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Authors

Premkumar, Ashish
Grobman, William A
Terplan, Mishka
et al.

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Methadone, Buprenorphine, or Detoxification for Management of Perinatal Opioid Use Disorder: A Cost-Effectiveness Analysis

Ashish Premkumar, M.D.[1], **William A. Grobman, M.D., M.B.A.**[1], **Mishka Terplan, M.D., M.P.H.**[2], **Emily S. Miller, M.D., M.P.H.**[1]

[1]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Feinberg School of Medicine, Northwestern University, Chicago, IL USA

[2]Division of General Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Virginia Commonwealth School of Medicine, Richmond, VA USA

Abstract

OBJECTIVE: To estimate whether methadone, buprenorphine, or detoxification treatment is the most cost-effective approach to the management of opioid use disorder during pregnancy.

METHODS: We created a decision analytic model compared the cost effectiveness (e.g. the marginal cost of the strategy in United States dollars divided by the marginal effectiveness of the strategy, measured in quality adjusted life years) of initiation of methadone, buprenorphine, or detoxification in treatment of opioid use disorder during pregnancy. Probabilities, costs, and utilities were estimated from the existing literature. Incremental cost-effective ratios (ICER) for each strategy were calculated and a ratio of $100,000/quality adjusted life year was used to define cost effectiveness. One-way sensitivity analyses and a Monte Carlo probabilistic sensitivity analysis were performed.

RESULTS: Under base assumptions, initiation of buprenorphine was more effective at a lower cost than either methadone or detoxification, and thus was the dominant strategy. Buprenorphine was no longer cost effective if the cost of methadone was 8% less than the base case estimate ($1,646/month) or if the overall costs of detoxification were 121% less than the base case estimate for the detoxification cost multiplier, which was used to increase the values of both inpatient and outpatient management of detoxification by a factor of 2. Monte Carlo analyses revealed that buprenorphine was the cost-effective strategy in 70.5% of the simulations. Direct comparison of buprenorphine to methadone demonstrated that buprenorphine was below the ICER in 95.1% of simulations, while direct comparison between buprenorphine and detoxification demonstrated that buprenorphine was below the ICER in 45% of simulations.

CONCLUSION: Under most circumstances, we estimate that buprenorphine is the cost-effective strategy when compared to either methadone or detoxification as treatment for opioid use disorder during pregnancy. Nonetheless, that in almost 1/3 of simulations buprenorphine was not the most

Corresponding author: Ashish Premkumar, M.D., 250 E. Superior Street, 05-2185, Chicago, IL 60611, ashish.premkumar@northwestern.edu, Phone: 312-472-4685, Fax: 312-472-4687.

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cost effective strategy suggests that the robustness of our model may be limited and that further evaluation of the most cost-effective approach to the management of opioid use disorder during pregnancy is needed.

PRÉCIS

Buprenorphine administration for pregnant women with opioid use disorder is the cost-effective management strategy when compared with methadone or detoxification.

INTRODUCTION

Opioid use disorder (OUD) is defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, as “a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems.”[1] OUD during pregnancy has become a major public health issue, rising more than 4-fold over a 15-year period (1.5/1,000 deliveries in 1999 to 6.5/1,000 deliveries in 2014).[1,2] From a perinatal perspective, the rise in OUD during pregnancy has been associated with a concomitant increase in the incidence of neonatal abstinence syndrome (NAS), with approximately 20,000 neonates affected yearly.[3,4]

Treatment of OUD during pregnancy is recommended by the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) for long-term maternal benefit, such as the reduced risk of withdrawal symptoms, recurrent opioid use, or opioid overdose.[3,7–9] Although clinical protocols vary, medication-assisted treatment (MAT) during pregnancy – the approach recommended by ACOG and SMFM – typically utilizes either methadone, which is dosed daily as a directly-observed therapy at an outpatient clinic, or buprenorphine, which is dosed as a take-home medication. However, detoxification, or medically-supervised withdrawal over five days to 16 weeks with medications such as buprenorphine or clonidine, is available as an alternative in certain areas in the U.S.[10–12] While case reports from the 1970s suggested that detoxification was associated with stillbirth or miscarriage, a recent systematic review demonstrated a similar frequency of stillbirth between women who did and did not undergo detoxification.[13–15] Given that detoxification may significantly reduce the incidence of NAS due to reduced fetal exposure to opioids, its use has been advocated by some practitioners as a viable treatment strategy.[3,16,17]

To date, the most cost-effective therapy to reduce both maternal and neonatal adverse events for women with OUD during pregnancy has not been determined. This is crucial, not only to improve the health of mothers and their newborns, but also to use healthcare resources in the most efficient manner. Thus, we performed a decision analysis to investigate whether methadone, buprenorphine, or detoxification treatment is the most cost-effective approach in the management of OUD during pregnancy.

