Clinical decision analysis of elective delivery vs expectant management for pregnant individuals with COVID-19–related acute respiratory distress syndrome

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BACKGROUND: Pregnant individuals are vulnerable to COVID-19–related acute respiratory distress syndrome. There is a lack of high-quality evidence on whether elective delivery or expectant management leads to better maternal and neonatal outcomes.

OBJECTIVE: This study aimed to determine whether elective delivery or expectant management are associated with higher quality-adjusted life expectancy for pregnant individuals with COVID-19-related acute respiratory distress syndrome and their neonates.

STUDY DESIGN: We performed a clinical decision analysis using a patient-level model in which we simulatedpregnant individuals and their unborn children. We used a patient-level model with parallel open-cohort structure, daily cycle length, continuous discounting, lifetime horizon, sensitivity analyses for key parameter values, and 1000 iterations for quantification of uncertainty. We simulated pregnant individuals at 32 weeks of gestation, invasively ventilated because of COVID-19–related acute respiratory distress syndrome. In the elective delivery strategy, pregnant individuals received immediate cesarean delivery. In the expectant management strategy, pregnancies continued until spontaneous labor or obstetrical decision to deliver. For both pregnant individuals and neonates, model outputs were hospital or perinatal survival, life expectancy, and quality-adjusted life expectancy denominated in years, summarized by the mean and 95% credible interval. Maternal utilities incorporated neonatal outcomes in accordance with best practices in perinatal decision analysis.

RESULTS: Model outputs for pregnant individuals were similar when comparing elective delivery at 32 weeks' gestation with expectant management, including hospital survival (87.1% vs 87.4%), life-years (difference, −0.1; 95% credible interval, −1.4 to 1.1), and quality-adjusted life expectancy denominated in years (difference, −0.1; 95% credible interval, −1.3 to 1.1). For neonates, elective delivery at 32 weeks' gestation was estimated to lead to a higher perinatal survival (98.4% vs 93.2%; difference, 5.2%; 95% credible interval, 3.5–7), similar life-years (difference, 0.9; 95% credible interval, −0.9 to 2.8), and higher quality-adjusted life expectancy denominated in years (difference, 1.3; 95% credible interval, 0.4–2.2). For pregnant individuals, elective delivery was not superior to expectant management across a range of scenarios between 28 and 34 weeks of gestation. Elective delivery in cases where intrauterine death or maternal mortality were more likely resulted in higher neonatal quality-adjusted life expectancy, as did elective delivery at 30 weeks' gestation (difference, 1.1 years; 95% credible interval, 0.1 – 2.1) despite higher long-term complications (4.3% vs 0.5%; difference, 3.7%; 95% credible interval, 2.4–5.1), and in cases where intrauterine death or maternal acute respiratory distress syndrome mortality were more likely.

CONCLUSION: The decision to pursue elective delivery vs expectant management in pregnant individuals with COVID-19–related acute respiratory distress syndrome should be guided by gestational age, risk of intrauterine death, and maternal acute respiratory distress syndrome severity. For the pregnant individual, elective delivery is comparable but not superior to expectant management for gestational ages from 28 to 34 weeks. For neonates, elective delivery was superior if gestational age was ≥30 weeks and if the rate of intrauterine death or maternal mortality risk were high. We recommend basing the decision for elective delivery vs expectant management in a pregnant individual with COVID-19–related acute respiratory distress syndrome on gestational age and likelihood of intrauterine or maternal death.

Keywords: acute respiratory distress syndrome, cesarean delivery, computer simulation, COVID-19, critical illness, decision analysis, neonatology, obstetrics, pregnancy, premature birth

Introduction

Pregnant individuals face increased mortality and morbidity from pandemic respiratory viral infections, including SARS-CoV-2 infection (COVID-19).[1–8] Among COVID-19–infected pregnant individuals, the rate of acute respiratory distress syndrome (ARDS) requiring invasive ventilation is 279 per 100,000, and the mortality rate is 148 per 100,000, with an odds ratio for mortality of 2.85 relative to nonpregnant COVID-19–infected women of reproductive age.[7,8]

Elective cesarean delivery is a strategy intended to improve maternal and neonatal outcomes in pregnant individuals with ARDS.[9–18] However, current evidence shows that the maternal benefit of delivery is uncertain.[19,20] After delivery, patients may improve because of changes in respiratory mechanics and reduced oxygen demand, or patients may deteriorate because of supine positioning, right ventricular overload from placental

Cite this article as: Resende MHF, Yarnell CJ, D'Souza R, et al. Clinical decision analysis of elective delivery vs expectant management for pregnant individuals with COVID-19–related acute respiratory distress syndrome. Am J Obstet Gynecol MFM 2022;4:100697.

2589-9333/$36.00

http://dx.doi.org/10.1016/j.ajogmf.2022.100697

AJOG MFM at a Glance

Why was this study conducted?

