ready-to-administer (RTA) syringe products may be safer in reducing the errors compared with the traditional vial-and-syringe IV push method; however, limited research exists assessing whether RTA syringe IV opioid products generate substantial cost savings for the hospital setting, such that they are cost-effective compared with the traditional vial-and-syringe IV push.

According to this cost-effectiveness study, manufacturer-prepared prefilled RTA syringe product was associated with an estimated savings of $182.61 per administration and a 94% reduction in errors compared with the traditional IV push vial-and-syringe method in an inpatient hospital setting. Manufacturer-prepared prefilled RTA syringe product was found to be superior to the traditional IV push vial and syringe, with an incremental savings of $22,554 per additional error avoided.

Integrating and adopting manufacturer-prepared prefilled RTA syringes within a health system could play an important role in improving care, building efficiency, increasing patient safety, and saving money.

## INTRODUCTION

Medication errors caused by injectable medications are common in an inpatient hospital setting and lead to more than 1 million hospitalizations annually, adding around $2.7 billion to $5.1 billion of medical costs to the US healthcare system [1]. About one-third to one-half of such medication errors that occur with intravenous (IV) medications are preparation and administration errors [2–4]. Medication errors are responsible for causing adverse drug events (ADEs) in an inpatient setting, some of which lead to severe harm and are life threatening and associated with high cost complications [1, 5, 6].

In an effort to reduce the probability of errors and mitigate patient harm, many solutions have been proposed and implemented [7, 8]. The guidelines of the American Society of Health-System Pharmacists (ASHP) on preventing medication errors in hospitals recommend that medications should be available in ready-to-administer (RTA) packaging to avoid further manipulation by the person administering the medication [9]. One such product that has been approved for IV use is Simplist, a ready-to-administer prefilled syringe. The Third Consensus Conference panel, which included representatives from The Joint Commission, ASHP, and the Institute for Safe Medication Practices (ISMP), concluded that RTA products are the safest intravenous drug delivery systems owing to their benefits and low risk profile [10]. Additionally, ISMP recommends that all stakeholders standardize their protocols to utilize RTA formulations and concentrations as much as possible to avoid the error-prone complexity of the traditional IV vial-and-syringe [11].

Although, the use of any IV push medication product can result in errors related to labeling, dilution, and disinfection of the vial stopper before use, past studies report lower error rates with RTA formulations [12, 13]. RTA products may be safer in reducing the errors compared with the traditional vial-and-syringe IV push method; however, limited evidence exists assessing the cost-saving associated with each product. Additionally, the extent of the harm caused by an error could be more severe for drugs like opioids. There is a scarcity of research assessing if RTA syringe IV opioid products generate substantial cost savings for the hospital setting, such that it is cost-effective

compared with the traditional vial-and-syringe IV push.

For the purpose of this study, comparators include manufacturer-prepared prefilled RTA syringe product (referred to as RTA) and the traditional IV vial-and-syringe for three drugs: fentanyl, hydromorphone, and morphine. The traditional vial-and-syringe comparator arm also included cartridge-based systems, or Carpuject, commonly used as a vial without the cartridge. Past research [12, 14] suggests that nurses withdraw the medication from the cartridge using a needle, making this practice similar to a traditional vial-and-syringe and common among practitioners. Other cartridge-based systems or ampules that were administered as directed by the package insert were excluded from this study.

The purpose of this research was to develop a cost-effectiveness model for the manufacturer-prepared prefilled RTA syringes versus the traditional IV push vial-and-syringe method for an inpatient setting. The study model focused on the administration of three drugs: fentanyl, hydromorphone, and morphine. The study determined the comparative cost-effectiveness of the two comparators by analyzing the net costs and number of errors.

## METHODS

The analysis was conducted from a health system perspective; focusing only on inpatient units, such as the medical/surgical, critical care, and operating/procedural areas. The model was designed using a time horizon of one year with a sample size of 15,727. A past study by Hertig et al. [15], which reported 15,727 total observations for a period of 1 year (i.e., 8327 with fentanyl, 7207 with hydromorphone, and 193 with morphine), was used to estimate the costs and errors over a duration of 1 year. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