METHODS

Using a decision-tree model from a health care payor perspective, we compared three strategies to manage OUD after 16 weeks of pregnancy among a cohort of women assumed

to be appropriate candidates for all three forms of non-residential OUD management: initiation of methadone, buprenorphine, or detoxification using a fourteen-day buprenorphine taper. A branch of the decision tree is displayed in Figure 1, and the format is replicated for all other treatment arms (Appendix 1).[13] The decision to specifically analyze a detoxification protocol that employed a buprenorphine taper was made in conjunction with data derived from a systematic review authored by two of the co-authors of this study (A.P. and M.T.), as well as consensus from the authors of this study after discussing detoxification options with key experts in perinatal OUD across the United States.[13] The decision tree cycled monthly throughout the course of pregnancy using a Markov structure, which is a method of incorporating transitions in health states (e.g. pregnancy to birth, stable methadone use to relapse) over the course of a fixed time period.[18]

The baseline probabilities and outcomes of each strategy were based on estimates from the literature. However, due to the limited data surrounding management strategies and outcomes of pregnant women with OUD, the decision was made to include probabilities and outcomes from both pregnant and non-pregnant participants, derived from a PubMed search using the search terms: “substance use,” “pregnancy,” “opioids,” “methadone,” “buprenorphine,” and “detoxification.” Probability and outcome estimates were pooled through the use of weighted averages, based on sample size of a given study. All reported probabilities, costs, and utilities were varied based on the upper and lower ranges reported in the literature for Monte Carlo simulations, which are used to model uncertainty within a given CEA by varying all costs, probabilities, and utilities along their predefined distributions, and univariable sensitivity analyses.[19] Given the limited quality and amount of data surrounding OUD in pregnancy, the decision was made to employ a triangular distribution – approximating a log-normal distribution – for Monte Carlo simulations, as data were available to approximate the most likely value, as well as minimums and maximums.[20] Probabilities that did not have multiple estimates in the literature were varied in the sensitivity analyses by 50% above and below the base estimate based on consensus of the authors that these threshold values would represent meaningful excursions (Tables 1 and 2). Monte Carlo simulations were run 100,000 times.

We assumed that initiation of all therapies would include a three-day hospitalization for coordination of pregnancy-related services and outpatient psychiatric care. For women undergoing detoxification, we assumed that they would have outpatient follow-up after discharge with their addiction specialist every 48 hours until their 14-day buprenorphine taper was complete, and then weekly thereafter. Women receiving methadone or buprenorphine followed-up with their providers on a weekly basis. Urine toxicology screens were performed at every outpatient visit to monitor for relapse. Although “relapse” is variably defined in the literature, we defined it to occur when a urine toxicology test was positive for opioids or when a woman self-reported opioid use during pregnancy. Due to limited information regarding the incidence of preterm birth, stillbirth, and miscarriage for pregnant women with OUD who experience relapse, we did not change the base case probabilities of these three outcomes in women with relapse. However, we did assume a higher rate of NAS among women who relapsed (Tables 1 and 2).

We assumed a base case for the frequency of maternal relapse of 4.6% for methadone, 8.3% for buprenorphine, and 28.1% for detoxification.[3,13,21,22] In line with the Substance Abuse and Mental Health Services Administration (SAMHSA) recommendations and expert opinion, if an individual relapses but does not overdose, they will continue with buprenorphine for an additional cycle and, if relapse reoccurs, they will transition to methadone in the next cycle.[23] However, if they are lost to follow-up or overdose in a given cycle, they will automatically transition to methadone in the subsequent cycle. All individuals who relapsed in the detoxification arm transitioned to methadone in the next cycle. As part of a sensitivity analysis, we reran the model assuming a residential treatment facility, rather than community-based, location of care for all three arms of the decision tree. In a residential treatment facility, costs for housing and ongoing clinical management were incurred, which would be different from a community-based treatment location. Of note, the cost of daily methadone in a residential treatment facility is lower when compared with community-based location of care, as it does not incur the additional cost of an outpatient nurse at a methadone clinic to administer the medication as administration of methadone occurs on-site.[24,25]

We assumed a similar loss to outpatient follow-up in each arm, and that loss to follow up also indicated relapse. Any woman lost to follow-up was assumed to engage in treatment in the subsequent cycle; for the buprenorphine arm, women were allowed to be lost to follow-up twice before switching to methadone. The same assumption was used for women who overdosed in a given cycle. The probability of fatal and nonfatal overdose during pregnancy was estimated from data derived from non-pregnant individuals, given the dearth of pregnancy-specific information.[8,13,26–30] Nonfatal maternal overdoses incurred the cost of both emergency stabilization services, along with a subsequent one-week inpatient hospitalization with (re)initiation of methadone.