We conducted a clinical decision analysis across a range of scenarios to determine whether elective delivery or expectant management leads to better outcomes for pregnant individuals with COVID-19–related acute respiratory distress syndrome (ARDS) and their unborn children.

Key findings

For pregnant individuals, elective delivery was not superior to expectant management across a range of scenarios, including gestational age ranging from 28 to 34 weeks. For neonates, elective delivery was associated with improved quality-adjusted life expectancy at ≥30 weeks' gestation, or if intrauterine death or maternal mortality were more likely.

What does this add to what is known?

This study provides evidence to recommend expectant management for pregnant individuals with COVID-19–related ARDS at <30 weeks of gestation in high-resource settings, and emphasizes the importance of basing delivery decisions on gestational age, maternal ARDS severity, and the risk of intrauterine fetal death.

autotransfusion, or postpartum hemorrhage.[21]

From the neonatal perspective, the net effect of elective delivery in the context of maternal COVID-19–related ARDS is also unclear. Benefit could accrue because maternal ARDS is associated with a high rate of fetal death—37% in 1 cohort[22]—and complications such as hypoxemic-ischemic encephalopathy.[23–26] However, prematurity also confers increased risks of mortality and long-term complications including cerebral palsy.[27–30] These risks increase with younger gestational age at birth.[30]

We undertook a clinical decision analysis to clarify the trade-offs involved in the decision to perform elective cesarean delivery vs expectant management of a pregnant individual with COVID-19–related ARDS.

Materials and Methods

We performed a clinical decision analysis from the perspectives of pregnant individuals and neonates. Health outcomes included long-term functional impairment (for pregnant individuals), cerebral palsy (for neonates), or death (both). Model outputs included hospital or perinatal survival, life expectancy, and quality-adjusted life expectancy denominated in years (QALYs). For neonates, perinatal survival required surviving the antepartum, intrapartum, and neonatal stage up to hospital discharge. Additional model outputs included fetal loss (intrauterine or intrapartum death) and gestational age at birth. We used a lifetime horizon and discounted outcomes by 1.5% annually.[31] We followed the Consolidated Health Economic Evaluation Reporting Standards guidelines.[32]

Model structure and patient population

We built a parallel, open-cohort individual-level simulation model to describe the daily dynamics of critical illness, delivery, and the subsequent course of both pregnant individuals and their neonates (Figure 1). A parallel open cohort was used to allow neonates to enter after their birth, potentially days or weeks after simulation outset. The base case for analysis was a pregnant individual at 32 weeks of gestation with a live single fetus, invasively ventilated in the intensive care unit (ICU) because of COVID-19–related ARDS. In the elective delivery strategy, pregnant individuals received immediate cesarean delivery. In the expectant management strategy, pregnancies continued until spontaneous labor or obstetrical decision to deliver.

The model cycled daily. In each cycle, pregnant individuals and neonates could live or die, and individuals still pregnant could deliver or continue pregnancy. If a pregnant individual died, their fetus may have still survived, approximating a

FIGURE 1
Model schematic

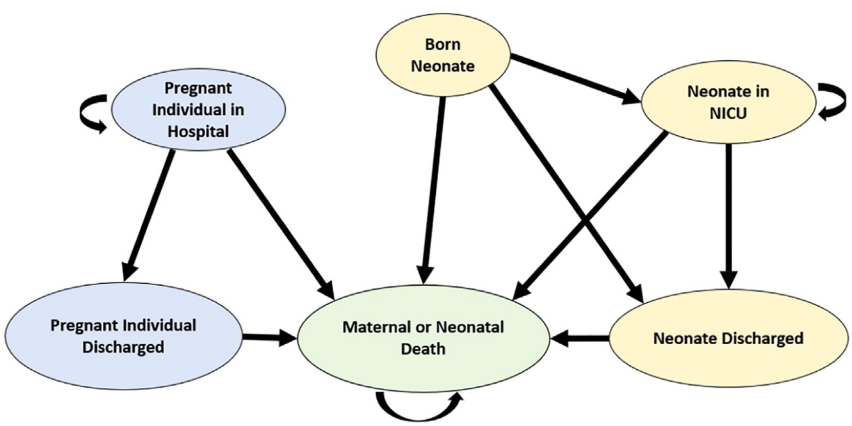

Figure shows a schematic representation of the model. *Arrows* represent possible transitions. Maternal states are *blue*, neonatal states are *yellow*, and states common to both are *green*. Note that neonates can be born alive or dead.

NICU, neonatal intensive care unit.

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perimortem or emergent delivery during terminal maternal deterioration. We also modeled location (ICU, ward, or discharged) and ventilation status (invasively ventilated or not) over time.