### Cost Parameters

Five cost parameters were included in the model. Table 1 outlines the sources used to obtain the model inputs for cost parameters. All of the cost parameters were converted to USD 2021 using Consumer Price Index. The first parameter was the cost of the drug, which included the average wholesale price (AWP) cost of manufacturer-prepared prefilled RTA syringe products and the AWP cost of the IV drug vial, obtained from Medi-Span [16]. Simplist products from Fresenius Kabi, Lake Zurich, USA were used as the manufacturer-prepared prefilled RTA syringe products in this study. AWP costs were used in this study because it is considered a benchmark for pricing and reimbursement of prescription drugs. The second parameter was the cost associated with drug preparation calculated as the amount of time spent by nurses to prepare the drug in terms of nurse's mean salary. The time spent preparing the drug was obtained from a past study conducted by Burger and Degnan [13] in 2019, where participants were asked to prepare an IV dose of diphenhydramine 25 mg/mL, ketorolac 30 mg/mL, and morphine 2 mg/mL using saline solutions for the RTA product, traditional-vial and-syringe, and cartridge-based syringe system (or Carpuject). The Burger and Degnan [13] study was simulated in an acute-care hospital setting, which is similar to the inpatient setting of our current study. Therefore, with the assumption that the nurse preparation time would not change or vary by the type of drug, Burger and Degnan [13] was considered an appropriate and valid source for our model. The third parameter was the cost associated with the administration of drugs calculated as the amount of time spent by nurses to administer the drug in terms of nurse's mean salary. The time spent administering the drug was obtained from unpublished data of a past study conducted by Hertig et al. in 2018 [12] for the RTA and traditional vial and syringe. The Hertig et al. 2018 [12] study was conducted in an inpatient setting which is the same as our current study. Therefore, with the assumption that the nurse administration time would not change or vary by the type of drug, Hertig et al. 2018 [12] was considered an appropriate and valid source for our model. The fourth parameter was the cost of drug waste. Cost of drug waste with the traditional vial and syringe was obtained for each drug from a past

**Table 1** Sources used to obtain the model parameters

| Parameters | Sources | |
|---|---|---|
| | **Traditional vial and syringe** | **RTA Simplist** |
| *Effectiveness* | | |
| Medication preparation and administration errors | Hertig et al. [12] | Hertig et al. [12] |
| *Cost* | | |
| AWP cost of the drug | Medi-Span [16] | Medi-Span [16] |
| Cost associated with the preparation of drugs | Burger and Degnan [13] | Burger and Degnan [13] |
| Cost associated with the administration of drugs | Hertig et al. [12] | Hertig et al. [12] |
| Cost of the drug waste | Hertig et al. [15] | Extrapolated from Hertig et al. [15] |
| Cost associated with errors (medication preparation and administration) | Hug et al. [17] | Hug et al. [17] |
| Cost associated with no errors | Hug et al. [17] | Hug et al. [17] |
| *Probabilities* | | |
| Probability of administering fentanyl, hydromorphone, morphine | Hertig et al. [15] | Hertig et al. [15] |
| Probability of medication preparation and administration errors per observation | Hertig et al. [12] | Hertig et al. [12] |
| Probability of errors leading to harm (or ADE) | Hug et al. [17] | Hug et al. [17] |
| Probability of errors categorized by severity: significant, serious, life-threatening | Hug et al. [17] | Hug et al. [17] |

study by Hertig et al. in 2020 [15], which was conducted at two hospitals in the State of Indiana. This parameter included cost of drug wasted and the time spent by the nurses wasting that drug. Since the study mentioned above did not collect information on the cost of drug waste with RTA products, extrapolations were made for the RTA arm using the raw data obtained directly from the study's authors. On the basis of the RTA products available in the market for hydromorphone (0.2 mg, 0.5 mg, 1 mg, 2 mg), morphine (2 mg, 4 mg, 5 mg), and fentanyl (50 μg, 100 μg), drug waste and time spent by nurse wasting the drug were extrapolated. The fifth parameter was the financial cost associated with severity of the error, i.e., significant, serious, and life threatening, calculated on the basis of the length of stay associated with each error type, as determined by a past study by Hug et al. in 2012 [17]. Cost of no errors was obtained from Hug et al. 2012 [17] as the average costs of hospitalization for all the patients in a specific setting. The base-case estimates of the cost parameters are presented in Table 2.