Given the gestational age of women upon entry into the decision tree (e.g. 16 weeks), miscarriage or fetal loss, while rare, was imputed to more accurately model costs of each strategy. Due to the association between preterm birth and use of opioids or MAT, women in either of these Markov states were assumed to have a 35% increased incidence of preterm birth; in sensitivity analyses, this value was varied from 0% to 41%.[13,31,32] We assumed all surviving neonates would be admitted to the NICU if they were born at a gestational age more than 24 weeks and less than 37 weeks. We also assumed all neonates would be admitted to the NICU for management of NAS if born at greater than 37 weeks. Due to the recent advances in management strategies for NAS, we performed a sensitivity analysis to simulate both rooming-in, or keeping the neonate with the mother 24 hours a day, versus management in the NICU. Previous studies have demonstrated that NAS managed in the NICU is associated with higher costs compared with neonates who room-in with the mother.[33] For our model, rooming-in would avoid the cost and disutility associated with NICU admission (Table 3).

All costs were derived from the Centers for Medicaid and Medicare Services (CMS), and were converted to 2017 USD (Table 4).[6,24,25,34–39] Due to lack of standardization of detoxification costs nationwide, we used data in the literature from Virginia, Florida, and Massachusetts.[25,37,40,41] For the purposes of univariable sensitivity analyses, we assumed

that the outpatient costs of detoxification during pregnancy would be twice those of outpatient costs outside of pregnancy, less medication costs, for both the buprenorphine and methadone arms due to limited cost data for detoxification in pregnancy, variation in reported protocols, and additional costs and monitoring that may be incurred due to limited reported experience with detoxification in pregnancy.[10–13] In order to ensure that this assumption did not drive the results of the model, we varied these costs widely (from 100% to 300% of base-case estimate) in sensitivity and Monte Carlo analyses based on consensus of the authors (Table 3).

In order to quantify adverse outcomes, maternal utilities, in the form of Quality Adjusted Life Years (QALYs) were computed for each outcome. QALYs are a standardized measure for understanding improvements and decrements in quality of life, and are computed by attributing different weights to the desirability of certain health states over the course of a year.[42] QALYs were derived from a maternal perspective. All utilities were derived from the existing literature or, when that was lacking, by consensus of the authors (Table 3).[42–48]

We assumed that an incremental cost-effectiveness ratio (ICER) of 100,000 USD/QALY defined cost effectiveness, which means that any cost greater than 100,000 USD for an additional QALY would indicate that a given strategy would not be cost effective.[49] When reporting strategies, they are described as dominant, in that the strategy is both cost saving and more effective than the other strategies, or cost effective, in that the strategy does not incur greater than 100,00 USD per QALY gained.[50] Outcomes evaluated in this model include maternal relapse, maternal overdose, maternal transition to methadone (if on either buprenorphine or after detoxification), maternal death, preterm delivery, NAS, and NICU admission. Costs expected to be saved by the cost-effective strategy per annum in the United States were determined by multiplying the marginal costs saved for one individual by 20,000, which is the estimated number of women in the United States per annum with OUD who have a child with NAS.[4] The model extended from entry at 16 weeks gestational age through 42 weeks' gestation, at which time all remaining subjects in the model would be delivered; due to this fact, the analytic horizon of the model only extended through the NICU stay of each neonate. Due to the limited analytic horizon of less than one year, we did not discount either costs or utilities. All analyses were performed in TreeAge (Williamstown, MA). IRB exemption was obtained from Northwestern University (STU00210552).

RESULTS

Use of buprenorphine was associated with a cost savings of 8,827 USD per person when compared to methadone, and 23,647 USD per person when compared with detoxification. Buprenorphine use resulted in higher total QALYs for a lower cost per QALY when compared to both methadone and detoxification (Table 5). These findings indicate that buprenorphine is a dominant strategy (i.e., results in lower costs and higher number of QALYs) when compared with methadone or detoxification.

For 20,000 women, the annual cost savings associated with use of buprenorphine is 177 million USD compared with methadone and 473 million USD compared with detoxification;

buprenorphine also results in 4,500 more QALYs compared with methadone, though detoxification did incur 2,600 more QALYs when compared with methadone. Approximately 75% of the QALYs accrued per strategy are derived from the maternal health state, whereas 25% of QALYs are maternal disutilities from the neonatal health state.