Each neonate was added to the population as either alive or dead (intrauterine death). All neonates born alive at <35 weeks of gestation were admitted to the neonatal ICU (NICU).[33]

The simulation ended for all individuals after a transition to the death state. Subsequent life expectancies for pregnant individuals and neonates who survived to hospital discharge were sampled from an age-at-death distribution. QALYs was calculated as the product of the subsequent life-years sampled for an individual and their long-term health utility. Further details are available in the Supplement.

Key assumptions

All patients were cared for in a tertiary hospital with access to obstetrics, adult ICU, and a NICU with capacity for neonates at <30 weeks of gestation. All pregnancies were singleton, with a live fetus, and uncomplicated before COVID-19 infection, and antenatal steroids for fetal lung maturation had been administered.[34] Maternal and intrauterine death were only possible while the pregnant individual was critically ill, marked by invasive ventilation. There was no reinitiation of invasive ventilation or readmission to the ICU. Neonatal COVID-19 caused no specific morbidity or mortality.[35]

Data sources

We performed a targeted literature search for each parameter. In the absence of sufficient evidence, we integrated available information with expert opinion from the author group Table 1.

Probabilities

Demographics. The age distribution of pregnant individuals was drawn from a registry of COVID-19 positive pregnant individuals.[36] Life expectancies for surviving pregnant individuals and neonates were drawn from a Gompertz distribution, the coefficients of which were based on lifetables from Ontario, Canada.[37]

Maternal COVID-19–related acute respiratory distress syndrome. The daily probabilities of ventilator liberation and mortality were based on the Kaplan–Meier curves of the RECOVERY dexamethasone study.[38] ARDS mortality was multiplied by a factor of 0.5 on the basis of an American administrative data study of pre–COVID-19 ARDS in pregnant individuals and observed mortality rates of pregnant individuals with COVID-19–related ARDS.[7,39,40] After 28 days of ventilation individuals received a tracheostomy[41] and were weaned from the ventilator with a probability of 0.1 each day, corresponding to a median of 7 additional ventilated days. The daily probability of ICU discharge after ventilator liberation was 0.35, corresponding to a median of 2 additional days for length of stay. Maternal long-term complication probabilities were based on a study of outcomes after ARDS.[42]

The effect of delivery on maternal ventilator liberation and mortality varied by patient according to a lognormal distribution with mean relative risk (RR) of 1 and standard deviation of 0.2 on the log scale.[19] This corresponded to a 95% probability that the RR for any individual fell between 0.68 and 1.45.[43]

Obstetrical. The daily probability of delivery was tabulated on the basis of the probability of preterm birth in COVID-19–positive pregnant individuals,[7] the gestational age distribution across preterm births,[44] and the gestational age distribution across term births.[45] The procedure-related mortality rate for cesarean delivery in individuals with ARDS is unknown because the scenario is rare, thus we used the probability (0.001) of severe postpartum hemorrhage requiring embolization or hemostatic compression suturing after cesarean delivery.[46] We reasoned that such a severe complication would be potentially fatal for an individual with ARDS. The probability of intrauterine death was based on data from the Centers for Disease Control and Prevention where 20 of 399 (5%) mechanically ventilated pregnant patients with COVID-19 experienced an intrauterine death.[47]

Neonatal. The rate of neonatal discharge from NICU according to gestational age at birth was based on the median NICU length of stay in a Canadian study.[29] The probability of cerebral palsy was based on a meta-analysis.[28] Probability of COVID-19 vertical transmission was 0.13.[48] The pregnant individual was infectious for 14 days.[49] The probability of an unborn fetus surviving maternal death was estimated at 0.75. This was based on a review of 80 cases of perimortem cesarean delivery with a survival rate of 86% among cardiac arrests that occurred in-hospital,[50] and a review of observational studies[51] with survival ranging from 0% to 89%. The hazard ratio of long-term mortality for neonates born preterm varied by gestational age at birth according to a multinational cohort study of 6.2 million people.[52]

Utilities. Health state utilities between 0 (death) and 1 (perfect health) were used to weight life-years by quality.[53] Survivors without long-term complications had a utility of 1. Pregnant individuals with long-term complications owing to ARDS were assigned a utility of 0.66 according to Cuthbertson et al.[54] Neonates with long-term complications were assigned the utility of moderate cerebral palsy, 0.76.[55]

For perinatal clinical decision models, it is recommended to incorporate joint maternal and fetal outcomes into maternal utilities.[56] We did so using utilities from a study focused on mothers taking anticoagulation for mechanical heart valves during pregnancy.[57] Maternal utility was multiplied by 0.95 if the neonate died and by 0.90 if the neonate had long-term complications.

