COVID-BIRTH study : Perinatal Impact of Maternal Covid-19

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Abstract

The perinatal impact of maternal COVID-19 disease and the hygienic and social distancing measures taken during the epidemic remain unclear. In this prospective study, the impact of SARS-CoV-2 infection and the social distancing measures on parental anxiety, depression and bonding in COVID-19 positive and COVID-19 negative pregnancies were evaluated.

We recruited pregnant women at delivery in a university hospital in Belgium between April and December 2020, both SARS-CoV2 negative and confirmed (current or previous) SARS-CoV2 positive during pregnancy. Baseline clinical information was retrieved from the patient's medical file. Women received questionnaires electronically at birth (Day 0-3) and 6 weeks after delivery.

In total, 240 individuals were included at delivery and 37 (15%) of them were COVID-19 positive pregnancies. No significant differences on maternal, neonatal, or breastfeeding outcomes between the COVID-19 positive and negative group were observed. Pregnancy, breastfeeding and neonatal outcome data were similar compared to reference values before COVID-19.

Elevated Edingburg Postpartum Depression Scale scores (>13) were seen in 11% of our patients. This number was significantly higher compared to data in pregnant women at the same hospital before the COVID-19 pandemic. Elevated GAD-7 (Generalized anxiety disorder score) was documented in 13.5% of all included patients. More than half of all women reported that the epidemic had an impact on the support they received post-partum.

It appears that the COVID-19 epidemic has a serious impact on the mental well-being of pregnant women and mothers. It is important to further explore the risk-benefit analysis of future measures during the epidemic.

Introduction

With over 600 million cases worldwide, as of March 2023, coronavirus infectious disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) set up a global public health crisis (1).

The impact of SARS-CoV-2 infection during gestation remained unclear at the beginning of the pandemic. The possibility of vertical transmission of SARS-CoV-2 has been a point of debate (2-6). Although rare, vertical transmission is possible, with the highest risk in the third trimester of pregnancy (7-9). The effect of the COVID-19 pandemic and its consequences on maternal and neonatal outcomes continued to be a knowledge gap (10-13). This uncertainty brought fear among healthcare providers and pregnant women.

Pregnancy, delivery of a baby, and early motherhood are crucial moments in the life of a woman. For the infant, the first 1000 days of life have been acknowledged as the base for mental and physical health in later life (14). When pregnancy and birth occur in uncertain times, when social distancing is the norm, when no visits are allowed, when thoughts of fear were overall present, it is unknown how these events affect mother-infant bonding, parental stress, breastfeeding rates, health problems during infancy and neurodevelopmental outcome of the infant (14). Different studies and reports addressed these indirect but potentially harmful consequences of the COVID-19 pandemic on pregnant women and neonates (15,16).

During the pandemic, the focus of healthcare and its resources shifted to the acute care of infection. A survey in the United Kingdom, conducted in maternity services, showed a reduction in both antenatal and postnatal appointments, as well as a shift to remote consultation methods (16). While these measures will likely protect both patients and staff against the acute effects of the virus, it remains essential to monitor pregnancy, maternal and neonatal outcomes during these challenging times. Reduced access to antenatal and postnatal care may impact the ability to screen for physical, psychological, and social problems. The risk-benefit analysis of these measures must be evaluated, as they risk amplifying and accentuating existing health and socio-economic inequalities (16,17).

A matched-control study in the United States of America showed acute traumatic stress symptoms in almost 50% of COVID-19 positive women in response to childbirth. They were twice as likely to have no visitors during delivery and hospitalisation and were separated more from their newborns in comparison with COVID-19 negative women (13). In addition, a Turkish cross-sectional study found pregnant women at high risk of antenatal depression during the COVID-19 pandemic (Edinburgh depression score >13) (18). A review including twelve studies about the impact of COVID-19 on breastfeeding plans showed positive experiences (increased time at home) as well as negative experiences (separation from newborn, decreased professional and family support, fear of vertical transmission). An Italian study showed a decrease in exclusive breastfeeding during lockdown and home confinement in non-infected mothers (19,20). Furthermore, breastmilk substitute companies capitalized on the uncertainty and fear among mothers during the COVID-19 pandemic by spreading debatable health claims and misinformation. These tactics violated the International Code of Marketing of Breast-Milk Substitutes (21).