In the hypothetical cohort of 20,000 women, the lowest incidence of overdose occurred in the buprenorphine arm, and the highest incidence of relapse was in the detoxification arm (Table 6). For women who did not start with the methadone strategy, the incidence of needing to switch to methadone was greater in the detoxification arm when compared with buprenorphine. The frequency of admission to the NICU (22.5%, 95% CI 17.4%−23.1%) or diagnosis of NAS (19.7%, 95% CI 19.1%−20.2%) were lowest among those in the detoxification strategy. There was no difference in incidence of preterm delivery among the different arms. The incidence of relapse was highest in the detoxification arm, with approximately 0.77 relapse events per woman (95% CI 0.76–0.79) during the duration of the analysis, and lowest in the buprenorphine arm (0.28 relapse events per woman, 95% CI 0.27–0.29). In the buprenorphine arm, approximately 2,087 women relapsed twice (95% CI 2,003–2,172) and were switched to methadone. Therefore, the number of women who were treated successfully with buprenorphine, either through a single relapse event or without relapse events, is approximately 17,913 (95% CI 17,828–17,997), or 89.6% (95% CI 89.1% −90.0%) of the buprenorphine arm.

In one-way sensitivity analyses, the large majority of alterations in 65 variable inputs resulted in no change in the conclusion – namely, that buprenorphine was the cost-effective strategy. Excursions in baseline estimates of two variables, however, resulted in buprenorphine no longer being the cost-effective strategy. Detoxification became cost effective if the assumption surrounding the increase in cost was less than 121% of the base case estimate for the detoxification cost multiplier, which was used to increase the values of both inpatient and outpatient management of detoxification by a factor of 2 (Figure 2; see Methods). Methadone became the cost-effective strategy if the monthly cost of medication administration was less than $1,514, or 8% less than the base case estimate ($1,646; Figure 3). As part of a sensitivity analysis for our model, we ran the decision tree assuming all women were part of a residential treatment program, rather than receiving community-based care, and that all neonates were roomed-in, rather than treated in the NICU. In all of the aforementioned scenarios, buprenorphine remained the cost-effective strategy.

To evaluate the robustness of our model, we performed a Monte Carlo probabilistic sensitivity analysis – sampling values across the prespecified ranges of costs, utilities, and probabilities – with 100,000 simulations. Buprenorphine was noted to be the cost-effective strategy in 70.5% of simulations, while methadone was cost-effective in 3.9% of runs and detoxification in 25.6% of simulations. Direct comparison of the ICER of buprenorphine to that of methadone demonstrated buprenorphine was below the ICER threshold in 95.1% of simulations, while direct comparison between detoxification and buprenorphine demonstrated that buprenorphine was below the ICER threshold in 45% of simulations.

DISCUSSION

Our study demonstrates that buprenorphine, under base-case circumstances, is a cost-effective strategy for management of opioid use disorder in pregnancy compared to methadone and detoxification. Indeed, variation in only two estimates – the medication cost of methadone or the cost of detoxification – resulted in other strategies becoming more cost effective. Within further sensitivity analyses, neither residential treatment nor rooming-in of neonates afflicted with NAS changed the findings of the initial analysis.

OUD during pregnancy has become one of the largest public health issues of the 21st century, generating a renewed effort to engage women in treatment for both maternal and neonatal benefit.[3,7] While strategies including MAT and detoxification have been used in an effort to improve maternal health and pregnancy outcomes, the most cost-effective treatment remains uncertain. Our decision analysis attempts to fill this void in the literature by comparing all three treatment strategies in order to elucidate which one is the most cost effective. Furthermore, our data are in line with a recent systematic review performed by members of our study team (A.P. & M.T.) demonstrating the benefits of pharmacotherapy over detoxification.

It is interesting to note that buprenorphine was the cost-effective strategy even though the frequencies of NAS and NICU admission were lowest in the detoxification arm. These findings suggest that while costs and disutilities generated by NAS and NICU admission may be substantial, they are offset by other costs (such as those of detoxification treatment) and other disutilities (such as those associated with maternal relapse or overdose) in the detoxification arm.

This study has several strengths. First, the decision analysis focuses on both maternal and neonatal outcomes, rather than simply one set of outcomes, in order to generate a cost-effectiveness assessment. This fact allows the decision analysis to attend to the unique problems posed by the maternal-fetal dyad when substance use is at play during pregnancy. Second, this study is one of the few that has been performed since the beginning of the opioid epidemic in the early 2000s and incorporates up-to-date data regarding both costs and probabilities of maternal relapse and overdose, as well as NAS.[51,52] Finally, our decision analysis utilizes a Markov strategy to mimic the dynamic nature of pregnancy itself, particularly as it relates to outcomes that are based on gestational age, such as risk of maternal overdose.[8]