## Effectiveness Parameters

The primary effectiveness endpoint was the number of errors per observation in each comparator arm. Two types of error were assessed: preparation errors and administration errors. A past study by Hertig et al. 2018 [12] was used to

**Table 2** Parameter estimates used in the cost-effectiveness model for scenario I

| Variable description | Lower bound | Base case or mean | Upper bound | Standard deviation |
|---|---|---|---|---|
| *Cost of drug preparation and administration* | | | | |
| Cost of drug preparation with RTA ($) | 0.238 | 0.292 | 0.348 | 0.028 |
| Cost of drug preparation with vial ($) | 0.587 | 0.670 | 0.752 | 0.042 |
| Cost of drug administration with RTA ($) | 0.728 | 0.918 | 0.995 | 0.068 |
| Cost of drug administration with vial ($) | 0.825 | 0.861 | 1.010 | 0.047 |
| *Cost of drug waste* | | | | |
| Cost of the drug wasted with RTA fentanyl ($) | 0.867 | 0.963 | 1.060 | 0.049 |
| Cost of the drug wasted with fentanyl vial ($) | 0.716 | 0.796 | 0.875 | 0.041 |
| Cost of the drug wasted with RTA hydromorphone ($) | 0.141 | 0.157 | 0.173 | 0.008 |
| Cost of the drug wasted with hydromorphone vial ($) | 2.978 | 3.308 | 3.639 | 0.169 |
| Cost of the drug wasted with RTA morphine ($) | 2.318 | 2.576 | 2.833 | 0.131 |
| Cost of the drug wasted with morphine vial ($) | 2.120 | 2.356 | 2.591 | 0.120 |
| *Cost of errors* | | | | |
| Cost of no errors ($) | 8155.097 | 8154.929 | 8155.452 | 0.091 |
| Cost of nonharmful errors ($) | 10,138.046 | 10,173.507 | 10,208.842 | 18.060 |
| Cost of serious errors ($) | 12,339.709 | 12,471.628 | 12,602.920 | 67.146 |
| Cost of significant errors ($) | 11,376.885 | 11,528.299 | 11,679.776 | 77.268 |
| Cost of life-threatening errors ($) | 17,067.359 | 17,742.127 | 18,416.948 | 344.283 |
| *Probabilities* | | | | |
| Probability of administering fentanyl | 0.477 | 0.53 | 0.583 | 0.027 |
| Probability of administering hydromorphone | 0.414 | 0.46 | 0.506 | 0.023 |
| Probability of administering morphine | c | 0.01 | – | – |
| Probability of harm | 0.099 | 0.11 | 0.121 | 0.006 |
| Probability of no harm | – | 0.89 | – | – |
| Probability of life-threatening errors | – | 0.096 | – | – |
| Probability of serious errors | 0.45 | 0.5 | 0.55 | 0.026 |
| Probability of significant errors | 0.3636 | 0.404 | 0.4444 | 0.021 |
| Probability of errors with RTA | 0.0225 | 0.025 | 0.0275 | 0.001 |

**Table 2** continued

| Variable description | Lower bound | Base case or mean | Upper bound | Standard deviation |
|---|---|---|---|---|
| Probability of errors with vial | 0.0936 | 0.104 | 0.1144 | 0.005 |
| Probability of no errors with RTA | – | 0.975 | – | – |
| Probability of no errors with vial | – | 0.896 | – | – |

Note: AWP costs of the manufacturer-prepared prefilled RTA syringe products and traditional vial and syringe included in the model were obtained from Medi-Span

obtain medication preparation and administration errors for RTA syringe and traditional vial and syringe. Under the traditional vial and syringe arm, Hertig et al. 2018 included those Carpuject observations where the Carpuject vial was used without the cartridge like a traditional vial. Table 1 outlines the sources used to obtain the model inputs for effectiveness parameters. A key assumption for this model was that only a proportion of preparation and administration errors can lead to patient harm, with some errors being nonharmful. The probability of an error causing harm was obtained from a past study by Hug et al. [17] Harmful error was categorized as those causing an ADE in a patient. The probability of harm was calculated as the proportion of patients experiencing an ADE of the total sample size. A harmful error was further categorized by severity as being "significant" (for example, a rash), "serious" (an episode of gastrointestinal bleeding with a need for two erythrocyte units), or life threatening (the need for transfer to an intensive care unit); and all the probabilities for each category were obtained from Hug et al. [17] The effectiveness was calculated as the number of errors at the end of each treatment arm. Errors were categorized as those that lead to patient harm, i.e., harmful errors, and those that do not lead to patient harm, i.e., nonharmful errors. Harmful errors were further categorized as significant, serious, and life-threatening errors. The number of errors for each arm is presented in Table 3 for the RTA syringe product and the traditional vial and syringe.