The purpose of this study was to obtain greater insight in the perinatal impact of maternal COVID-19. Primary objectives were to examine the association between COVID-19 infection and the social distancing

measures on parental anxiety, depression, and mother-child bonding. Secondary, we wanted to assess the association between the COVID-19 pandemic and the measures of social distancing on breastfeeding outcomes, breastfeeding complications and health complications in the neonatal period in COVID-19 positive pregnancies, as well as in COVID-19 negative pregnancies.

Methods

Study-design

A prospective observational study was conducted in the University Hospitals Leuven, a tertiary care university hospital in Belgium. We recruited pregnant women who delivered in the University Hospitals Leuven between April 2020 and December 2020. COVID-19 negative pregnancies were defined as patients with a recent (<1 week) negative polymerase chain reaction (PCR) for SARS-CoV-2 on nasopharyngeal swab or with no recent swab but asymptomatic. COVID-19 positive pregnancies were defined as patients with current or previous SARS-CoV-2 infection confirmed by PCR on nasopharyngeal swab, or with current suspected SARS-CoV2 infection because of suggestive signs and/or symptoms. All patients admitted for delivery were screened for SARS-CoV-2 infection by nasopharyngeal swab, as specified in the standard clinical protocol. This was done either the day before hospitalization in patients with planned deliveries, or at admission in patients with spontaneous labor. As some unscheduled patients might deliver before the results of the test, and since the sensitivity of the PCR test for SARS-CoV-2 is not 100%, symptomatic patients with or without available test results were also included.

The study was carried out in accordance with the latest version of the Declaration of Helsinki. The study was approved by the Ethics Committee Research of the University Hospitals Leuven (internal study number S63942). Written informed consent was obtained on admission in labor ward for delivery.

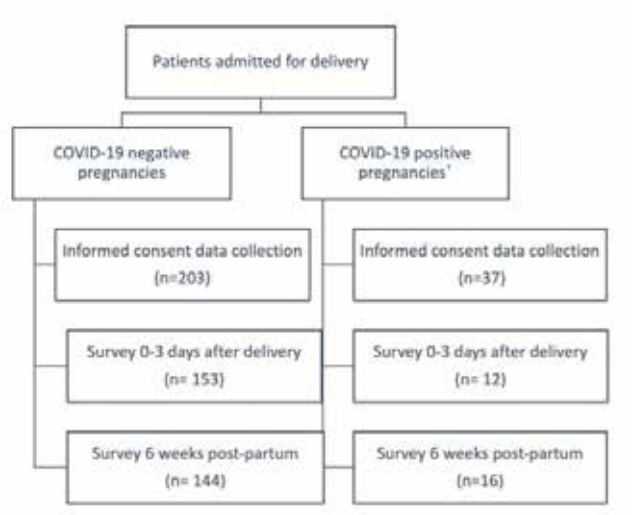
Since this was an observational study and the evolution of the COVID-19 pandemic was still unknown, it was not possible to calculate a required sample size. Sample size was estimated based on the average deliveries per month at our hospitals (200/month), participation rate for questionnaires during pregnancy in other studies (25-40%) and the rate of COVID-19 positivity among patients admitted for delivery at that time (5-10%). We estimated to recruit 540 patients.

An electronic database was set up within the safe environment of a clinical server at the hospital (REDCAP). Baseline clinical information (including demographics, comorbidities, pregnancy history) was retrieved from the patient's medical file at admission. Women received questionnaires electronically on admission, at birth (Day 0-3), and 6 weeks after delivery. They received questions about demographics, education and social environment, medical and obstetrical history, mental health, pregnancy and neonatal complications, as well as COVID-19 related questions (Figure 1). Women who were admitted to University Hospitals Leuven after a stillbirth or a termination of pregnancy due to severe congenital malformations were excluded from the questionnaire part of the study.