Nevertheless, our study has important limitations. First, our decision analysis is predicated on the assumption that all women entering the tree were both eligible for and able to access all three forms of therapy. The conclusions, therefore, cannot be generalized to apply to women with OUD who may have comorbid conditions that may lead one particular strategy to be more clinically indicated[53,54] or to women who live in regions with lack of access to any of the examined strategies.[55] Although we defined reasonable approaches for any of the strategies, there is no single standard to initiation of methadone, buprenorphine, or detoxification during pregnancy.[13] Due to the limited published data on detoxification costs, derived from a few states, there exists a possibility for regional variation in costs that could

change the findings of our decision analysis, although given the robustness of the model in sensitivity analysis, this would only be likely at large cost excursions. Furthermore, our analytic horizon was limited to the end of a NICU stay. Extending the horizon further would have required the incorporation of assumptions that could no longer be based on available evidence. Long-term developmental outcomes of the offspring associated with each of the strategies remains unknown, and there are limited data focusing on adherence in the postpartum period for women using methadone or buprenorphine, and no data for detoxification.[13] There are few data to guide our QALY estimates, and, given the limited analytic horizon of our model and narrow constraints on QALY variation within the model, our findings depend heavily on our QALY assumptions. Finally, our Monte Carlo analysis did demonstrate that buprenorphine was cost effective in 70.5% of runs and direct comparison between buprenorphine and detoxification demonstrated a lower frequency of being below the ICER threshold. These findings suggest that the robustness of our model may be limited, and further research must be performed to clarify economic costs and probability estimates in order to update this cost-effective assessment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX 1

A schematic of the decision tree constructed to compare methadone, buprenorphine, or detoxification in the management of perinatal opioid use disorder

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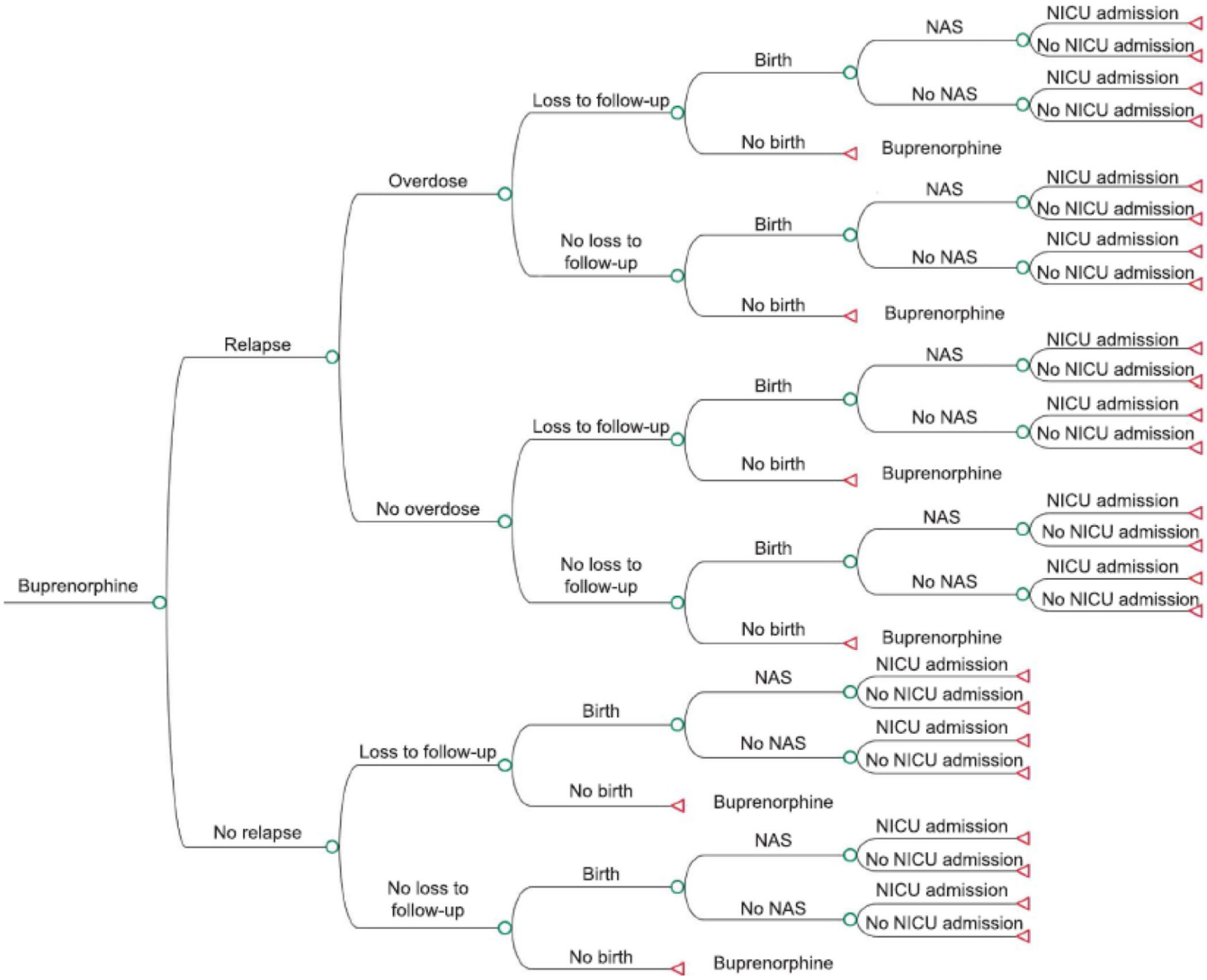

FIGURE 1.