Analysis. Sensitivity to specific parameters was assessed by varying parameter values through plausible ranges. We considered scenarios where:

1. Delivery conferred maternal benefit (RR, 0.7) or harm (RR, 1.4).

2. Gestational age was 28, 30, or 34 weeks.
3. The probability of intrauterine death was lower (0.01) or higher (0.1).
4. Maternal utilities of neonatal death or complication were lower (0.5).
5. The survival rate for unborn fetuses in case of maternal death was lower (0.5).
6. The NICU mortality rate was doubled.
7. The long-term mortality risk for neonates born at <34 weeks of gestation was doubled.

The model was built in TreeAge Software, Williamstown, MA R v4.0.3[58] and plots were generated in R (R Foundation for Statistical Computing, Vienna, Austria).[59] We used 1000 iterations of 1000 pregnant individuals and reported the mean and 95% credible intervals (CIs) for all outcomes. The model is available at https://doi.org/10.5281/zenodo.6435090.

Results

For the pregnant individual, model outputs were estimated to be similar when comparing elective delivery at 32 weeks' gestation with expectant management (Table 2), including hospital survival (87.1% vs 87.4%), life-years (31.5 vs 31.6), and QALYs (29.7 vs 29.8) (Figure 2). For the neonate, elective delivery at 32 weeks' gestation compared with expectant management resulted in higher perinatal survival (98.4% vs 93.2%; difference, 5.2%; 95% CI, 3.5−7.0), similar expected life-years (44.6 vs 43.2), and similar probability of long-term complications (0.7% vs 0.2%; difference, 0.4%; 95% CI, −0.2 to 1.0). Expectant management was expected to result in a mean gestational age at birth of 38 weeks (37.9−38.3 weeks).

Model outputs for joint outcomes differed between the 2 strategies. When maternal and neonatal outcomes were considered together, there was no difference in the probability that both mother and infant would survive. However, the probability of maternal survival with neonatal death was lower with elective delivery at 32 weeks' gestation compared with expectant management (1.4% vs 3.5%; difference, −2.2%; 95% CI, −3.5 to −0.8). The percentage of pairs where both the pregnant individual and their neonate died was lower with the elective delivery strategy (0.2% vs 3.3%). The estimated percentages of pairs with joint survival were similar (86% vs 84%). With the expectant management strategy, 72% (95% CI, 69−75) of pregnant individuals were estimated to survive hospitalization and deliver at term.

Scenario analyses

Different scenarios were explored to test the robustness of the model conclusions to its input parameters (Table 3). For pregnant individuals, when the effect of delivery on mortality and ventilator liberation was varied from moderate benefit (RR, 0.7) to moderate harm (RR, 1.4), the estimated difference in mean QALYs between elective delivery and expectant management varied from benefit (1.4; 95% CI, 0.3−2.4) to harm (−1.8; 95% CI, −3 to −0.6) (Figure 2). At 28 weeks of gestation, increased neonatal mortality and long-term complications created a larger gap in maternal QALYs between elective delivery and expectant management, although the CI included equivalence (−0.4 QALYs; 95% CI, −1.6 to 0.6). When maternal utilities of neonatal outcomes were lower, elective delivery was superior, but the CI included equivalence (0.2; 95% CI, −1 to 1.4).

Model outputs for neonates improved at higher gestational ages in both strategies. Comparing elective delivery with expectant management, the difference in neonatal QALYs ranged from possible harm (−0.3; 95% CI, −1.5 to 0.8) at 28 weeks of gestation to benefit (1.6; 95% CI, 0.7−2.6) at 34 weeks. At 30 weeks of gestation, elective delivery was estimated to lead to benefit in terms of QALYs (1.1; 95% CI, 0.1−2.1) but harm in terms of an increased proportion with long-term complications (4.3% vs 0.5%; difference, 3.7%; 95% CI, 2.4−5.1).

Across other scenarios, elective delivery compared with expectant management was associated with increased neonatal QALYs except in the scenario with a higher risk of long-term mortality for neonates born at <34 weeks of gestation (−0.2; 95% CI, −1.1 to 0.7). The estimated benefit in neonatal QALYs associated with elective delivery was largest for the scenarios incorporating higher rates of intrauterine death, neonatal perimortem delivery mortality, or maternal mortality from ARDS (Figure 2).

Comment

Principal findings

For a pregnant individual at 32 weeks of gestation with ARDS from COVID-19, our clinical decision analysis estimated that elective delivery compared with expectant management yielded a similar number of maternal quality-adjusted life years and an increased number of neonatal quality-adjusted life years. Expectant management resulted in a higher rate of perinatal mortality, but elective delivery caused universal prematurity with a shorter estimated life expectancy. Elective delivery between 28 and 34 weeks of gestation resulted in outcomes comparable to those of expectant management for the pregnant individual. However, elective delivery also resulted in improved neonatal outcomes at ≥30 weeks of gestation, and in cases where the risk of maternal or intrauterine death was high.