## Decision-Analytic Model

A simple decision tree was designed (Fig. 1) for the study. The decision nodes included choosing between the types of syringe (RTA versus traditional vial-and-syringe), types of drug (fentanyl, hydromorphone, morphine), whether a preparation and administration error occurred or not, types of error (harmful versus nonharmful), and types of harmful error (significant, serious, and life threatening). Effectiveness was assessed in terms of number of errors occurring at the end of each arm. Costs included cost of the drug, drug waste, drug preparation, and administration. Incremental cost-effectiveness ratio (ICER) was reported as the main outcome for this cost-effectiveness analysis. ICER, which represents the additional cost per one unit of outcome gained by the new technology or drug, has been the most widely accepted outcome for a cost-effectiveness analysis [18–21].

**Table 3** Effectiveness or number of errors for each arm of the cost-effectiveness model

| Effectiveness parameter | Traditional vial and syringe | RTA Simplist |
|---|---|---|
| *Harmful errors* | | |
| Significant errors | 0.0046 | 0.0011 |
| Serious errors | 0.0057 | 0.0014 |
| Life-threatening errors | 0.0011 | 0.00026 |
| Nonharmful errors | 0.0922 | 0.022 |

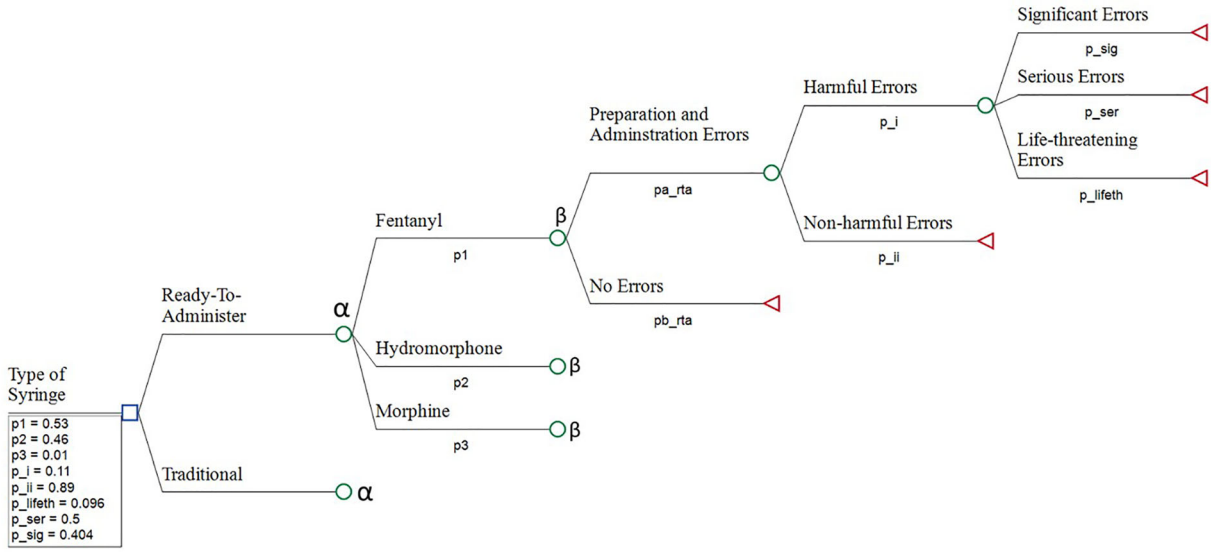


**Fig. 1** Simple decision tree displaying the decision nodes, probabilities, and payoffs for the ready-to-administer and traditional vial and syringe

For the current study, ICER was calculated as the incremental errors per observation with RTA compared with traditional vial-and-syringe. The costs and outcomes were reported separately for each arm. The costs and outcomes were combined to calculate the ICER with the following equation:

$$\frac{C1 - C2}{E1 - E2}$$

In the equation, C1 and C2 are the costs, and E1 and E2 are the number of errors associated with RTA syringe product and traditional vial-and-syringe, respectively. For the ICER value calculations, all the cost variables were included in the numerator part of the equation and the number of errors were included in the denominator part of the equation. The parameter estimates used for the base-case analysis is presented in Table 2. The calculations of all the input values for the parameters are presented in Supplementary Material 1. Two methods of sensitivity analysis were conducted to address the uncertainty in certain key inputs and test the robustness of the model: one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA). OWSA was conducted by varying each parameter in the model one at a time between two extreme values, and then recalculating the ICER value with the new inputs. The process was repeated for all the variables in the model. Variables that have a substantial impact on the costs, effectiveness, and ICER values are reported in the form of a tornado diagram. Tornado diagrams help compare the relative importance of different parameters and provide a graphical way to display the varying effects of different parameters. For the OWSA, estimates for the lower-bound, base, and upper-bound values are required for each parameter being considered [22]. The lower- and upper-bound values for all the parameters were obtained from the 95% confidence interval reported in the literature. If a 95% confidence interval was not reported in the literature for a parameter, base-case estimates were varied using 10% margin of error (scenario I). Additionally, to further test the robustness of the model, base-case estimates were also varied using 50% margin of error (scenario II).

PSA was conducted using Monte Carlo simulations, which help vary all the input parameters simultaneously to assess overall variability of the model. Each input parameter was assigned a probability distribution (e.g., gamma, beta, or Dirichlet) obtained from the mean and standard deviations of the parameters. To run a

single Monte Carlo simulation, a random value is drawn out from each of the probability distributions assigned to the parameters and model outcomes are recalculated. This process was repeated 10,000 times for this study, yielding a distribution of ICER values. Table 2 displays the lower bound, base case (or mean), upper bound, and standard deviations of the parameter estimates used in the sensitivity analysis for scenario I. The results of the OWSA and PSA for scenario II are included as appendices 2 and 3. TreeAge Pro software [23] was used to create the decision model and run the analyses. This study was in compliance with the ethics guidelines.

## RESULTS

The results of the base-case analysis with values for incremental costs, incremental effectiveness, and ICER are presented in Table 4. Base-case analysis showed that the cost of each RTA administration was $8216.97; and the cost of each traditional vial-and-syringe administration was $8399.58. RTA was the least costly option between the two, with an incremental cost difference of $182.61. Also, the number of errors in the RTA arm was lower by 94% compared with the traditional vial arm (0.0005 versus 0.0086 per administration). Overall, this cost-effectiveness study found that the manufacturer-prepared prefilled RTA syringe product was superior to the traditional IV push vial-and-syringe, with an incremental savings of $22,554 per additional error avoided. Estimated over a period of 1 year in an inpatient setting with 15,727 administrations [15], the study found that the RTA arm had the potential to prevent 127.3 errors (incremental errors) and save $2871,889 in costs annually (incremental costs), compared with the traditional vial-and-syringe (Table 4).

The results of the OWSA for scenario I are shown in a tornado diagram in Fig. 2. It depicts how variations in each model input parameter affect the outcome. The vertical line represents the ICER for the base-case analysis ($22,554 per additional error avoided), and the horizontal bars represent the variation of the ICER obtained by varying the key parameters (costs and effectiveness) of the model. The range of ICER variations are represented by lower (gray bars) and higher (red bars) ICER values. Input parameters are arranged from top to bottom in the tornado diagram such that the parameter with the highest ICER range is at the top of the diagram and has the biggest impact on the outcome.

For scenario I, the ICER values for the OWSA ranged from −$21,947 to −$23,119 and were most sensitive to the probability of errors with

**Table 4** Base-case results of the cost-effectiveness analysis of ready-to-administer (RTA) Simplist versus traditional vial-and-syringe

| Strategy | Cost | Incremental cost | Errors | Incremental errors | ICER |
|---|---|---|---|---|---|
| $n$ = 1 | | | | | |
| Ready-to-administer Simplist | $8216.97 | | 0.0005 | | |
| Traditional vial-and-syringe | $8399.58 | $182.61 | 0.0086 | 0.0081 | DOMINATED |
| $n$ = 15,727 (1-year time horizon) | | | | | |
| Ready-to-administer Simplist | $129,228,286.03 | | 7.75 | | |
| Traditional vial-and-syringe | $132,100,175.30 | $2,871,889.27 | 135.08 | 127.33 | DOMINATED |

Notes: Incremental costs were calculated as the difference between the costs of the two comparators. Incremental errors were calculated as the difference between the numbers of errors for the two comparators. ICER is calculated as the ratio of incremental costs to incremental errors