A schematic depicting the buprenorphine arm of the decision analysis, which is part of Appendix 1

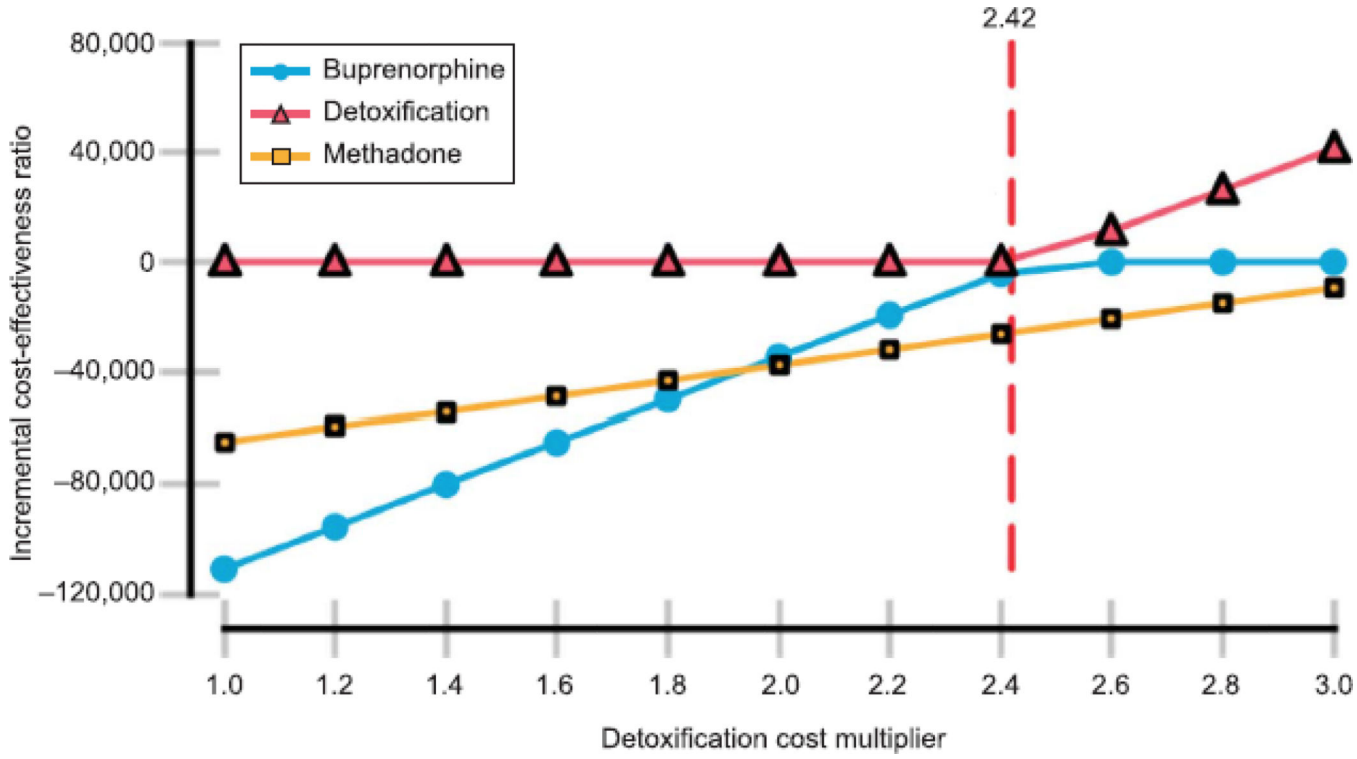

FIGURE 2.