Psychological measurements

Parental anxiety, depression and bonding were assessed using the Edinburg Postpartum Depression Scale (EDPS), Mother Infant Bonding Scale (MIBS) and the Generalized Anxiety Disorder-7 (GAD-7). These were included in the questionnaires at birth (day 0-3) and 6 weeks after delivery. The GAD-7 is a valid and efficient tool for screening for GAD (generalized anxiety disorder) and assessing its severity in clinical practice and research. The GAD-7 items include: 1) nervousness; 2) inability to stop worrying; 3) excessive worrying; 4) restlessness; 5) difficulty in relaxing; 6) easily irritated; and 7) fear of something awful happening. The GAD-7 asks participants to rate how often they have been troubled by each of these 7 core symptoms over the past 2 weeks. The total score of the GAD-7 ranges from 0 to 21. A score of 10 or greater on the GAD-7 represents a reasonable cut-off point for identifying cases with GAD. A cut-off of 13 is proposed in pregnancy. The EPDS was developed

Figure 1: Flow chart of participants included in the study



to determine postnatal depression symptoms and the critical cut-off point is 13. It is a self-reporting 10-item scale. The total score ranges between 0 and 30. MIBS is an 8 item self-rating mother-to-infant bonding questionnaire that has been designed to assess the feelings of a mother towards her new baby (22). Breastfeeding outcomes were assessed with focused questions about breastfeeding duration, breastfeeding support, and breastfeeding complications. Infancy health was evaluated with focused questions about growth evolution and hospital admissions.

Data Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 26 for Mac. Descriptive statistical analyses were performed for the clinical data. Also, for the data collected by the questionnaire, descriptive statistics (percentages, means, standard deviations, medians, ranges) were used. Summary statistics for all variables were calculated using means and standard deviation for continuous variables, when normally distributed, and frequency and proportions for categorical variables. Pregnancy and neonatal outcome data in COVID-19 positive and negative women were compared with each other and with reference values available from 2019 in Flanders (SPE) (23).Chi-Square and Fisher-exact test were used when comparing proportions between both groups (e.g., COVID-19 positive vs COVID-19 negative patients or reference values from SPE). Unpaired t-test was used to compare means between COVID-19 negative and positive groups. Significance level was accepted if $p < 0.05$.

Results

Baseline data

In total, 240 women were included in our study. Data from the medical records are summarized in Table 1. The medical record was not fully completed for each patient resulting in missing data for some variables. There were significantly more non-Caucasian women in the COVID-19 positive group. There were no other statistically significant differences in baseline demographics between the COVID-19 positive and COVID-19 negative group.

COVID-19 Infection

Thirty-seven of all patients (15.3%) had a current or previous COVID-19 infection. Thirty-four were confirmed by PCR, three had only strong clinical suspicion. Nasopharyngeal swab was used for PCR testing in all cases. Reported symptoms were cough (41%), rhinorrhea (33%), tiredness/lethargy (26%), sore throat (15%), dyspnea (15%), fever (15%), headache (11%). Anosmia was reported in two patients. No gastro-intestinal symptoms were reported. Almost one fifth (18.5%)

had no suggestive symptoms. Three women were hospitalized in the third trimester of the pregnancy due to COVID-19 infection and received intensive care. There was one preterm delivery and one stillbirth after pre-eclampsia and HELPP.

Current Pregnancy and birth

Table 1: Baseline characteristics of patients

	COVID-19 negative pregnancies (n=203)	COVID-19 positive pregnancies (n=37)	P-value*
Age (years)	32±3,6	32±4,3	1.0
Race			
Caucasian	185/194 (95.4%)	30/36 (83.3%)	0.02
Medical History			
None	113/197 (57.4%)	23/35 (65.7%)	0.46
Psychiatric disorders	6/197 (3.0%)	0/35 (0%)	0.59
Conception			
Spontaneous	167/194 (86.1%)	35/36 (97.2%)	0.09
In vitro fertilization (IVF)	6/194 (4.1%)	1/36 (2.8%)	1.0
Pregnancy Complications			
None	119/197 (60.4%)	20/36 (55.6%)	0.58
Gestational diabetes	11/197 (5.6%)	5/36 (13.9%)	0.08
Stillbirth	0/197 (0.0%)	1/36 (2.8%)	0.15
Steroids for fetal lung maturation	7/195 (3.6%)	2/37 (5.4%)	0.63
Delivery Type			
Spontaneous	100/195 (51.3%)	16/37 (43.2%)	0.47
Planned	92/195 (47.2%)	18/37 (48.6%)	1.0
Urgent	3/195 (1.5%)	3/37 (8.1%)	0.06
Anesthesia			
None	30/195 (15.4%)	7/36 (19.4%)	0.62
Spinal/Epidural	163/195 (83.6%)	28/36 (77.8%)	0.47
General	1/195 (0.5%)	1/36 (2.8%)	0.29
Complications at birth			
None	182/195 (93.3%)	32/37 (86.5%)	0.18
Shoulder dystocia	6/195 (3.1%)	4/ 37 (10.8%)	0.06
Postpartum hemorrhage	3/195 (1.5%)	1/37 (2.7%)	0.50
Birthweight (gram)[1]	3287±478	3240±673	0.61
Breastfeeding at birth	162/197 (82.2%)	30/35 (85.8%)	0.81
NICU/Medium care admission	27/197 (13.7%)	9/36 (25.0%)	0.13