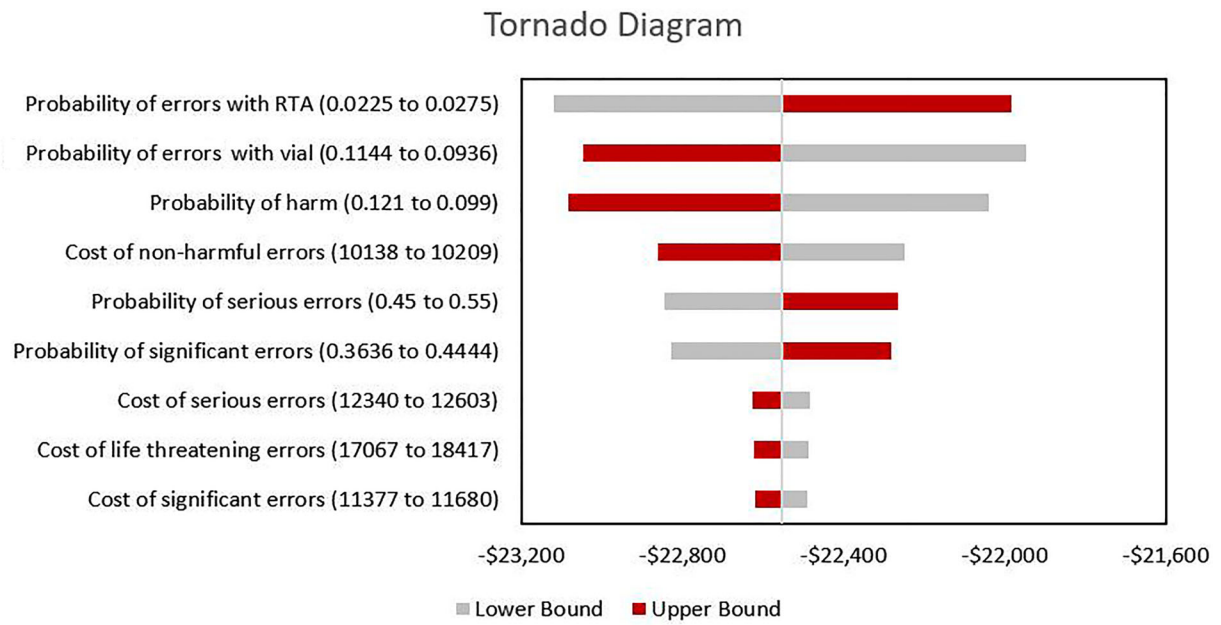


**Fig. 2** Tornado diagram depicting the one-way sensitivity analysis of ready-to-administer (RTA) versus traditional vial and syringe for scenario I

the RTA and the traditional vial and syringe, the two topmost parameters in the tornado diagram (Fig. 2). With the highest reported value of the probability of errors in the RTA arm (upper bound 0.0275), the ICER value decreased by $572 (i.e., to $21,983). However, with the highest reported value of the probability of errors in the traditional arm (upper bound 0.1144), the ICER value increased by an amount of $491 (i.e., to $23,045). Additionally, the ICER value was also sensitive to the probability of harm. With the highest reported value of the probability of harm (upper bound 0.121), the ICER value increased by an amount of $529 (i.e., to $23,083). ICER value was least sensitive to the AWP cost of the three drugs, cost of the drug waste, cost of drug preparation, and cost of drug administration.

The results of the PSA for scenario I are shown in Fig. 3, which depicts the Monte Carlo probability distribution of ICER values with 10,000 iterations. It shows that, after varying all the input parameters simultaneously, the ICER value ranged from −$19,700 to −$30,700, with more than 80% of the likelihood for the ICER to range from −$21,200 to −$23,200. Additionally, a scatter plot with incremental costs on the *y*-axis and incremental effectiveness on the *x*-axis and acceptability curves was also created. Since the RTA method dominated the traditional IV push vial-and-syringe method for all the iterations, the scatter plots and the acceptability curves did not provide any additional insights into the ICER measure and therefore, the results were not shown.

For scenario II, the results of the OWSA and PSA are shown in Supplementary Material 2 and 3, respectively. Applying the 50% margin of error under scenario II, the results showed a higher range of uncertainty for the ICER values. The ICER values ranged from −$16,777 to −$25,329 for the OWSA and were most sensitive to the probability of errors with the traditional vial-and-syringe and the RTA (Supplementary Material 2). The ICER values for the PSA ranged from −$11,000 to −$41,000, with more than 80% of the likelihood for the ICER to range from −$20,000 to −$26,000 (Supplementary Material 3). None of the sensitivity analysis scenarios changed the preferred option, and RTA syringe remained the most cost-effective choice between the two comparators under both the scenarios.