Results in the context of what is known

These findings support existing guidelines and expert opinion for pregnant individuals with COVID-19−related ARDS recommending expectant management at earlier preterm gestational ages and elective delivery at later preterm gestational ages.[18,21,60,61] This model adds to insights gleaned from a previous decision analysis of steroid administration for pregnant individuals with COVID-19 infection.[62] Unlike randomized trials and decision analyses studying the timing of elective delivery for pregnant individuals with other medical conditions such as previous uterine rupture,[63] hypertensive disorders of pregnancy,[64] or placenta previa,[65] we did not identify a clear

TABLE 1
Input parameters

Category	Variable	Base-case value	Source
Demographic	Age	Empirical distribution (median, 30 y)	Money,[36] 2021
	Life expectancy	Gompertz distribution	Naimark 2021, Ontario lifetables[37]
Maternal	Ventilator liberation	Empirical (median, 28 d)	RECOVERY 2020
	Mortality	Empirical $\times$ 0.5 (median, 14.5%)	RECOVERY 2020; Rush et al,[39] 2017; Kalafat et al,[40] 2022
	ICU discharge, daily	0.35 (median LOS, 2 d)	Assumption
	Hospital discharge	0.1 (median LOS, 7 d)	Assumption
	Long-term complication—probability	0.2/0.1/0.05 based on risk	Herridge et al,[42] 2016
	Long-term complication—utility	0.66	Cuthbertson et al,[54] 2010
	Fetal/neonatal death— utility from maternal perspective	0.95	D'Souza,[57] 2019
	Neonatal long-term complicatio—utility from maternal perspective	0.9	D'Souza,[57] 2019
	RR of ARDS outcomes postdelivery	Lognormal: mean 1, SD 0.2 (in log space)	Lapinsky et al,[19] 2015
Obstetrical	Delivery	Empirical distribution by gestational age	Allotey et al,[7] 2020; Chawanpaiboon et al,[44] 2019; Ananth et al,[45] 2018
	Fatal delivery complication	0.001	Mehrabadi et al,[46] 2014
	Intrauterine death	0.05 over 28 d	CDC MMWR 2021
	Neonate survives perimortem delivery	0.75	Einav et al,[50] 2012; Drukker et al,[51] 2014
Neonatal	NICU discharge	Empirical distribution by gestational age	Rios et al,[29] 2021
	NICU survival	0.958/0.961/0.986 | GA 28/29/$\geq$30	Canadian Neonatal Network 2020
	Long-term complications—probability	0.0432/0.00675/0.00014 | GA 28–31/32–36/$\geq$37	Oskoui et al,[28] 2013
	Long-term complications—utility	0.76	Tonmukayakul et al,[55] 2019
	HR long-term mortality for GA <34	1.44/1.23/1.12/1| GA <34/34–36/37–38/>38	Risnes et al,[52] 2021

"Assumption" denotes the use of expert opinion for a parameter.

ARDS, acute respiratory distress syndrome; *CDC*, Centers for Disease Control and Prevention; *GA*, gestational age; *HR*, hazard ratio; *ICU*, intensive care unit; *LOS*, length of stay; *MMWR*, Morbidity and Mortality Weekly Report; *NICU*, neonatal intensive care unit; *RR*, relative risk.

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TABLE 2
Base case (32 weeks' gestation) results

	Mean (95% credible interval)		
Maternal outcome	Elective delivery	Expectant management	Difference
Ventilation duration	22.7 (21.7–23.7)	22.8 (21.8–23.7)	−0.1 (−1.4 to 1.3)
Long-term complications	0.136 (0.116–0.157)	0.138 (0.116–0.158)	−0.002 (−0.031 to 0.028)
Hospital survival	0.871 (0.849–0.891)	0.874 (0.852–0.894)	−0.004 (−0.035 to 0.027)
Hospital length of stay	48.5 (46.4–50.6)	48.7 (46.5–50.9)	−0.15 (−3.15 to 2.79)
Life-years	31.5 (30.6–32.3)	31.6 (30.7–32.4)	−0.1 (−1.4 to 1.1)
QALYs	29.7 (28.9–30.6)	29.8 (28.9–30.7)	−0.1 (−1.3 to 1.1)
Joint outcome			
Gestational age at delivery/birth	32 (32–32)	38 (37.9–38.3)	−6 (−6.3 to −5.9)
Maternal survival, neonatal death	0.014 (0.007–0.022)	0.035 (0.025–0.046)	−0.022 (−0.035 to −0.008)
Both survive	0.857 (0.834–0.878)	0.839 (0.816–0.861)	0.018 (−0.015 to 0.049)
Neonatal outcome			
Proportion admitted to NICU	0.998 (0.995–1)	0.163 (0.14–0.187)	0.835 (0.811–0.859)
NICU length of stay	26 (25–28)	3.6 (2.9–4.4)	23 (21–25)
Neonatal COVID-19	0.13 (0.11–0.152)	0.019 (0.011–0.028)	0.111 (0.09–0.134)
Long-term complications	0.007 (0.002–0.012)	0.002 (0–0.006)	0.004 (−0.002 to 0.01)
Perinatal survival	0.984 (0.976–0.992)	0.932 (0.916–0.947)	0.052 (0.035–0.07)
Life-years	44.6 (44.1–45)	43.2 (42.4–44)	1.3 (0.4–2.2)
QALYs	44.5 (44–45)	43.2 (42.4–44)	1.3 (0.4–2.2)

Data are presented as mean and 95% credible interval of the mean.