[1] *Mean ± SD*
** obtained by t-test for continuous and chi-square or Fisher's exact test for categorical variables*

There were no statistical differences between the COVID-19 positive group and COVID-19 negative group for pregnancy and birth characteristics. Comparing our total population to the reference values of SPE 2019, we saw similar values for most characteristics, including number of spontaneous pregnancies (89.8%, p=0.33) and percentage of diabetes (5.8%, p=0.68). We saw statistically significant differences in the average use of epidural analgesia in Flanders vs our population (69.3% vs 82.7%, p=0.01) and in the number of planned deliveries (25.4% vs 47.4%, p=0.01.

Postpartum/Postnatal period

More than 83% of all patients decided to (indirect) breastfeed after birth. Fifteen percent decided to start with formula feeding. When questioned, maternal or neonatal COVID-19 infection was never given as a reason for choosing between breastfeeding or bottle feeding at birth. Rates of breastfeeding at birth did not differ between the COVID-19 positive group and the COVID-19 negative group (p=0.81).

Sixteen percent of all babies were admitted to the NICU or medium care neonatal ward. Respiratory distress (43.0%) and prematurity (33.4%) were the most common reasons for admission. There was no statistically significant difference in admissions to the NICU between the COVID-19 positive and negative group (p=0.13). There were no statistical differences in admissions between our population and reference values of 2019 in Flanders (p=0.72) (23).

Twelve babies (5.1%) received a COVID-19 PCR test. Eight of them received the test when they were admitted to the NICU or medium care neonatal ward. They all had COVID-19 positive mothers. None of them tested positive. Four neonates were screened pre-operative or on readmission because of infection or hyperbilirubinemia. One of these four neonates tested positive. The mother of this neonate tested positive one week earlier. There was no difference in abnormalities at physical examination. Neonatal complications were rare, no differences were documented between the two groups.

Questionnaires at discharge & six weeks postpartum

The survey on day 0-3 was completed by 165 women (70% of initial population), 160 women completed the survey at 6 weeks. One patient was excluded from the survey because of stillbirth. Only 32% (n=12) and 43% (n=16) of patients with a current or previous COVID-19 infection completed the survey on day 0-3 and 6 weeks, respectively. This difference is statistically significant (p<0.05) (Figure 1). Questionnaires were not always fully completed by patients, causing some answers to be missing for some patients. Nearly all women were married or living together (98%). Higher education was completed by 86%. Almost half of the women (48%) had completed university studies. Close to 30% of our study population (45/165) worked in the healthcare sector. More than 20% of them had direct contact with COVID-19 patients. They worked, in average, until 28 weeks of pregnancy.

At discharge, 80.4% of all women were breastfeeding. Six women indicated the pandemic to be of influence for their decision, in favor of breastfeeding. At 6 weeks, almost 75% were still breastfeeding. None of them indicated the pandemic to be of influence to stop breastfeeding. At discharge more than 75% of all patients had a midwife service at home, 12% had maternity care. More than half of the women (52%) reported that the COVID-19 pandemic had played a negative role in the level of support they received at home (familial or professional).

From the 165 women who completed the survey at discharge, 12 patients had a proven COVID-19 infection during pregnancy. Another 20 patients indicated that they possibly experienced a COVID-19 infection during pregnancy (cough, cold, fever, difficulty breathing). There was no statistical difference between the COVID-19 positive (proven and/or suspected) group and the negative group in maternal educational level, occupancy in healthcare, postnatal support or rates of breastfeeding (Table 2).