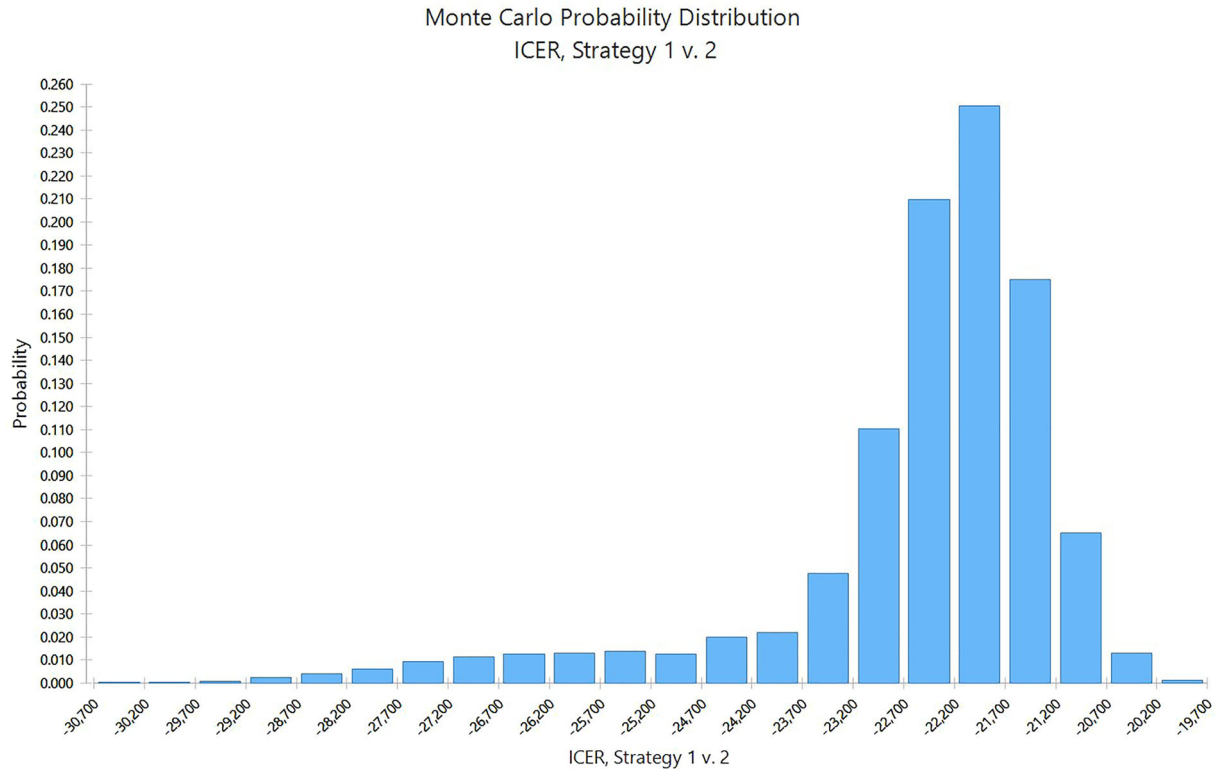


**Fig. 3** Monte Carlo probability distribution diagram depicting the range of incremental cost effectiveness ratio (ICER) of ready-to-administer (strategy 1) versus traditional vial-and-syringe (strategy 2) using the probabilistic sensitivity analysis for scenario I

## DISCUSSION

The results of the study showed that using RTA syringe product in an inpatient hospital setting was associated with an estimated savings of $182.61 per administration and a 94% reduction in errors compared with the traditional IV push vial-and-syringe method. Accounting for medication errors that lead to adverse events or patient harm, this equates to a saving of $2.9 million when extrapolated to 15,727 administrations over a duration of 1 year. The sensitivity analysis results demonstrated that the ICER value was robust to the large variations in the costs and effectiveness parameters and RTA syringe remained the most cost-effective choice. Although the range of the ICER values was large for the PSA, more than 80% of the times the ICER values ranged from −$21,200 to −$23,200 for scenario I and −$20,000 to −$26,000 for scenario II.