A graph of the one-way sensitivity analysis of the cost multiplier of detoxification against the incremental cost-effectiveness ratio

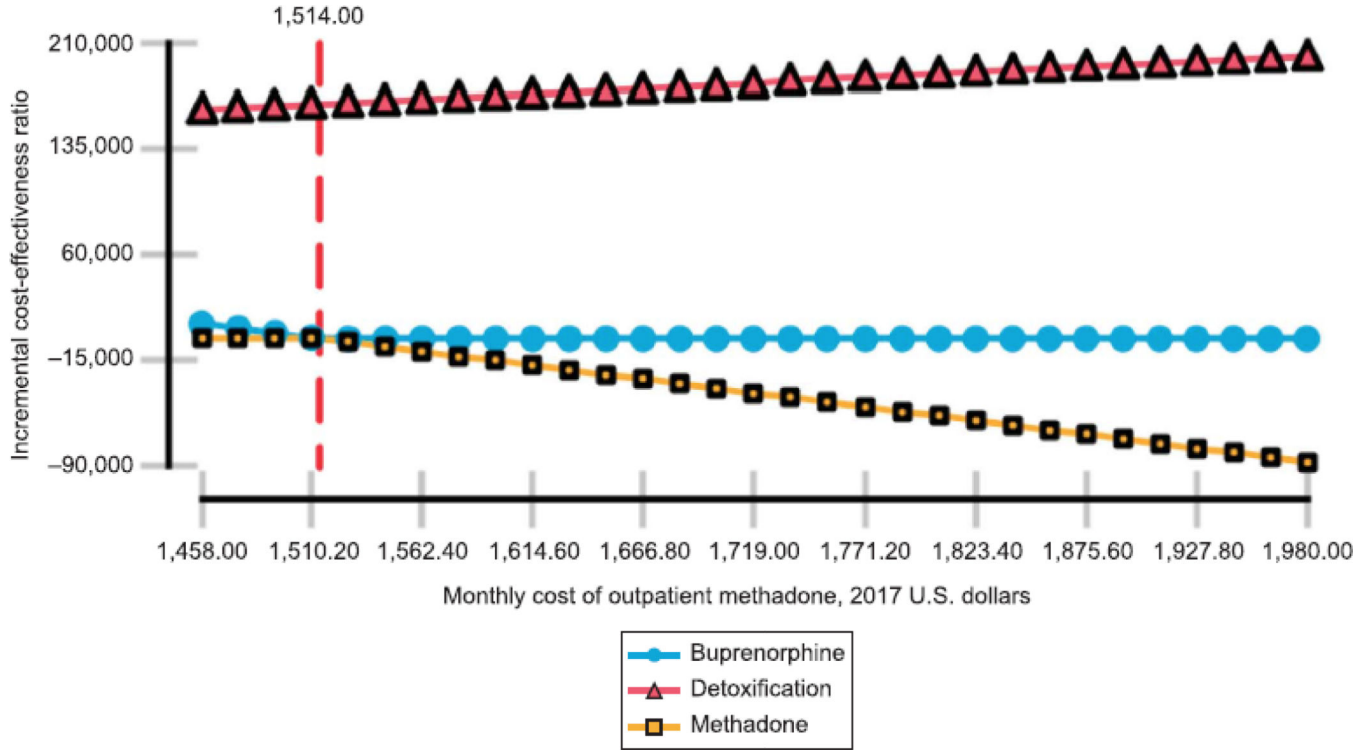

FIGURE 3.

A graph of the one-way sensitivity analysis of the monthly outpatient cost of methadone against the incremental cost-effectiveness ratio

Table 1.

Treatment-dependent probabilities

Variable	*Probabilities per monthly cycle (with ranges used in sensitivity analysis)*		
	Methadone	**Buprenorphine**	**Detoxification**
Rate of relapse	0.046 (0.0039–0.051)[21,22]	0.0829 (0.041–0.124)[21]*	0.281 (0.0625–0.5)[3,13]
Rate of overdose (fatal and nonfatal)	0.001 (0.000045–0.003)[8,26]	0.00118 (0.000045–0.003)[8,26]	0.0314 (0.00486–0.0314)[27]
Rate of fatal overdose	First cycle: 0.00233 (0.000975–0.007125)[29,30] Subsequent cycle: 0.0015 (0.001125–0.002025)[29,30]	First cycle: 0.000675 (0.000075–0.00255)[29,30] Subsequent cycle: 0.001125 (0.00075 – 0.001575)[29,30]	0.00063 (0.0001–0.01)[29,56]
Rate of NAS among offspring of women who do not relapse	0.51 (0.13–0.94)[21,57–60]	0.41 (0.22–0.67) [21,57–59]	0 (0–0.094)[10,12]

Table 2.