A total of 14.5% (n=23) of all women experienced isolation or quarantine because of COVID-19 virus infection during pregnancy. Women in COVID-19 positive pregnancies were significantly more likely to have been quarantined or isolated.

The GAD-7 was higher than 10 in 13.5% of all women, and higher than 13 in 8.6% of all cases. There was no statistical difference between the COVID-19 positive group and COVID-19 negative group in the mean result or cut-off points of 10 or 13. The EPDS was 13 or higher in 11% of the women who completed the survey at birth. No statistical differences were observed between the COVID-19 positive group and COVID-19 negative group in EPDS scores.

Table 2: Questionnaires outcomes

	COVID-19 negative pregnancies	COVID-19 positive pregnancies	P-value*
Social situation			
Married or living together	147/150 (98.0%)	12/12 (100%)	1.00
Maternal Education Level			
Secondary School	17/149 (11.4%)	3/12 (25.0%)	0.17
College	74/149 (49.7%)	4/12 (33.3%)	0.37
Healthcare worker	44/153 (28.8%)	2/12 (16.0%)	0.51
Breastfeeding			
At discharge	118/149 (79.2%)	10/11 (90.9%)	0.69
6 weeks	102/143 (71.3%)	14/16 (87.5%)	0.24
Postpartum Care			
Midwife	113/149 (75.8%)	10/12 (83.3%)	0.73
Maternity care	20/149 (13.4%)	0/12 (0%)	0.36
Isolation/Quarantine	13/145 (9.0%)	7/11 (63.6%)	0.001
GAD-7	4.7±4.8[1]	4.1±4.5[1]	0.69
>10	20/148 (13.5%)	1/11 (9.1%)	1.00
General	12/148 (8.1%)	1/11 (9.1%)	1.00
EDPS	6.1±4.7[1]	8.7±6.2[1]	0.09
>13	16/142 (11.3%)	1/10 (10%)	1.00

[1] *Mean ± SD*

* *obtained by t-test for continuous and chi-square or Fisher's exact test for categorical variables*

GAD-7: Generalized Anxiety Disorder-7

EDPS: Edinburg Postpartum Depression Scale

Discussion

No significant differences in pregnancy or neonatal outcome between COVID-19 positive pregnancies and negative pregnancies were documented. However, we did see higher GAD-7 and EPDS scores in our study population, than before the COVID-19 pandemic (24). Generalized anxiety disorder (GAD) and postpartum depression have different consequences for mother and child. Studies describe decreased quality of life, disrupted mother-child attachment, and emotional and developmental problems in the child. Moreover, GAD would also have a negative effect on birth weight and increased risk of prematurity (25-29). Prevalence of GAD in pregnancy and postpartum varies in reported studies. Prevalence of GAD during pregnancy varies between 8.5% and 10.5%. In the postpartum period there appears to be more variance in the reported prevalence (4.4% to 10.8%) (26,27). Our percentages are at least at the upper end of this interval (8.6% and 13.5% depending on the chosen cut-off point of the GAD-7). Eleven percent of our study population scored higher than the EDPS cut-off point of 13 at birth. This is significantly higher and more than double, compared to a study performed before the COVID-19 pandemic conducted in 2013 at the same hospital (University Hospital Leuven, Belgium) in pregnant women (EPDS >13 in 4.5%, p<0.05) (24).

Almost one-fifth (18.8%) of all women of our study, were placed in isolation or quarantine during pregnancy or in the 6 weeks post-partum. More than half of mothers indicated that the COVID-19 pandemic had an impact on the level of support provided at home after birth. So, it seems likely that the uncertainty of the COVID-19 pandemic, the potential impact on mother and neonate, the isolation and lack of social contact, impaired mental well-being of all pregnant women and mothers. Two other studies conducted in Europe during the pandemic using GAD-7, reported even higher rates of moderate anxiety (GAD-7 >10), 34.9% and 24.8%, respectively (30,31). A cross-sectional, web-based study conducted in several Western European countries during the pandemic, in pregnant and lactating women, showed GAD-7 (>10) and EDPS (>13) scores similar to our study (in 11% and 15% of pregnant women, respectively) (32). We did not specifically question why women felt more anxious. The importance of prenatal questioning and management of anxiety and depression symptoms, is therefore emphasized. This can impact the mother-infant bonding which can have lifelong consequences for the baby (cfr. first 1000 days of life) (14). Hygiene measures during the pandemic were necessary, but they possibly had an impact on the mental well-being of pregnant women and mothers. It may be interesting to conduct a risk-benefit analysis of the measures introduced during the pandemic, so that this can be factored into decisions in the (hopefully distant) future.