NICU, neonatal intensive care unit; *QALYs*, quality-adjusted life years.

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gestational age at which elective delivery becomes a superior strategy to expectant management from the maternal perspective. This is likely because the maternal benefit of elective delivery is uncertain for pregnant individuals with ARDS, whereas it is more established in the conditions mentioned above. By contrast, we did identify a threshold gestational age (30 weeks) at which the estimated neonatal QALYs was higher with elective delivery than with expectant management.

Clinical and research implications

Our findings highlight 4 main points about care for pregnant individuals with COVID-19–related ARDS. First, high-quality management of ARDS from COVID-19 for pregnant individuals is essential. Maternal mortality limits outcomes for both pregnant individuals and neonates because elective delivery exchanges the risks of ARDS for the risks of prematurity. Severe COVID-19 pneumonia care for pregnant individuals should include glucocorticoids and interleukin-6 blockade.[21,60] ARDS care should include lung-protective ventilation, positive end-expiratory pressure optimization, prone positioning, muscle paralysis, and consideration of extracorporeal life support.[66–69] Minimizing maternal organ dysfunction from ARDS may also reduce the rate of intrauterine death, another influential factor with respect to neonatal model outputs. Further research should focus on improving ARDS care for pregnant individuals.

Second, the maternal utilities of life after neonatal death or complication are relevant, but were less influential in this study. The influence of maternal utilities for neonatal outcomes was best observed in the 28 weeks' gestation scenario, which estimated lower maternal QALYs with the elective delivery strategy because of increased neonatal morbidity and mortality. The utilities used in this study were derived from a survey of pairs of pregnant individuals and their partners.[57] Other work that surveyed only pregnant individuals recorded substantially lower utilities for maternal life after fetal loss,[70] and work that surveyed parents of children aged <18 years found lower parental utilities for children with disabilities.[71] However, even lowering the maternal utilities of neonatal outcomes by almost 50% did not induce a substantial change in maternal QALYs because at gestational ages of >30 weeks poor neonatal outcomes were rare.

Third, high-quality management of preterm neonates is important because if the risks associated with prematurity can be attenuated, then elective delivery

TABLE 3

Absolute differences between strategies across scenarios and outcomes

	Postdelivery relative risk of ARDS outcomes		Gestational age (wk)		
Maternal outcome	**0.7**	**1.4**	**28**	**30**	**34**
Long-term complications	−0.007 (−0.036 to 0.022)	−0.001 (−0.033 to 0.03)	−0.003 (−0.032 to 0.026)	−0.002 (−0.032 to 0.028)	−0.001 (−0.03 to 0.028)
Hospital survival	0.035 (0.007−0.062)	−0.052 (−0.083 to −0.022)	−0.009 (−0.039 to 0.019)	−0.003 (−0.033 to 0.025)	−0.003 (−0.031 to 0.025)
Life years	1.3 (0.2−2.3)	−1.9 (−3.1 to −0.7)	−0.3 (−1.6 to 0.8)	−0.1 (−1.3 to 1.1)	−0.1 (−1.3 to 1)
QALYs	1.4 (0.3−2.4)	−1.8 (−3 to −0.6)	−0.4 (−1.6 to 0.6)	−0.2 (−1.3 to 1)	−0.1 (−1.3 to 1)
Joint outcome					
Maternal survival, neonatal death	−0.021 (−0.034 to −0.007)	−0.022 (−0.035 to −0.01)	0 (−0.018 to 0.016)	−0.024 (−0.036 to −0.011)	−0.019 (−0.032 to −0.006)
Both survive	0.056 (0.025−0.087)	−0.029 (−0.062 to 0.003)	−0.009 (−0.043 to 0.025)	0.02 (−0.01 to 0.053)	0.015 (−0.016 to 0.047)
Neonatal outcome					
Long-term complications	0.004 (−0.002 to 0.01)	0.004 (−0.002 to 0.01)	0.035 (0.023−0.049)	0.037 (0.024−0.051)	0.005 (−0.001 to 0.01)
Perinatal survival	0.052 (0.034−0.069)	0.052 (0.036−0.069)	0.024 (0.003−0.045)	0.055 (0.037−0.074)	0.048 (0.032−0.066)
Life years	1.3 (0.4−2.2)	1.3 (0.4−2.3)	0 (−1.1 to 1.1)	1.5 (0.5−2.5)	1.7 (0.8−2.6)
QALYs	1.3 (0.4−2.2)	1.3 (0.4−2.2)	−0.3 (−1.5 to 0.8)	1.1 (0.1−2.1)	1.6 (0.7−2.6)