This study is a novel economic evaluation that analyzed costs of using manufacturer-prepared prefilled RTA syringe IV opioids to incremental benefits in terms of reduced errors, adverse events, and their associated costs. The existing published literature used to populate the data on costs and probability were designed in a similar inpatient setting. However, obtaining accurate estimates of the frequency of harmful errors and their costs was challenging. Clinical trials measuring error rates and costs are limited. Most published studies that exist are retrospective observational or prospective case–control designs conducted in smaller populations in a single hospital setting, and have reported estimates of the probability of errors leading to harm ranging from as low as 3% to 13% [2, 24–26]. The current model used the study by Hug et al. [17] since it reported the error rates and associated costs categorized by severity of errors. The errors that cause patient

harm could result in a possible increase in the hospital length of stay, and were included as an additional costs in the Hug et al. study. [17]

In the absence of direct-observation-based studies, several models such as decision tree models, probability pathway models, or simulations have been used in the past to assess the impact of various healthcare interventions including drugs [27–29], imaging technologies [30], and procedures and guidelines [31, 32], but limited literature exists in the USA evaluating the types of IV administration techniques. A past study by Larmene et al. in 2019 [25] conducted in a Dutch hospital reported cost savings (in euros) with the use of ready-to-administer prefilled sterilized syringes (PFSSs) compared with the conventional preparation method for parenteral administration. The study suggested that a decrease in medication errors and cases of bacteremia were the main contributors to the cost savings of PFSSs. Our study, in agreement with the Dutch study, found that the probability of preparation and administration errors was the main parameter contributing to the ICER value. Adding to the existing literature, our study focused on three opioid drugs, and was designed to account for the differences in opioid waste caused by RTA versus traditional vial and syringe.

The results of the study support RTA syringe product being a cost-effective option, demonstrating cost savings and reductions in error rates when compared with the traditional IV push vial-and-syringe, which could significantly drive up the cost after accounting for adverse events. Our results were sensitive to large variations in the probability of errors and the probability of harm caused by the errors. Our findings are in concordance with a past cost-effectiveness study by Westbrook et al. [33] that compared an electronic medication management system (eMMS) with paper-based prescribing. The past study [33] found that eMMS reduced the potential ADEs by 71% and was cost-effective in comparison with the paper-based prescribing. The study also found that the amount of savings was more sensitive to the probability of potential ADEs, probabilities of intercepting an error, and of non-intercepted errors resulting in actual ADEs. Therefore, assessing rates of errors leading to harm is a crucial parameter of interest while evaluating a new method of delivery or administration. The common errors associated with intravenous medication errors include dilution errors, labeling, and disinfection errors, all of which could be life threatening and expensive to manage clinically. Since RTA reduces the probability of dilution, labeling, and disinfection errors, the occurrence of administration and preparation errors is relatively low in the RTA arm compared with the traditional vial-and-syringe arm [12].

Our results suggest that the probability of harm caused by serious or life-threatening errors had a significant impact on the ICER value. However, the cost parameters including the AWP costs of the drugs, cost of the drug waste, cost of drug preparation, and cost of drug administration had the least impact on the ICER value. These findings suggest that the probability of harm and cost of errors are more important parameters in guiding the decision-making to choose between the RTA versus traditional vial-and-syringe, rather than the cost of the technology.

Owing to the limited availability of clinical studies assessing the RTA and traditional vial, the effectiveness and cost parameters of this study were obtained from observational studies. Although RTA remained the cost-effective choice, our model was sensitive to large variations in the probability of harm. One of the reasons could be that the input probabilities used to link the preparation and administration errors to the severity of harm were obtained from a single study conducted in a middle-size community hospital in Massachusetts. This fact can limit the external validity and generalizability of our study results to other settings such as outpatient or emergency departments. Another limitation of the study is that it compared only two types of methods; therefore, cost savings from this model cannot be applied to other technologies [such as electronic medication management systems (eMMS), automated robotic technology, etc.] which might have different error rates. Additionally, the range of the estimates published in the past literature are limited with a paucity of good-quality research

reporting errors and adverse events specific to opioids, which warrants caution to the generalizability of this cost-effectiveness study.

## CONCLUSION

The use of manufacturer-prepared prefilled RTA syringes can reduce healthcare costs by decreasing errors compared with the traditional vial-and-syringe. Integrating and adopting ready-to-administer products like the RTA prefilled syringe within a health system could play an important role in improving care, building efficiency, increasing patient safety, and saving money. With an increase in the marketing of the RTA syringe products on a larger scale, cost-effectiveness studies like these could help decision-makers, including administrators and clinicians, ascertain the importance of RTA prefilled syringe and the associated benefits in terms of return on investment for a health system.

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***Compliance with Ethics Guidelines.*** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

***Data Availability.*** All data generated or analyzed during this study are included in this published article or in supplementary information files.



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