We observed a trend of more urgent deliveries in COVID-19 positive pregnancies. Pregnancy and neonatal outcome data were similar compared to reference values available from 2019 in Flanders (SPE) (23). More epidural analgesia was used as average in our population, but large dispersion was seen between hospitals in Flanders (12.1%-86.5%). The higher percentage of planned deliveries than the average in our population reflects the reality of a tertiary university hospital with its specific pathologies, but was higher than the spread in Flemish hospitals in 2019 (12.4%-36.7%). We cannot exclude that patients with planned deliveries were more easily included in our study due to the study protocol. A large proportion of our pregnant women were caregivers (30%). In comparison, fifteen percent of the general active population in Belgium works in the healthcare sector. It seems reassuring that they were not more likely to be COVID-19 positive. Finally, the COVID-19 pandemic does not appear to have had a negative effect on breastfeeding choice and adherence in our population. Percentages are similar to those of the years before the COVID-19 pandemic in our hospital. Most women reported that the epidemic did not affect this choice. Moreover, the few women who did get influenced by the COVID-19 pandemic, all chose breastfeeding.

Limitations of our study were firstly the limited size of our COVID-19 positive group. As a result, we may not have been able to confirm significant differences that were found in previous studies (e.g., NICU admissions), or have enough power to be sure these differences were really not present (11). Other pregnancy, delivery or neonatal complications were rare, so possible differences were difficult to demonstrate with the current sample of our population. For these data, we were also partially dependent on the accuracy and completeness of the medical record, which resulted in missing date for some patients. We could not include as many patients as we had initially envisaged. There was no record of how many patients were asked to join the study and how many did not want to participate. It is thus unclear whether informed consent wasn't systematically asked or whether many patients didn't want to participate. Selection bias can thus not be ruled out. COVID-19 positive women answered significantly less to the questionnaires at birth and after 6 weeks. This possibly also weakened the difference between the two groups. One might wonder why these women responded less frequently. Perhaps women, whose conditions were more difficult, were less likely to answer, and a form of selection bias has developed as a result (nonresponse bias). COVID-19 positive mothers were also less likely to be Caucasian. Perhaps there were language and cultural barriers for completing the questionnaires. Our study took place during a period when there was still limited PCR testing capacity. A proportion of women reported possible COVID-19 infection without PCR confirmation. It is

unclear if this had an impact on our results. The impact of the COVID-19 pandemic hit socioeconomically disadvantaged communities harder (17). Our study population was very highly educated (almost half of all women had college degrees) and there were almost no single mothers. This is a good representation of our hospital's patient population, but not the general population. It is possible that our population was less affected by the measures taken in the pandemic and the true impact of the COVID-19 pandemic on pregnant women is even greater. The study was performed during the first and second waves of COVID-19 in Belgium, including the summer months of 2020 where there were very few corona infections and measures were much less stringent. How this affected the results is unclear. No sub analysis by period occurred. On the other hand, our study happened during a period where there was still very much uncertainty and conflicting reports about COVID-19 during pregnancy, possibly causing more stress and anxiety then later during the pandemic.

Conclusion

We conducted a prospective observational study during the first and second waves of the COVID-19 pandemic in a tertiary centre. We looked at the possible association between, on the one hand, COVID-19 infection during pregnancy and social measures during the pandemic and, on the other, maternal anxiety and depression, as well as breastfeeding and maternal and neonatal outcomes. We found no statistical differences between COVID-19 positive and negative pregnancies for clinical maternal, neonatal, or breastfeeding outcomes. However, higher levels of generalized anxiety and depressive symptoms were observed in our population compared to the period before the pandemic. This study emphasizes the importance of monitoring mental health in pregnancy and postpartum. It would be interesting to see if now, after the pandemic, anxiety and depression scores are back to pre-pandemic levels.

Conflict of interest

The authors have no conflicts of interest in relation to the subject matter of this manuscript.

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