Data are presented as the difference in QALYs between elective delivery and expectant management strategies (elective delivery−expectant management). On the left, outcome differences are shown for 2 potential impacts of delivery on maternal outcomes—benefit (relative risk, 0.7) or harm (relative risk, 1.4). On the right, outcome differences are shown for 3 additional gestational ages (results for 32 weeks available in Table 2). Blue shading denotes estimated benefit with elective delivery; red shading denotes estimated benefit with expectant management; white shading denotes estimated differences with 95% credible intervals overlapping equivalence.

ARDS, acute respiratory distress syndrome; *QALYs*, quality-adjusted life years.

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FIGURE 2

Probability distribution of difference in QALYs by benefit of delivery and gestational age at birth

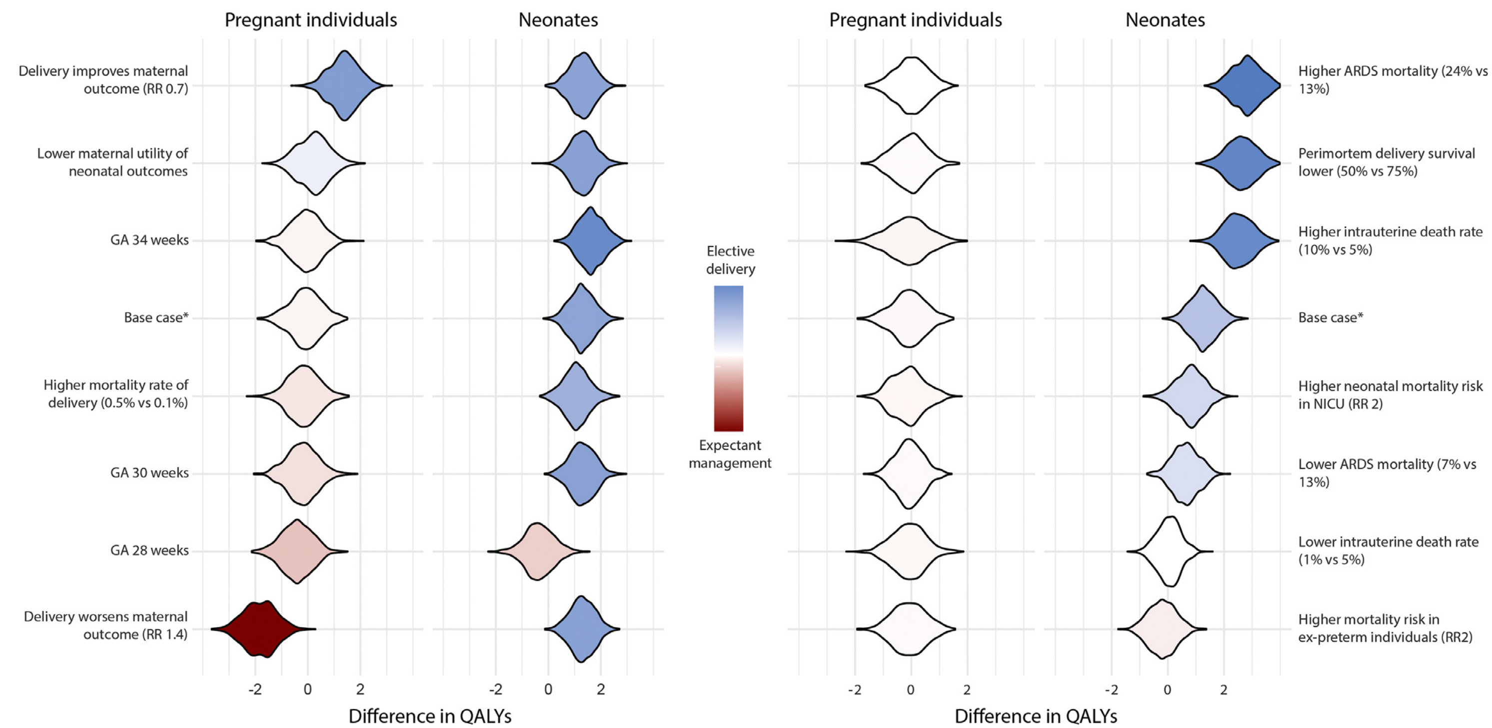

Figure shows the distribution of mean difference in QALYs for both pregnant individuals and neonates by scenario. The left column shows scenarios with important variation in maternal QALYs. The right column shows scenarios that are largely equivalent with respect to maternal QALYs, with important variation in neonatal QALYs. The height of each shape depicts the probability density for that value of the mean difference. Shading is based on the mean difference over all iterations. Blue shading indicates scenarios where elective delivery is favored, red shading indicates scenarios where expectant management is favored, and white denotes equivalence.