Treatment-independent probabilities

Variables not dependent on OUD therapy	Probabilities per monthly cycle (with ranges for sensitivity analysis)
Loss to follow-up without overdose	0.016 (0.008–0.024)[12,21,26,58,61] *
Loss to follow-up after overdose	0.0717 (0.056–0.126)[26,62]
Rate of preterm birth	0.0068–0.0709l[13,31,32], dependent on gestational age
Rate of NAS with relapse	0.835 (0.55–0.94)[63–65]
Rate of miscarriage	0.00605 (0.003025–0.0121)[66] *
Rate of neonatal death for neonates > 24w	0.00154–0.64, dependent on gestational age[67,68]
Rate of neonatal death in setting of NAS, > 37w	0.000253 (0.0001265–0.0003795)[57] *

NAS, neonatal abstinence syndrome

* Due to limited data derived from pregnant women with OUD, these variables were varied by 50% above and below the base case estimate

Table 3.

Cost estimates

Variable	Cost (in 2017 USD, range for sensitivity analysis)
Methadone, initial month	$22,612 (22,584–23,114)[25,34–37]
Methadone, subsequent month	$2,540–6,400, based on gestational age[25]
Buprenorphine, initial month	$22,306 (21,088–24,014)[25,34–37]
Buprenorphine, subsequent month	$968–5,257, based on gestational age[25]
Detoxification, initial month	$10,366 (9,488–11,640)[25,34–37,41]
Detoxification, subsequent month	$920–4,780, based on gestational age[25,34–37,41]
Detoxification cost multiplier *	2 (1–3) (consensus)
Cost of methadone treatment, residential, initial month	$6,354 (2,448–10,114)[24,25]
Cost of methadone treatment, residential, subsequent month	$7,117 (2,751–11,283)[24,25]
Cost of residential treatment, initial month	$6,968 (3,114–10,823)[24,25]
Cost of residential treatment, subsequent month	$7,787 (3,504–12,069)[24,25]
Medication cost of methadone outpatient (including outpatient nursing administration), per month	$1,646 (1,458–1,980)[25]
Medication cost of buprenorphine, per month	$200 (58–558)[35]
Maternal overdose	$40,496–41,606, based on gestational age[25,34–37]
Birth	$3,841 (3,810–3,986)[6]
Treatment of fetal loss/miscarriage	$1,402[38]
NAS treatment, NICU	$19,340 (18,290–20,390)[6]
NAS treatment, rooming in	$8,795 (5,327–14,203)[33]
Admission to NICU < 37w	24w-28w: $90,978[39] 28w-32w: $53,880[39] 32w-36w: $16,780[39]

NAS, neonatal abstinence syndrome; NICU, neonatal intensive care unit

* Detoxification cost multiplier was used to vary the cost of inpatient and outpatient management for women undergoing detoxification

Table 4.

Utility estimates

Variable	QALY
Initial cycle of detoxification	0.72[44]
Initial cycle of buprenorphine	0.87 (0.86–0.87)[45]
Initial cycle of methadone	0.70 (0.70–0.75)[48]
Maintenance in treatment, all arms	0.92 (consensus)
Relapse	0.68 (0.59–0.81)[45]
Loss to follow-up	0.68 (0.68–0.81)[45]
Initial cycle of maternal overdose	0.19 (0.09–0.29)[42]
Maternal death	0[42]
Preterm birth	0.71 (0.60–0.82)[42]
NAS	0.92 (0.70–0.92) (consensus)
Admission to NICU	0.92 (0.87–0.98)[47]
Miscarriage	0.90 (0.70–0.92)[43]
Stillbirth/Neonatal death	0.92 (0.85–0.95)[46]
Healthy, term newborn	1 (consensus)

NAS, neonatal abstinence syndrome; NICU, neonatal intensive care unit

Table 5.

Base case results

Strategy	Cost per person, in 2017 USD	Incremental cost, in 2017 USD	Effectiveness per person, in QALYs	Incremental effectiveness, in QALYs	Incremental cost-effectiveness
Methadone	$61,715	$8,827	9.06	−0.23	Dominated
Buprenorphine	$52,888	-----	9.28	------	------
Detoxification	$76,535	$23,647	9.41	0.13	Dominated

QALY, quality adjusted life years

Table 6.

Events among 20,000 women

Outcome	***Event number per strategy: n(95% CI)***		
	Methadone	**Buprenorphine**	**Detoxification**
Maternal relapse	13,153 (12,633–13,676)	5,541 (5,365–5,721)	15,459 (15,161–15,761)
Overdose, fatal and nonfatal	25 (16–35)	9 (4–15)	178 (152–205)
Preterm birth (<37 weeks)	642 (593–691)	642 (593–691)	642 (593–691)
NAS	9,739 (9,602–9,878)	8,085 (7,949–8,222)	3,930 (3,819–4,040)
NICU admission	9,926 (9,789–10,065)	8,379 (8,242–8,518)	4,502 (3,486–4,618)
Switch to methadone	N/A	2,087 (2,003–2,172)	6,878 (6,746–7,011)

NAS, neonatal abstinence syndrome; NICU, neonatal intensive care unit