The *asterisk* denotes in order from top to bottom, left to right, base-case parameters: delivery impact on outcomes mean RR, 1; maternal utilities of 0.9 (neonatal long-term complication) and 0.95 (neonatal death); gestational age, 32 week; 0.1% cesarean delivery mortality; 13% ARDS mortality; 75% perimortem delivery survival; 5% intrauterine death rate; and RR of 1 for both NICU mortality and long-term mortality risk in ex-preterm individuals.

ARDS, acute respiratory distress syndrome; *GA*, gestational age; *NICU*, neonatal intensive care unit; *QALY*, quality-adjusted life-year; *RR*, relative risk.

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provides a less harmful alternative to expectant management. Recommendations to improve health outcomes for preterm neonates include delivery in a tertiary perinatal center,[57] use of maternal antenatal steroids for lung maturation and magnesium sulfate for neuroprotection, use of oxygen, continuous positive airway pressure and surfactant administration for neonates with respiratory distress syndrome, and adequate nutritional support including use of human donor milk in the absence of maternal breast milk.[58,59] There is more uncertainty on how to attenuate the long-term increased risk of mortality for individuals born preterm, which is an important area for future research.

Last, the best scenario for a pregnant individual is to avoid COVID-19−related ARDS. Vaccination reduces the severity of COVID-19 pneumonia and is recommended for all pregnant individuals to protect them from both infection and severe outcomes.[72,73]

Strengths and limitations

The findings have several limitations. The model applied to individuals who have received antenatal steroids. The benefits of expectant management would likely be greater for those who had not yet taken antenatal steroids.[34] The model did not include deteriorating nonintubated pregnant individuals, although that situation is comparable because the maternal benefit of elective delivery remains uncertain. The model considered individuals without comorbidities, although an increased burden of comorbidities could translate to a higher mortality for pregnant individuals, and in that scenario analysis, elective delivery had a relatively greater benefit for neonates. The model did not incorporate pregnancy-related complications such as preeclampsia, known to have an association with COVID-19 infection.[7,74] Although we did not include 3 important consequences of preterm birth (blindness, deafness, and severe neurodevelopmental delay), these are extremely rare at gestational ages of ≥28 weeks and do not affect the validity of the model. Extracorporeal life support was not modeled; however, it has been associated with a 35% intrauterine death rate, thus our findings suggest that the optimal neonatal strategy in that scenario would shift toward elective delivery at lower gestational ages.[75,76] Variation in the incidence of severe disease has been documented across different waves and variants of the pandemic,[77] but in our model we incorporated any available data because ARDS in pregnant individuals is rare.

The results are limited by uncertainty in key parameters, including the effect of delivery on maternal outcomes, the probability of fetal survival after maternal death, the risk of intrauterine death in the setting of maternal COVID-19−related ARDS, and the impact of neonatal COVID-19 infection. There was no utility penalty for separating mother and neonate at birth, which advantaged the elective delivery strategy. Our results assume a high-resource setting and may not generalize to lower-resource settings with higher maternal and perinatal mortality.[78] The model itself gives the average or expected outcomes with each strategy, but it does not replace clinical judgment nor obviate the need to account for the nuances of an individual patient.

Despite limitations, our model has several strengths. It addresses a high-stakes clinical question that has been distressingly common worldwide.[7] We were able to demonstrate the maternal and neonatal trade-offs involved in the decision for elective delivery or expectant management. Lastly, we provide scientific support for prevailing obstetrical critical care recommendations regarding delivery in pregnant individuals with COVID-19−related ARDS.

Conclusion

For pregnant individuals with COVID-19−related ARDS, elective delivery was comparable but not superior to expectant management for gestational ages from 28 to 34 weeks. For neonates, elective delivery was superior if gestational age was ≥30 weeks, if the rate of intrauterine death was high, or if maternal mortality risk was high. We recommend basing the decision for elective delivery vs expectant management in a pregnant individual with COVID-19−related ARDS on gestational age and likelihood of intrauterine or maternal death. We also recommend continued research into obstetrical critical illness, including COVID-19−related ARDS, to inform key parameters and help clinicians and families to make better decisions. ■

ACKNOWLEDGMENTS

We thank Beate Sander, PhD, for helpful comments.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2022.100697.

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Received July 11, 2022; accepted July 12, 2022.

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The authors declare no conflict of interest.

C.J.Y. reports funding from the Canadian Institutes for Health Research Vanier Scholar program, the Eliot Phillipson Clinician-Scientist Training Program, and the Clinician Investigator Program of the University of Toronto. No endorsement by any of the funding agencies is intended or should be inferred.

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